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CONTENT

EDITORIAL

A CHALLENGE FOR ANESTHESIOLOGISTS: OBSTRUCTIVE SLEEP APNEA

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Obstructive sleep apnea (OSA) is a commonly seen disease characterized by apnea attacks during sleep due to chronic, repeated partial or complete obstruction of upper airway (1, 2). Apnea attacks, lasting more than 10 seconds, are usually spontaneously terminated by brief cortical arousals or awakenings which lead to excessive sleepiness during day-time (3). Impaired ventilatory control, low arousal threshold, hyporesponsive genioglossus muscle, anatomical abnormalities all contribute to the pathogenesis of the disease (4). The estimated incidence varies between 9-24% in females-males at ages between 30-50 years. However, it increases nearly to 50% in patients with severe obesity. Besides obesity and male gender; advanced age, chronic alcohol consumption and smoking are among the other factors that increase the risk (3). As a result, currently, more patients with diagnosed or undiagnosed OSA come to the operating theatre for several procedures.

There are several screening tests such as ASA checklist, Belin questionnaire and STOP-Bang score. Polysomnography is the tool for definitive diagnosis and it also determines the severity of the disease. Apnea-hypopnea index (AHI=number of apnea/ hypopnea events per hour) 5-15 events/hour is defined as mild OSA, 15-30 events/hour as moderate OSA and AHI>30 events/hour as severe OSA (3). The lowest SpO_2 value, O_2 desaturation index, duration of O_2 desaturation, simultaneous cardiac changes could also give additional idea about severity of the disease (4).

Perioperative safety of OSA patients is a matter of concern for anesthesiologists in many aspects. First of all, autonomic stimulation, due to chronic hypoxia and hypercarbia, leads to increased association with systemic and pulmonary hypertension, coronary artery disease, cerebrovascular accidents and type 2 diabetes mellitus (5, 6). Postoperative cardiopulmonary complications, such as atrial fibrillation, myocardial infarction, O_2 desaturation events, unplanned re-intubations, delirium and pneumonia are increased in OSA patients. Studies even relate OSA to the increased 30 days mortality (3). Higher prevalence of difficult airway is another major problem.

Anesthesiologists should be aware of the risks, however delaying the surgery with complex and time-consuming tests for definitive diagnosis of OSA is not recommended due to insufficient evidence. STOP-Bang has been found as the most validated preoperative screening tool in surgical patients (7-9). STOP-Bang >4 or STOP ≥2 + BMI>35 kg/m^2 or male gender is associated with greater risk of OSA (3). Since it is an easy and fast applicable test, STOP-Bang should be considered for all possible cases during preoperative screening, and patients with suspected OSA should be approached with care as if they have diagnosed OSA. However, in case of uncontrolled or significant systemic disease or ventilation problems, the patients would benefit preoperative cardiopulmonary evaluation and optimization and CPAP therapy (3).

Perioperative CPAP therapy has been proven to decrease complications and length of hospital stay. Patients who are already on CPAP therapy should be encouraged to bring their own CPAP machines to the hospital and use the same perioperative. The need for postoperative modifications due to edema of the face and upper respiratory tract is possible. The fact that the use of CPAP perioperatively does not eliminate the need for close monitoring, should be always kept in mind (4, 10).

OSA has been proven to be an independent risk factor for both difficult mask ventilation and intubation. Supraglottic airway devices are usually good rescue devices, however two studies also indicated increased risk of failed supraglottic airway (11, 12). An upright or ramped position, with the aid of proper preoxygenation and apneic oxygenation techniques would improve the conditions during airway management. Awake intubation techniques are commonly preferred in OSA cases with possible difficult airway. However, the increased risk of impaired upper airway reflexes with topical anesthesia and unexpected deep sedation causing loss of airway, should be handled carefully in these patients. CPAP is a good aid for oxygenation during sedation (4, 13).

Due to increased risk of postoperative residual neuromuscular blockade; minimizing the dose, monitoring the level of the blockade and reversal of neuromuscular blockade, preferably with sugammadex gains importance (10). The evidence about opioids is not certain enough, but there are studies supporting the fact that opioids worsen apneas in a dose-dependent manner. Relatively short acting anesthetic drugs such as propofol, remifentanil, volatile agents, dexmedetomidine and midazolam could be used safely with a careful titration and depth of anesthesia monitoring. Regional anesthesia techniques could be better alternatives in appropriate patients, both for anesthesia and postoperative analgesia to decrease drug doses and spare residual effects of general anesthesia (10).

Early postoperative period is critical because the most events usually occur during the first 24 hours. Extubation should be performed in a fully-awake patient, following appropriate preoxygenation and reversal of neuromuscular blockade. If needed, CPAP should be initiated as early as possible. As supine position worsens apneas; upright, semi-upright or lateral positions should be encouraged during extubation and in the postoperative period, especially during sleep. Close monitoring and opioid sparing analgesic techniques are among essential principles. Patients might benefit restricted fluid therapy because rostral fluid shifts during the perioperative period due to intravenous fluids, spending much time in supine position and compression stocks is one of the leading causes of postoperative airway collapse (14-16).

Patients with OSA should be considered at risk perioperatively, regardless of the type of the surgery and anesthetic technique. But still it seems that there is a lack of institutional policy about perioperative management strategies of OSA patients in many countries, despite the evidence of increased perioperative complications and published guidelines (1, 17). Understanding the pathophysiological mechanisms, an attentive and well-planned perioperative care with an integrated multidisciplinary team approach would be critical to avoid complications.

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MEETING THE NEEDS WHILE KEEPING THE SOURCE-BLOOD INVENTORY MANAGEMENT

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ABSTRACT

Background: Blood inventory management is the critical step between the blood supply and blood transfusion. Its main role is to keep the balance between shortage and wastage of blood. Evaluation of our current blood supply and inventory management with an intention to identify the weak points and to propose models to establish the best practices that will ensure optimal blood supply with minimal wastage of blood.

Material and Methods: We evaluated data concerning the number of whole blood units collected, the number and ABO/D phenotype of the produced, issued and expired blood components (BC), using the donor information system.

Results: The linear trend of produced and issued BC shows an increment, while the trend of expired BC shows a decrement over the period of 12 months in 2019. The overall rate of produced, issued and expired units is 126, 120 and 6RBC/day and 78, 67 and 11PLT/day. The expired RhD negative RBC (25%) and PLT (33%) are significantly greater in comparison to the produced and issued, being 2 times greater for the RBC and 3 times greater for the PLT. The expired AB RBC (16%) and PLT (27%) are significantly higher in comparison to the produced (8.2%) and issued (7.3%) RBC, as well as to the produced (5.7%) and issued (7.3%) PLT. From the total number of expired O RBC (688) and PLT (710), 28% and up to 50% are RhD negative respectively. From the total number of expired AB RBC (340) and PLT (1075), 26.5% and 22% are RhD negative respectively. The"universal" O negative RBC and AB negative PLT expire in significantly greater proportion than the produced and issued BC of the same blood type.

Conclusion: Blood transfusion experts should work together with the clinicians and the hospitals in setting the indicators for monitoring the blood inventory management in order to minimize the shortage and outdating of the blood and to meet the patients' needs for transfusion.

Key words: blood inventory management, expiry rate, universal red blood cell.

Introduction

Blood transfusion is lifesaving medical procedure especially for critical trauma patients and for all other patients who need urgent or chronic treatment with different blood products. Providing safe and adequate blood should be an integral part of every country's national health care policy and infrastructure. WHO recommends that all activities related to blood collection, testing, processing, storage and distribution, should be coordinated at the national level through effective organization and integrated blood supply networks according to the availability of resources, with the aim of achieving self-sufficiency (1).

Our national blood transfusion establishment (BTE) is responsible for the provision of an adequate supply of safe blood for all patients requiring transfusion. The national health and blood program develops policies and strategies to collect enough blood while maintaining the pool of regular blood donors. According to the WHO, these strategies should also include: prevention, early diagnosis and effective treatment of conditions that could result in the need for transfusion, use of good surgical and anesthetic techniques, pharmaceuticals and medical devices to reduce blood loss, availability and use of simple alternatives for volume replacement, including intravenous replacement fluids (crystalloids and colloids), appropriate prescribing of blood and blood products in accordance to the national guidelines, safe pre-transfusion procedures, safe administration of blood and blood products.

The Council of Europe also provides policy guidance and technical assistance to countries for ensuring safe blood and blood products, and works towards self-sufficiency in safe blood based on voluntary unpaid blood donation to achieve universal health coverage (2).

The primary goal of blood establishments is to recruit and to maintain sufficient pool of voluntary and no remunerated blood donors who give blood on regular basis. Blood safety starts with the donor. Donor selection process should meet well established criteria to ensure both the safety of the donor and the patient in a way which would not produce shortage of the blood supply.

Rational clinical use of blood products is the other crucial process in providing enough blood for transfusion. Blood inventory management is the critical step between the blood supply and blood transfusion. Its main role is to keep the balance between shortage and wastage of blood. Having in mind that the labile blood components such as red blood cells (RBC) and platelets (PLT) have short storage time in terms of days (35-42 days for RBC and 5-7 days for PLT), keeping optimal stock to meet 100% of the needs with minimal loss of blood due to expiry is very challenging (3).

Even more, blood products are still mainly from human origin which is why it is very important to optimize the supply according to the demands. To achieve that, two processes are of main importance and need constant monitoring. One of them is the sufficiency and safety of the blood supply which is the responsibility of blood establishments. On the other side of the coin is the rational clinical use of blood which must be based on well-established indications for prescribing blood and the optimal use of the alternatives to blood transfusion by the clinicians.

Unnecessary transfusions not only expose the patients to the recognized and hidden transfusion risks, but also reduce the availability of blood products for patients who are in need.

Blood inventory management is crucial chain that connects these two processes. Having in mind that there are several blood inventories at our BTE (one in the capital of Skopje, 3 regional and 20 local), their management becomes even more challenging.

For that reason, this article focuses on the evaluation of our current blood supply and inventory management with an intention to identify the weak points and to propose models to establish the best practices that will ensure optimal blood supply with minimal wastage of blood.

Material and Methods

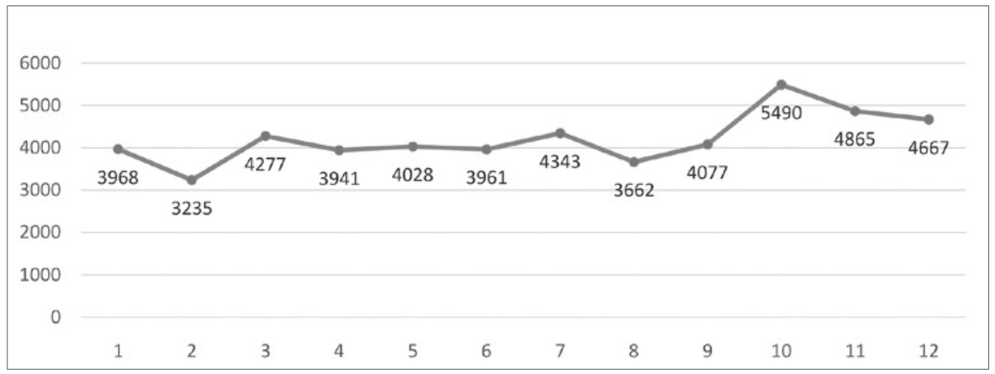
We evaluated the dynamics of blood supply as well as the blood shortage and wastage levels as key indicators for the blood bank performance. Detailed statistical analysis of the data concerning the number of blood donors (accepted and deferred), whole blood units collected, as well as the number of labile blood components (BC), such as red blood cell (RBC) fresh frozen plasma (FFP) and platelets (PLT) which were produced, issued and expired during 2019, was performed. ABO and RhD distribution of the produced, issued and expired cellular blood components was also analyzed. Data were obtained from the donor information system (eDelphyn).

Results

In the period of 2019 there were 56028 registrations for blood donation, from 27450 blood donors, from which 5270 (9.4%) were deferred for medical reasons and other conditions which could impact the safety of the donor or the recipient.

The total of 50600 whole blood units were collected with the average number of 4200 collected unites per month, ranging from the lowest number of 3235 observed in February to the highest number of 5500 observed in October.

Graphic 1. *Number of donations per month*



The total of 4500 (8.9%) units were eliminated. The blood testing laboratory eliminated 1350 (2.7%) units from which 53.5% because of transfusion transmissible infection marker reactivity, 9.5% had positive RBC antibody screening and 37.0% blood samples were unsuitable for testing. The production unit eliminated other 3150 (6.2%) units which did not meet the production criteria mainly because of insufficient volume (70.6%) and other reasons such as the presence of fat in plasma components or too many red blood cell in platelet components. The number of obtained primary blood components (BC) from the rest of the 46100 whole blood units, such as red blood cell (RBC), platelets (PLT) and fresh frozen plasma (FFP) which were labelled for clinical usage and entered the inventory is shown in Table 1.

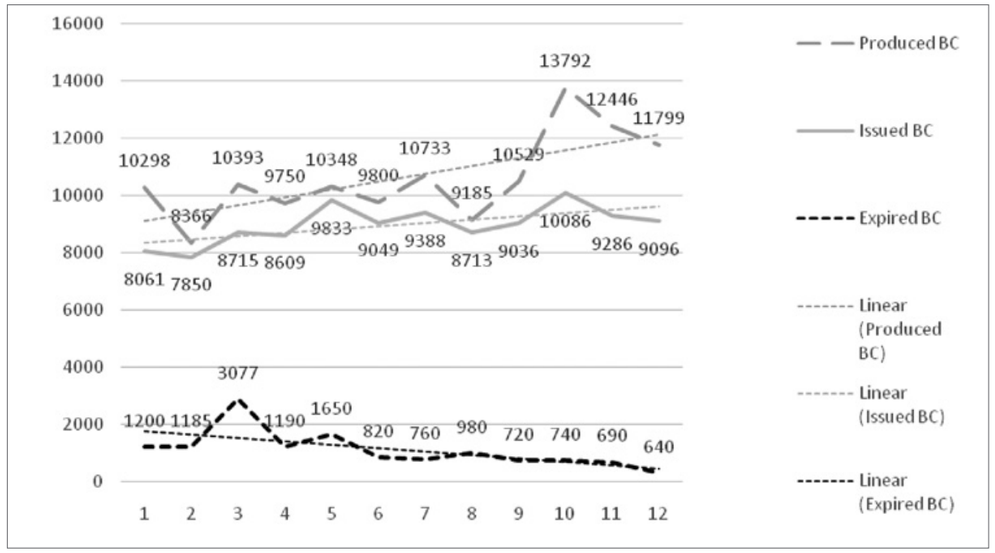
Table 1. *Produced, issued and expired blood components in the period of 2019.*

Blood component	Produced No (%)	Issued No (%)	Expired No (%)
RBC	46000 (99.7)	44000 (95.5)	2100 (4.5)
PLT	28409 (61.6)	24442 (91.5)	3967 (15.0)
FFP	46000 (99.7)	38300 (83.3)	7700 (17.0)
Total	120.500 (100.0)	106742 (88.5)	13767 (11.5)

The linear trend of produced (labelled for clinical usage) and issued BC shows an increment while the trend of expired BC shows a decrement over the period of 12 months.

The overall rate of produced, issued and expired RBC is 126, 120 and 6 units/day. The overall rate of produced, issued and expired PLT is 78, 67 and 11 units/day respectively.

Graphic 2. *Distribution of the produced, issued and expired BC per month*



(The figures represent the produced and issued primary BC, as well as and the modified BC such as filtered and pediatric RBC and Cryoprecipitate.)

According to the RhD phenotype, the percentage of produced and issued RhD positive in comparison to RhD negative cellular blood components is similar. The percentage of expired RhD negative RBC and PLT is significantly greater in comparison to the percentage of produced and issued RhD negative blood components, being 2 times greater for the RBC and 3 times greater for the PLT (Table 2).

Table 2. *Produced, issued and expired RBC&PLT according to the RhD phenotype*

RhD	Produced (%)		Issued (%)		Expired (%)	
	RBC	PLT	RBC	PLT	RBC	PLT
Positive	86.0	89.0	88.0	90.0	75.0	67.0
Negative	14.0	11.0	12.0	10.0	25.0	33.0

According to the ABO/RhD phenotype frequency distribution, there was no significant difference between the produced and issued RBC and PLT. The ABO/RhD distribution of the expired RBC and PLT significantly differ from the one observed in the produced and issued BC (Table 3). In general, there were significantly more RhD negative blood components among the expired cellular blood components of all ABO types, especially O RhD negative RBC and AB negative PLT in comparison to produced and issued blood components of the same blood group.

Table 3. *ABO and RhD phenotype distribution of RBC and PLT*

Blood group	Produced (%)		Issued (%)		Expired (%)	
	RBC	PLT	RBC	PLT	RBC	PLT
A+	35.0	36.0	36.4	36.3	24.0	23.2
A-	5.3	4.3	5.0	4.0	7.0	12.0
O+	29.0	33.0	29.5	34.0	24.0	9.0
O-	5.0	4.0	4.7	4.0	9.0	9.0
B+	15.0	15.0	15.0	15.0	15.5	14.0
B-	2.4	1.9	2.0	1.7	4.0	6.0
AB+	7.0	5.0	6.3	4.5	12.0	21.0
AB-	1.2	0.7	1.0	0.5	4.0	6.0

According to the ABO phenotype, the greatest difference between the expired, on one side and the produced and issued BC, is observed in blood group AB. The percentage of expired AB RBC (16%) and PLT (27%) is significantly higher in comparison to the produced (8.2%) and issued (7.3%) RBC, as well as to the produced (5.7%) and issued (7.3%) PLT.

From the total number of expired O RBC (688) and PLT (710), 28% and up to 50% are RhD negative respectively. From the total number of expired AB RBC (340) and PLT (1075), 26.5%

and 22% are RhD negative respectively. The "universal" O negative RBC and AB negative PLT expires in significantly greater proportion than the produced and issued BC of the same blood type (Table 3).

The greatest expiry rate among RhD negative RBC is observed in blood group O (15.6 units/month). The expiry rate of AB negative PLT is lower in comparison to other RhD negative PLT, but in relative terms it is still very high as shown on Table 4.

Table 4. *Expiry rate of cellular BC according to the ABO/D phenotype*

Expiry rate	A+	A-	O+	O-	B+	B-	AB+	AB-
RBC/month	42.0	12.5	41.6	15.6	27.0	7.0	20.8	7.5
PLT/month	73.5	38.5	29.6	29.6	49.0	20.2	67.0	19.6

From the total of the distributed BC from the BTE, about 66% of the RBC, 77% of the FFP and 96% of the PLT were issued for the hospitals in the city of Skopje. More than half of the RBC and FFP are used in surgery, while 90% of the PLT are used in non-surgical setting (mainly for hematology and oncology) as it is shown in Table 5. About 30% of the PLT used in surgery are for the cardio-surgical patients and another 30% are used in gynecology.

Table 5. *Clinical use of blood*

Blood component	Surgery No (%)	Non-surgical setting No (%)	Private hospitals No (%)*
RBC	22350 (58.5)	15600 (41.5)	6050 (13.7)
FFP	21970 (68.7)	10050 (31.3)	6315 (16.5)
PLT	2260 (10.0)	20640 (90.0)	1542 (6.3)
CRYO	472 (58.0)	342 (42.0)	440 (35.0)

**Percentage from the total number of issued blood component*

Discussion

It is well known that every blood inventory should keep a certain amount of O negative RBC and AB plasma and platelets for urgent blood transfusion when there is no time or possibility to determine the patient blood group.

According to our results, the ABO and RhD distribution of the produced and issued RBC and PLT is similar like in the general and the donor population being about 86% RhD positive and 14% RhD negative. The percentage of expired RhD negative RBC and PLT was significantly higher, being 25% and 33% respectively.

From the total of 2048 issued O negative RBC, 63% were used by hospitals in Skopje (26% were for surgical patients, 18% for non-surgical patients, 19% were issued to the private hospitals) and 36% were issued through the regional blood transfusion facilities to the regional and local hospitals. Private and regional hospitals used 1143 O negative RBC which is 56% from

the total. Having in mind that only 47% of the issued RBC is used by the private and regional hospitals, their usage of 55% of the O negative RBC is significantly greater in comparison to the other users. From the total of 188 outdated O negative RBC, 75 (39%) expired in the blood establishment in Skopje and 113 (61%) expired in the blood inventories in the regional and local BE which supply the correspondent hospitals.

All of these rise the question why RhD negative blood components, especially O negative RBC expire in relatively greater number compared to the RhD positive ones?

The possible explanation is poor inventory management at local level having in mind that there are about 20 blood banks in the local BE and some of them are distant from the correspondent regional BE which is probably why they keep more O negative RBC than the actual need.

Even more, some of the blood bank laboratories perform only several cross-matches per month, but still must keep, "minimum" quantities of RBC from all blood groups, especially O negative.

On the other side, the private hospitals are completely dependent on the supply from BTE and they also probably keep RhD negative blood components in excess in their blood inventory.

To overcome this problem, several measures were undertaken such us:

- detailed assessment of the number of cross-matched versus issued RBC, as well as the number of requested/ reserved and issued RBC, FFP and PLT on regular basis,
- issue of blood components on the principle, "first in, first out" on regular basis,
- introduction of blood inventory management program with regular RBC replacement with fresh RBC on the principle "ten days to expiry" in the blood inventories of the local BE,
- time and cost-effective regional routing of the blood establishment vehicles.

From the graphs which show the distribution of collected, produced, issued and expired blood units, it is obvious that in the first six months of the year the blood supply was greater than the needs which resulted with two peaks of supply and expiry of blood components. In the next six months the blood supply was in the concordance with the utility with declining trend of expiry which indicated better inventory management due to the undertaken improvements.

The number of RBC units in the main inventory has proved to be a good predictor for outdating of RBC. The principle "first in, first out" which is currently in use in our everyday practice, means that if a RBC unit enters the inventory, every one which enters the inventory afterwards would be issued after that unit. This principle is well working to the threshold of about 800 RBC in the inventory, but if the number exceeds 1000 units, with an average of 150 RBC issued per day, the average age of cross-matched and transfused units is about 25 days and there still might be lack of some of the RhD negative ABO phenotypes. For this reason, we managed the blood supply in a way which enabled more consistent blood collection without peaks of too many or too less collected units with the consideration of the donors' blood type as well.

However, there is still much to be done from both counterparts, the BE as a supplier and the hospitals as a consumer.

BE should adjust the supply according to the demand and there are some blood inventory management models which are focused on the management of blood supply with certain types of blood donation such as the apheresis, especially thrombopheresis (4, 5).

To achieve these, hospitals should send regular report about their needs, especially when the need for certain blood components, especially platelets, from certain rare blood groups is expected to be greater. This is very important information for the blood establishment to prepare and call suitable voluntary blood donors with rare blood groups when such blood is needed and to educate the donors to retain from donation otherwise.

Other models to prevent expiry were proposed such as those defined by a single threshold: rather than transfusing the oldest available blood that is younger than 42 days, to transfuse the oldest blood that is younger than the threshold, and if there is no blood younger than the threshold then to transfuse the youngest blood that is older than the threshold. To assess this policy, a simulation model focused on the trade-off between the mean age of transfused blood and the fraction of transfused blood that is imported was used (6).

Whether the age of RBC affects mortality after transfusion in critically ill patients is controversial, but still affects the decisions concerning the blood inventory management. One large study in which 8467 critically ill patients were enrolled compared fresh RBC transfusion with the current standard practice. The study concluded that age of red cells for transfusion did not affect the outcomes in critically ill patients (7).

Programming, software based models for defining optimal periodic review policies for red blood cells inventory management that focus on minimizing operational costs, as well as blood shortage and wastage due to outdating, have also been proposed (8).

The effective clinical use of blood is another important step to the ability of the health system to cope with the demand and to prevent the shortage of blood. Hospital should have well established maximal blood ordering schedules (MBOS). National guidelines on rational clinical use of blood should also be in place to help clinicians to avoid unnecessary transfusions and unsafe transfusion practices which expose patients to the risk of adverse transfusion reactions and in the same time reduce the availability of blood products for patients who are in need (9). For that purpose, WHO recommends the development of systems, such as hospitals transfusion committees (HCT) and haemovigilance, to monitor and improve the safety of transfusion processes. In this regard WHO reports that 124 countries have national guidelines on the appropriate clinical use of blood, transfusion committees are present in 45% of the hospitals performing transfusions. Haemovigilance system have 46% of the reporting countries from which 76% are in the European region (10).

Concerning the rational clinical use of blood, we also propose ABO compatible RBC and PLT to be widely accepted by the clinicians which means not only in periods of shortage, but also when BE is in need to balance the inventory. Recent studies suggest managing RBC inventory with more restrictive maximal shelf life policy of RBC (up to 21 days) which also takes into account the potential savings offered by ABO compatible substitution, even though the group O

RBC are going to be needed more frequently. It was observed that ABO/RhD compatible blood substitution can reduce RBC wastage due expiry up to 16% (11).

Another mathematical model for blood ordering and issuing management also considers the substitution relations among various blood types in the blood transfusion process in order to minimize blood shortage and wastage (12).

Blood establishments and hospital blood banks should implement performance indicators for the use of blood and blood components which is very important for efficient blood inventory management. These indicators include detailed numerical data for the numbers of units of RBC, FFP and platelets issued and transfused (13).

In 2014, European Directorate for the Quality of Medicines (EDQM) conducted a project on the Quality indicators for monitoring the clinical use of blood in Europe. Among the key items in the questionnaire were: the number of hospital beds, the number of patients admitted, and the number of patients transfused. Only 5% of the total number of hospitalized patients were transfused. The number of transfused units per 1000 population was 10-60 units of RBC, 5-20 units of FFP and 3-15 units of platelets. The number of units transfused per hospital bed was 3-18 for RBC, 2-7 for FFP and 2-5 for platelets (6-28 all component units per bed). The blood units transfused in onco-haematology and in surgery as proportion of total transfusions in the hospital were 10-30% and 20-70% respectively (14).

As a quality indicator for the distribution of blood units from blood establishments to hospital blood banks, and the management of hospital blood bank stocks, the ratio of the number of units distributed to those actually transfused was calculated. It was 1.2 with a blood loss ranging as high as 20%. The ideal ratio of 1:1 even under the best conditions and practice is practically impossible to achieve (14). In our practice it is impossible to calculate the above mentioned ratio because of the lack of the information about the actual number of transfused units from the hospitals.

Useful data for the blood inventory management are data concerning the number of blood components in stock, units of blood components discarded (in total and separately because of poor storage, expiry or poor transportation) and the number of group O Rh negative units that were outdated or transfused to Rh positive patients. Percentage distribution of causes of discarding blood units due to poor storage is 2-10%, due to expiry is 25-88% and due to poor transportation is 25-80% in different hospital blood banks (15).

Implementation of reservation period for cross-matched RBC and on-time recall of blood transfusion requests, which in our transfusion practice exists only in few hospital based blood banks, has proved its efficacy as a method for rational use of blood with positive impact on the blood inventory.

Currently, it is very difficult to provide data on blood inventory management in the hospitals, especially the actual number of transfused and discharged blood units on hospital level. This is mainly due to the fact that hospitals' transfusion committees, which although mandatory, are not functional in the most of the hospitals. Also, there are no national guidelines on the clinical use of blood which would define strict and measurable quality indicators.

Conclusion

Human blood is rare and valuable source and every drop of it should be used wisely. For that reason, further efforts towards good planning and collaboration between blood transfusion experts and the clinicians are essential in setting the indicators for optimizing the blood inventory management in order to minimize shortage and outdating of blood and to meet the patients' needs for transfusion.

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LIPOSUCTION WITH ANALGOSEDATION AND TUMESCENT LOCAL ANESTHESIA VS. GENERAL ANESTHESIA: COMPARATIVE STUDY

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ABSTRACT

Introduction: Liposuction is one of the most popular cosmetic surgery with unique anesthetic considerations. It may be performed with local tumescent anesthesia and analgosedation, regional or general anesthesia, depending on volume aspirated, region treated and patient's preference.

Objectives: To present our experiences with liposuction on patients using analosedation and local luminescent anesthesia in comparison to general anesthesia.

Material and Methods: Study analyzes 40 patients, ASA I-II with a mean age of 39.3 ± 5.6 years that underwent liposuction. All patients were divided in two groups. In the first group we have 20 patients operated with general anesthesia and 20 patients (Group-2) operated with analgosedation and tumescent local anesthesia. Formula for tumescence fluid that we used is modified Klein's solution, comprising 15 ml 2% lidocaine and 1 ml 1:1000 adrenaline in a 500 ml warmed up saline.

Several attributes were analyzed among the groups: gender, age, amount of aspirated fat, postoperative pain, by using VAS score at 5 points-2 hr, 4 hr, 6 hr, 12 hr and 24 hr, cumulative 24 hours morphine consumption after the operation, operative time (minutes) and aspirated fat.

Results: There was no statistical significance in age, gender and the amount of the aspirated fat among the groups (Group I-3300 vs. Group II-3550 ml, P=0.02853). Operative time (minutes) was significantly higher in group I (p=0,0005).

There were statistically significant differences in VAS scores between the groups I and II at all postoperative time points-2 hr, 4 hr, 6 hr, 12 hr and 24 hr. ($P < 0.00001$).

The cumulative 24 hours morphine consumption after the operation was significantly lower in the Group II (mean = 4.83 ± 1. 31) than the Group I (mean = 12 ± 2.41). This difference was statistically significant **(**p=0.0001).

Conclusion: Analgo-sedation and local tumescent anesthesia is as effective as general anesthesia in terms of amounts of liposuction fat. Allowing patient's cooperation during intervention this new anesthesia technique decreases patient's postoperative morphine consumption, operation time and VAS score at all postoperative points.

Keywords: analgosadation, liposuction postoperative pain, tumescent local anesthesia.

Introduction:

Suction assisted lipectomy or liposuction is one of the most popular cosmetic surgical procedures being the second most frequent in the last few years (1). It has gained high popularity due to its efficacy with almost invisible surgical incisions and low morbidity rates, being one of the safest among aesthetic procedures (2).

During liposuction, risk of severe complications rises with the amount of fat aspirated (3). Depending on the volume aspired, liposuction is divided in high volume (>4,000ml aspired) or low volume liposuction (<4,000ml aspired). Depending on the amount of wetting solution used, there are four main types of liposuction techniques: dry, wet, super-wet and tumescent. The essential differences between these techniques focus on the amount of infiltrating solution injected into adipose tissue and the resultant blood loss as a percentage of aspirated fluid (4,5,6). Modern guidelines are focused on super wet and tumescent infiltration. In these procedures, very large volumes of dilute local anesthetic along with additives, such as epinephrine and sodium bicarbonate, are injected into the subcutaneous tissue to enlarge the tissues and make them solid, swollen, and turgid, i.e., the final endpoint of strong tissue turgor. This creates a plane, from where suction of fat becomes easier, with lesser blood loss (7). Decreasing the blood loss significantly, makes liposuction safe and effective procedure (4,3,7). The higher the amount of fat that have to be aspirated is, the larger the volume of tumescence local anesthesia have to be infiltrated. As Klein stated, these remarks make liposuction an ambulatory procedure, without necessity of additional general anesthesia what makes lowering the risk of severe complications (6).

Liposuction may be performed in local tumescent anesthesia and analgosedation, regional or general anesthesia.

The anesthesia technique depends on the site and extent of the liposuction as well as patient's preference. Ideal anesthesia in liposuction is the one allowing the patient cooperation during painless intervention in different body parts at the same time. General anesthesia is often asked by the patients and sometimes it is needed especially when massive liposuction is planned. This always prolongs the operative time (8).

The combination of analgosedation and local tumescent anesthesia shows great patient comfort, cooperation during operation and abolishes the need of hospital overnight. Furthermore, this combination is safe and does not interfere with the efficacy of the procedure and endpoint result.

Vasoconstrictor and local anesthetic infiltration reduces bleeding and provides intraoperative analgesia, reduced recovery period, quicker discharge and low patient cost (9,10).

The objective of the study is to present our experience with liposuction driven with analgosedation and local tumescent technique, comparing to previous cases where general anesthesia was utilized.

Material and methods:

This is a retrospective comparative study that analyzes 40 patients with approval of ethic committee, ASA I-II that underwent liposuction at the University Clinic for Plastic and Reconstructive Surgery in Skopje, in the period of last two years (2018-2019). Patients were divided in two groups: patients operated under general anesthesia (Group I) and patients operated with analgosadation and local tumescent anesthesia (Group II). Several attributes were analyzed among the groups: gender, age, amount of aspirated fat (in ml.), postoperative pain (by using VAS at 5 points-2 hr, 4 hr, 6 hr, 12 hr and 24 hr), cumulative 24 hours morphine consumption after the operation, and duration of operation.

Exclusion criteria included age <18 , ASA class III-IV, known allergy to paracetamol, chronic hepatic or renal failure, any contraindications to regional techniques (allergy to amino amide local anesthetics, infection around the site of the block, and coagulation disorder), history of analgesics dependence and patients with body mass index (BMI) >35 kg/m^2.

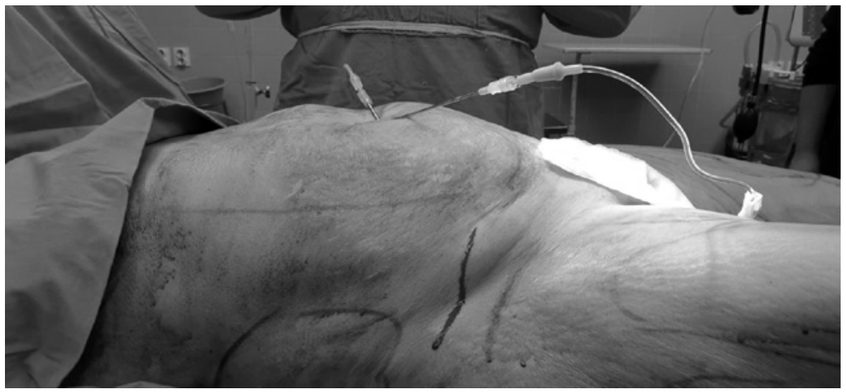
Within the group of analgosadation and tumescent anesthesia (Group II), there are two subgroups of patients: 9 patients with large volume of fat aspiration and 11 patients with small volume of fat aspiration. Indications for operation were localized fat deposits on one or more body parts such as abdominal wall, waist, back, thighs and arms. Some of the patients have concomitant fat grafting procedure, which was not in conflict with the type of anesthesia. Prior operation, usual blood count lab tests, coagulation profile and anesthesiologist counseling were done. No patient had serious comorbidity that will contraindicate the intervention. General anesthesia was given according to patient's preference. Prevention with low molecular heparin for every massive liposuction was given one day prior surgery. One hour before operation, all the patients got single shot wide spectrum antibiotic intravenously and premedication with midazolam in dose of 0.02 mg/kg intravenous (IV) before surgery.

Induction of general anesthesia to all 20 patients (in Group I) was performed with 2% propofol-1-2 mg/kg, lidocaine 40 mg, and fentanil 2-3 mcg/kg. After unconsciousness, rocuronium 0.6 mg/kg was injected and then endotracheal intubation was done following the 90 seconds mask ventilation. Pressure controlled ventilation was done by providing oxygen 50% and air 50% at the flow rate of 2 L per min. Maintaining the anesthesia was done by sevoflurane at 05-1 MAC. Intermittent pneumatic compression (IPC) devices was used in all patients to help prevent blood clots in the deep veins of the legs.

Patients (in Group II) with analgosdation and tumescent local anesthesia during liposuction received ketamine at dose of 25 mg, paracetamol 1 g, remifentanil in dose of 0.025-0.2 mcg/kg/min IV and propofol at dose of 0.1-0.15 mg/kg/min IV for 3-5 min; administered as slow infusion with monitoring of cardiorespiratory function.

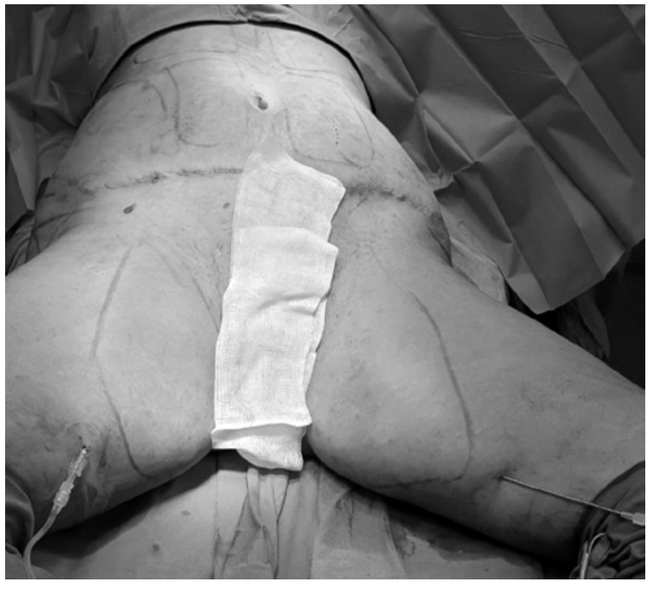
Formula for tumescence fluid that we use is modified Klein's solution, comprising 15 ml 2% lidocaine and 1 ml 1:1000 adrenaline in a 500 ml warmed up saline. Several liters (2 – 6 l.) are administrated in the regions to be treated using blunt multi-holes infiltration cannulas Ø2-3 mm. Infiltration goes slowly, finishing when bleaching effect and strong tissue turgor is achieved while fluid leakage via entry ports starts.

Figure 1: *Fat Infiltration with local tumescent anesthesia*



At this moment, since the painful event is finished, sedation can go superficial, and in the following 40 minutes, patient is awakened. This is the time necessary to wait in order fatty tissue to get soaked prior liposuction. Liposuction is conducted via the same entry incisions using Mercedes suction cannulas Ø4-6 mm, 30-50 cm long (Byron) connected with plastic tubes to suction vacuum machine (PSI – TEC III Aspirator, Byron).

Figure 2: *Liposuction with Mercedes suction cannulas*



Usually, lidocaine is well distributed locally during the waiting period and patient does not feel any pain when liposuction starts. However, sometimes they complain the discomfort of for and back cannula movements, feeling even some pain, and this is the time when analgosedation might go deeper. The level of analgosedation can be adjusted depending on surgical procedure. The analgosedation has to be superficial when patients have to be turned in prone position.

End point of liposuction is achieved when bloody aspirate starts to come out or the result is achieved. Dressing follows with or without vacuum pumps and finally a compressive garment is put on. If fat grafting is planned, sedation can be deeper at that point while filling the fat cells in selected areas.

Statistical Analysis

Data was statistically analyzed in SPSS software package, version 22.0 for Windows (SPSS, Chicago, IL, USA). The qualitative series were processed by determining the coefficient of relations, proportions, and rates, and were shown as absolute and relative numbers. Quantitative series were analyzed with measures of central tendency (average, median), as well as with dispersion measures (standard deviation, standard error). Normality of distribution was tested by Shapiro-Wilk W test. Mann-Whitney U Test was used for analysis of differences between the two numerical variables. To determine the association between qualitative variables Pearson Chi square test and Fisher exact test was used. A two-sided analysis with a significance level of $p<0,05$ was used to determine the statistical significance.

Results

In the study sample of 40 (100%) patients, the mean age was 42,5±6,9 years with min/max age of 32/56 years and 50% patients younger than 42 years for Median IQR 42 (37-47). The min/max age of patients in Groups I/ II was 32/56 with 50% younger than 41,5 years vs. 33/56 with 50% younger than 42,4 years respectively. More than 50% of the patients in both groups had BMI higher than 31 kg/m^2. There were no statistically significant differences in age (years), ASA (I/II) and BMI (kg/m^2), neither significant association with gender (F/M). Operative time (minutes) was significantly higher in Group I (p=0,0005). In 50% of the patients in both groups the amount of aspirated fat was higher than 4025 ml vs. 4125 ml with no significant differences between the groups among the groups (p=0,2853).

Table 1. *Demographic and Clinical Characteristics*

Parameters	Group I (general anesthesia)	Group II (analgosadation + local tumescent anesthesia)	p-value
Age (years)	42,4 ± 6,9 Median IQR=41,5 (37-45,5)	42,5 ± 7,1 Median IQR=41,5 (38-47,5)	Mann-Whitney U test: Z=0,1217; p=0,9031
Gender (F/M)	18 (90%) / 2 (10%)	13 (65%) / 7 (35%)	Fisher exact test: p=0,0583
ASA (I/II)	11 (55%) /9 (45%)	8 (40%)/ 12 (60%)	Pearson Chi-square: 0,9822; df=1; p = 0,3422
BMI (kg/m2)	31,1 ± 1,8 Median IQR=31 (29-32,5)	30,8 ± 2,1 Median IQR=31 (29-32,5)	Mann-Whitney U test: Z=-0,4193; p=0,6750
Operative time (minutes)	113,5±9,9 Median IQR=110 (110-120)	138,5±11,4 Median IQR=140 (135-145)	Mann-Whitney U test: Z=-4,7608; p=0,00005*
Aspirated fat (ml)	3977,1±288,6 Median IQR= 4025 (3875-4175)	4060,4±546,3 Median IQR=4125 (3850-4425)	Mann-Whitney U test: Z=-1,0685; p=0,2853

* significant for p<0,05
Abbreviations: F, female; M, male; ASA, American Society of Anesthesiologists; BMI, body mass index.

There were statistically significant differences in VAS scores between Group I and Group II at all postoperative time points-2^{hr}, 4^{hr}, 6^{hr}, 12$^{hr.}$ and 24$^{hr.}$ ($p < 0,00001$). VAS scores in Group II are significantly lower at all points. (Table 2)

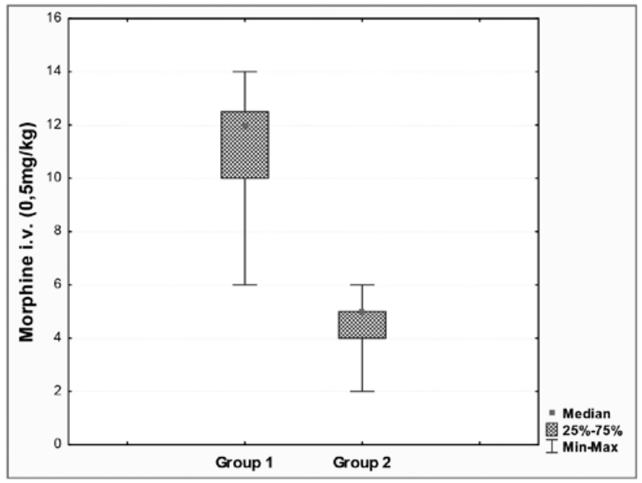
Table 2. *VAS scores in Group I and II at all postoperative time points*

Groups	VAS 2 h	VAS 4 h	VAS 6 h	VAS 12 h	VAS 24 h
Group 1	5,1± 0,4	5,5± 0,6	5,6± 0,7	5,7± 0,6	5,4± 0,7
Group 2	1,3±0,6	2,1±0,6	1,7±0,6	1,9±0,3	1,6±0,5
Mann-Whitney U test:	Z=-5,4100; p=0,00006*	Z=-5,4200; p=0,00001*	Z=-5,3900; p=0,00001*	Z=-5,4000; p=0,00005*	Z=-5,5885; p=0,00001*

*** significant for p<0,05**

The cumulative 24 hours morphine consumption after the operation was significantly lower in the group of patients who underwent local tumescent anesthesia and analgosedation (Group II – 4,8± 1,31) than the group of patients who underwent only general anesthesia (Group I – 12± 2,41). This difference was statistically significant (Z=-5,3556; p=0,00001*). (Figure 2.)

Figure 3. *Cumulative 24 hours morphine consumption after the operation in Group I and II*



No differences concerning complications among the two groups were noted.

Disscusion

Liposuction may be performed under local tumescent anesthesia and analgosedation, regional, or general anesthesia. No single anesthesia technique has been proven to be superior over another in terms of effectiveness, but all deaths that have been reported are linked to liposuction done under general anesthesia (11,12). However, general anesthesia was not directly accused in the most cases, but it was the extensiveness of the liposuction or combination of unrelated procedures at the same time done (11). General anesthesia is always an option in massive liposuction, but several studies pointed out the higher morbidity and mortality rates in general anesthesia in comparison to the pure local tumescent or superficial analgsedation (2,6).

Complication risk is proportional with the volume of lipoaspiration. Therefore, 5000 ml lipoaspirate of pure liposuction and 2000 ml of lipoaspirate as an adjuvant procedure, are confined as cut off points, according to American Society of Plastic surgeons (13). Since, strong supportive scientific data are lacking, these limitations are debatable.

The anesthetic procedures differ depending on the region being operated on, the liposuction volume being aspirated and patient's preference. For small volumes liposuction, analogization or tumescent anesthesia solely is preferred. We managed to conduct large volume liposuctions combining these methods, resulting in effective and safe liposuction. Our tendency is to conduct these procedures as day care, to recover psychomotor and cognitive functions quickly, ensuring that patients are discharged early. By using tumescent anesthesia, the need for general anesthesia can be annulled, as reported by others, even for other non-liposuction procedures (14,15).

Lidocaine is the most widely used local anesthetic in tumescent solutions, with a maximum dose of 7 mg/kg in combination with adrenaline when used undeluded. When deluded in

tumescent solution, doses may be significantly greater with recommended lidocaine maximum within the range of 35-55 mg/kg (7,16). The lidocaine concentration varies depending on the areas treated: dosage may be raised up to 1,500 mg/L in more sensitive areas such as breast and abdomen or lowered down to 500 mg/L in less sensitive areas such as the thighs (17). Vasoconstrictor and local anesthetic infiltration prevents bleeding and, respectively, provides intraoperative analgesia. Following these recommendations, despite large amount of lidocaine injected, we should not have high concerns regarding lidocaine toxicity (3). We use Hunstad modification of original Klein tumescence comprising 1000 ml of saline with 50 ml of 1% lidocain and 1 ml 1:1000 adrenaline. When specific more sensitive regions, like chin or face, are treated, we use 400 ml NaCl 0.9% with 0.8 ml Adrenalin and 35 ml 2% Lidocaine. In this manner, liposuction can be done as an ambulatory procedure when small volumes are addressed (18).

Monitored anesthesia carries the desired technique, useful for liposuction in small volumes. We conduct analgosedation by using midazolam (1-3 mg), low-dose ketamine (0.25-0.5 mg/kg), fentanyl (1-10 mcg/kg) or remifentanil (0,005-0,25 mcg/kg) for liposuction in small volumes. Propofol (0.5-1 mg/kg) may be given for controlling anesthesia treatment on an intermittent basis or in a continuous infusion (19).

Clonidine in dose of 2-5 mg/kg, is also a useful adjuvant in sedation techniques (7,16,20). However, in massive liposuctions additional anesthesia is needed, especially when the procedure is combined with fat grafting (20, 21,22).

With superficial or no sedation, patient cooperates during procedure, especially when she/he has to turn around in a prone position and this fact is shortening operation time. When patient is not comfortable enough, sedation goes deeper.

In abdominal liposuction, the quality of the epidural analgesia provided is higher than that of local tumescent infiltration and analgosedation. An extensive epidural blockade, however, is often associated with hypotension and must be restricted to patients with good cardiac reserve (22). We have not use it in our patients.

Precautions should be taken prior any massive liposuction since complications and unpleasant adverse effects are much higher. Intravenous fluids should be used with extreme caution in high-volume liposuction procedures as there is significant fluid changes due to the amount of tissue extracted, with the risk of developing pulmonary edema (16,23).

An increase in cardiac index, heart rate, mean pulmonary arterial pressure, stroke volume index and right ventricular stroke function index was observed along with a decrease in mean arterial pressure and systemic vascular index (24). Epinephrine, which is used in large doses routinely during liposuction, may be responsible for tachycardia and increased cardiac index (25).

Furthermore, in patients with large volume liposuction, there is an increased risk of hypo-thermia (26).

The reasons are: exposure of large body surfaces, infusion of large volumes of cold wetting solutions, long duration, general anesthesia, heat loss during mechanical ventilation, ambient room

temperature, and intravenous fluids all contribute to hypothermia in these patients. Hypothermia aggravates complications such as cardiac dysrhythmias, coagulopathies, oliguria, and electrolyte imbalances. We normally heat the saline plastic bottles before preparing them for infiltration. Both the hemodynamic and thermoregulatory changes may persist after the start of surgery for more than 24 hours (24,27).

Any drug that interferes with lidocaine metabolism such as statins and blockers of calcium channels should either be stopped before liposuction or the total lidocaine dose should be reduced (7,26,27). Perioperative thromboprophylaxis with low molecular weight heparin is essential in obese patients (20).

Conclusion

Analgo-sedation and local tumescent anesthesia is as effective as general anesthesia in terms of amounts of liposuction fat. Allowing patient's cooperation during intervention this new anesthesia technique decrease operation time, patient's postoperative morphine consumption and VAS score at all postoperative points.

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CASE REPORT UDK: 616-089.5-032:611.82]:616.98:578.828.7

SPINAL ANESTHESIA FOR A PARTURIENT INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV)

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ABSTRACT

Since both pregnancy itself and HIV infection may complicate management of anesthesia and obstetric interventions of these patients, we aimed to present anesthetic management of a HIV positive term parturient focusing on choice of delivery mode and choice of anesthesia technique by taking into account antiretroviral drug features and infectious precautions.

Key Words: Cesarean delivery, HIV, obstetrics, pregnancy, spinal anesthesia.

Introduction

Modern treatment regimens prolong lives and improve quality of life of human immunodeficiency virus (HIV) infected patients. Acquired immunodeficiency syndrome (AIDS) was first described in 1981 in adults followed by the isolation of the causative agent, HIV in 1983 which cause a disease known as without borders and moral codes (1-3). According to the most recent United Nations Update, there are 34.5 million adults with HIV, and 51% of them has been reported to be at childbearing age (4). Moreover, everyday nearly 2,000 women aged between 15 and 24 years are having new HIV infection diagnosis. Fortunately, with the dramatic success rate of highly active antiretroviral (ARV) treatment, the disease has evolved from a fatal condition to a chronic state. Since the HIV survivors increase by time, we, the anesthesiologists are more likely to come across to manage these challenging patients. Therefore, we aimed to present management of a term parturient receiving ARV treatment due to positive HIV, scheduled to undergo cesarean section (CS) under spinal anesthesia in our institution.

Case Report

A 39 year-old parturient having AIDS diagnosis and currently under ARV treatment with raltegravir (ISENTRESS 400 mg tablet, MSD İlaç, İstanbul) was scheduled for CS at 39 weeks' gestation after obtaining her written consent. According to her preoperative laboratory results HIV RNA was negative with CD4: 590/mm and CD4/CD48: 0.63/1. She was anemic ([Hb] was 10.8 g/dL with serum iron: 319 µg/dL, serum iron binding capacity: 538 µg/dL and serum ferritin: 4 µg/dL). In her physical exam on admission, she had fatigue, oral/genital ulcerations and vaginal discharge. There were no other remarkable findings in her medical history except receiving oral sidatria (200mg emtricitabine ve 245 mg tenofovir disoproxil, Santafarma-Zentiva Sağlık Ürünleri Ticaret ve Sanayi A.Ş., İstanbul) for the last three years by the control of the Department of Infectious Diseases in our hospital before pregnancy.

After establishing intravenous (IV) route, aspiration prophylaxis including 10 mg metochlopramid+50 mg ranitidine was administered. After providing standard monitoring (ECG, heart rate, non-invasive blood pressure and peripheral oxygen saturation), single shot spinal anesthesia was performed in the sitting position between L3-4 intervertebral space with a 27 G Whitacre needle using 10 mg hyperbaric bupivacaine + fentanyl 10 µg + morphine 100 µg. Operation table was tilted to 15° left to prevent supine hypotensive syndrome. In case of detecting spinal anesthesia induced hypotension, incremental doses (10mg) of IV ephedrine was planned for treatment. Four minutes after skin incision, a healthy male baby (3,120gram & 50 cm) was born. Apgar scores of the newborn were 9 and 10 at 1 and 5 minutes, respectively. After umbilical cord clamping oxytocin (10 IU/500 mL Ringer lactate solution) was given by IV infusion. Operation lasting 35 minutes was uneventful.

Discussion

Hereby, we present our first anesthetic management of a HIV positive term parturient focusing on choice of delivery mode and anesthesia technique by taking into account ARV drug therapy and infectious precautions in our institution.

Anesthesiologists caring for HIV infected parturient should have a knowledge on the clinical manifestation, organ involvement and treatment of the disease, features of ARV drugs and vertical transmission of the virus from mother to child and healthcare workers. It is essential to plan a safe anesthesia management of the parturient infected with HIV (5). Although transmission of HIV occurs generally with secretions and/or blood, heterosexual transmission is the most common way as it was in our case. Since vertical transmission from mother to child during pregnancy as a result of vaginal labor/delivery and, breastfeeding are the most important issues, CS decision was made by consensus of obstetricians and the physicians of infectious diseases in the present case and breastfeeding was not allowed in order to avoid vertical transmission from mother to newborn.

During the preoperative evaluation drug abuse, which is considered as an important coexisting problem in patients with HIV was carefully questioned for safe anesthesia management (6) and our patient was not using any other medications and did not have drug abuse habit.

Detailed history of the patients including ARV drug therapy and adverse events, other sexually transmitted diseases such as syphilis and Hepatitis B was also checked (7).

Additionally, multiple organ/system involvement associated with cardiovascular, respiratory, gastrointestinal, renal, central nervous, endocrine and hematologic system are summarized in Table 1 (5,8). When we examined our patient, there was only anemia which is commonly mediated by bone marrow suppression as a result of direct HIV infection, or secondary to opportunistic infections, malignancies and adverse drug reactions. We did not encounter any abnormality in laboratory studies including coagulation parameters and blood biochemistry tests in the present case.

Choice of the anesthetic technique for elective CS in an otherwise healthy parturient has been still regional anesthesia (epidural, spinal or combined spinal epidural: CSE) (9). However, one can ask whether it is safe to use it in HIV positive patients due to concern on the risk of spreading the infection into the central nerve system or worsening the preexisting neurological symptoms if any. Yet, to our knowledge, there are no data related to progression of the disease or increased risk of peri-and/or postoperative complications associated with regional anesthesia. When 30 HIV infected parturients delivered under neuraxial analgesia and anesthesia (18 labor, 12 CS) were evaluated, no neurologic complications or alterations in immune functions were recorded in the postpartum 4-6 month follow up (10). Additionally, when spinal anesthesia in 44 HIV infected patients were compared to 45 healthy parturients undergoing CS, no significant differences were found in terms of intraoperative hemodynamic stability or postoperative complications (11). Based on these evidences though either epidural or CSE technique has the advantage of a catheter for effective postoperative pain control, single shot spinal anesthesia using local anesthetic plus opioids which would be a better option because of the potential risk of infection related to in situ catheters like we did and we did not observe any peroperative and/or postoperative adverse outcome.

In case of any medical contraindication to neuraxial anesthesia, there is a major concern in choosing general anesthesia due to possible immune depressant effects of any drug or condition in immunosuppressed HIV infected patients. According to the reports, both general anesthesia may lead to transient immune depression, and pregnancy itself may suppress cell mediated immune system. However, no complications related to general anesthesia and worsening of the HIV infection were observed (12-14). Fortunately, there was no contraindication for neuraxial anesthesia in our case and we had a successful spinal anesthesia management without any adverse events or complications likewise in otherwise healthy parturients.

There is a number of antiretroviral drugs for treating the primary disease and/or providing both prophylaxis and treatment against opportunistic infections in HIV infected patients. Extensive use of these drugs during pregnancy has significantly decreased the incidence of vertical transmission from mother to child less than 2% (15,16). In general, antiretroviral drugs with different mechanism of actions are preferred to improve outcome of the HIV infected patients by minimizing development of resistance (17). Our patient was preoperatively using raltegravir, an integrase enzyme inhibitor, which is capable of decreasing viral load and

increasing CD4 cells. Before pregnancy she used to receive sidatria which is a nucleoside reverse transcriptase enzyme inhibitor. According to released statement related to prevention of HIV transmission from mother to child by Public Health Authority of Turkish Ministry of Health, CS is the accepted delivery mode in patients with HIV (+) and zidovudine (nucleoside reverse transcriptase inhibitor) therapy is recommended pre-/per-/postoperatively for planned CS at[3]38 weeks' gestation (18).

Anesthesiologists should be aware of the consequences of drug related adverse effects (5). Although raltegravir has been known with its hepatotoxicity, liver enzymes were within normal limits in the present case. Also, ARV therapy and its possible interactions with local anesthetic drugs might be a concern. Bupivacaine (a racemic mixture of R and S enantiomers) has been known as a safe local anesthetic for epidural anesthesia and/or analgesia due to its low placental transfer in healthy pregnant women. Both bupivacaine and ARV drugs are highly protein bound, and plasma level of alpha1 gycoprotein is less in partureints with HIV than control (40g/dL vs 57.5 g/dL). Thus, placental transfer of 15 mL epidural bupivacaine (R and S enantiomers) was found to be 100% higher in HIV infected pregnant women received long-term ARV therapy (lopinavir/ritonavir) when compared to otherwise healthy parturients for CS (19). In our case spinal anesthesia was preferred which is safer in terms of placental transfer because nearly 1/10 of the epidural local anesthetic dose is used for spinal route.

Anesthetists might play an important role for preventing or decreasing the risk of transmission of HIV infection to uninfected patients. Transfusion associated transmission of blood borne infections including HBV and HCV can be reduced by minimizing allogenic blood transfusion. Other route of transmission includes contamination of the anesthesia machine and equipment where laryngoscope blades, face masks and endoscopes can be the source in case of general anesthesia with endotracheal intubation is required. Despite HIV may survive up to 7 days outside the body, it is quite sensitive to disinfection with sodium hypochlorite and heat (20). Therefore, equipment contaminated with blood, should be immediately washed and disinfected according to ASA (American Society of Anesthesiologists) Subcommittee on Infection Control Policy. Even though routine hospital sterilization techniques are usually enough, ASA highly recommends meticulous sterilization or disinfection methods (21). Of note, healthcare workers' undesired contact by patient's body fluids, universal safety precautions should be taken during anesthesia management regardless of the HIV status/stage of the disease and protecting other patients from contamination should be taken into consideration.

In conclusion, choice of cesarean delivery in order to avoid vertical transmission being the mainstay strategy along with choice of spinal anesthesia because of general anesthesia associated risk of immune suppression particularly in HIV infected parturient is a rational option unless there is no medical contraindication to neuraxial anesthesia.

Table 1. *Clinical findings of organ involvement in HIV infection.*

Organ systems	Problems associated with HIV infection	
Cardiovascular system	Pericardial effusion	Acute coronary syndrome
	Dilated cardiomyopathy	Vasculitis
	Endocarditis	Pulmonary hypertension
	Valvular lesions	Kaposi sarcoma
Respiratory system	Obstruction (tumor/infection)	Pneumonia
	Bronchitis	Pneumothorax
	Sinusitis	Atypical infections (Tuberculosis)
Gastrointestinal system	Esophagitis/dysphagia	Biliary disease
	Regurgitation	Malnutrition
	Hepatitis	Diarrhea
Renal system	Drug induced nephrotoxicity	HIV associated nephropathy
Neurological system	Headache	Meningitis
	Photophobia	Diffuse encephalopathy
	Meningoencephalitis	Focal CNS lesions
	Cognitive changes	Myelopathy
	Demyelinating neuropathy	Peripheral neuropathy
	Abnormal CSF findings	Myopathy
Hematological system	Anemia	Thrombocytopenia
	Leukopenia	Coagulation disturbances
Endocrine and metabolic system	Lipodistrophy	SIADH
	Metabolic syndrome	Hypo/hyperthyroidism
	Adrenal insufficiency	Lactic acidosis

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Authors' Contributions

BG handles the patient and write the paper, HKP critics and comments, GE prepares literature search, ET operates the patient and refers to us, HSO provides the medical treatment of the patient and follow up.

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NEONATAL SIDE EFFECTS DURING PATIENT CONTROLLED INTRAVENOUS REMIFENTANIL FOR LABOR ANALGESIA

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ABSTRACT

Introduction: Remifentanil is becoming more and more popular as alternative method for labor analgesia. There are limited studies about the neonatal safety of remifentanil for labor analgesia.

Materials and Methods: Our study included 80 pregnant women, at term, receiving intravenous PCA with remifentanil for labor analgesia. Our primary goal was to examine neonatal safety when using remifentanil. During analgesia fetus was monitored through continuous cardiotocography recording. After delivery we recorded neonatal Apgar scores in 1st, 5th and 10th minute, acid-base status, use of naloxone and any neonatal resuscitation. Parturients all the time during labor analgesia have one-to-one care and complete haemodynamic monitoring (SaO_2, respiratory rate, non-invasive blood pressure, and heart rate).

Results: Fetal heart rate (FHR) abnormalities were recorded in 12 patients, 4 of them had pathological continuous cardiotocograph (CTG) records. The most common Apgar score in the 1st minute was 8, in the 5th it was 9 and in the 10th minute it was 10. Intermediate values of all parameters from the umbilical acid-base status of newborns were within normal limits.

Conclusion: Neonatal side effects during patient-controlled intravenous analgesia with remifentanil are minimal. One-to-one care, appropriate continuous monitoring of the parturient and neonate with available resuscitation kit are mandatory.

Introduction

In many countries today, the possibility of painless delivery is considered a reflection of the development of obstetric care.

Remifentanil was firstly used in obstetric anesthesia in 1998, and since then it is becoming more and more popular as effective and safe alternative. Remifentanil is an ultra-short acting opioid, metabolized by non-specific plasma and tissue esterases. It crosses the placenta very rapidly and extensively, but on the other hand it is eliminated quickly in neonates because of rapid metabolism and redistribution (1).

Due to remifentanil's pharmacokinetic characteristics, it has become an effective agent in the neonatal population allowing the provision of intense analgesia and anesthesia with a rapid recovery profile in various clinical scenarios (2).

There are limited studies about the neonatal safety of remifentanil for labor analgesia. Almost all available studies about the use of remifentanil in labor analgesia are presenting remifentanil as a safe option for neonates. But still, cardiovascular instability and respiratory depression immediately after birth were noticed in some cases.

The aim of our study is to analyze neonatal side effects during PCA remifentanil for labor analgesia.

Materials and Methods

This was a prospective clinical study performed at the University Clinic for Gynecology and Obstetrics in the period from January 2016 to January 2018. The study was approved by the Ethic Committee for Human Research of the "Ss Cyril and Methodius" University-Medical Faculty, Skopje. All patients signed an informed consent before entering the study. They were all primiparous, at term, healthy pregnant women, without any known obstetric complication during pregnancy. All parturients were respectively prepared. A peripheral venous catheter was placed and appropriate monitoring was provided to all of them. We began with labor analgesia at 4-5 cm cervical dilatation, always in communication with the obstetrician.

All parturients received intravenous remifentanil in bolus doses on a pump for patient controlled analgesia (PCA) with 2 minutes locked interval. We started the remifentanil analgesia with smaller doses and increased them gradually. We started with 0.2 μg/kg remifentanil (solution 20 μg/ml), gradually increased for 0.1 μg/kg up to the maximum bolus dose of 1 μg/kg. All patients were explained how to operate the pump and when to give the bolus dose. We advised all patients to apply the bolus when they feel that there was pain coming. Few labor pains were enough, and the patients knew when to give the bolus. Analgesia was stopped 10 minutes before the expected expulsion of the newborn. All the time during the analgesia with remifentanil anesthesiologist or experienced nurse remained in the delivery box with the laboring parturient. And all the time parturients were monitored: oxygen saturation and heart rate continuously, respiratory rate and noninvasive blood pressure every 15 minutes.

For neonatal safety fetal heart rate (FHR) was monitored with continuous cardiotocography (CTG) recording. The CTG recording gives us very important data on the condition of the fetus. Loss of variability is a typical finding of opioid analgesia during childbirth, but it is always innocent and probably it is a result of the direct effect of the opioid on the central nervous system of the fetus, with no association with fetal oxygenation. But if the FHR recordings became pathological (fetal bradycardia, late decelerations), we temporarily stopped with remifentanil analgesia.

After the delivery Apgar scores at 1st, 5th and 10th minute were determined by the neonatologist. Any neonatal interventions in the immediate postnatal period were recorded. Naloxone was always prepared, and any use of it was recorded.

Blood from the umbilical artery (UA) was taken immediately after delivery and the acid-base status (ph, pCO_2, pO_2, bicarbonate and base excess) was measured. Acid-base status of the newborn taken from the umbilicus gives us information about placental function and fetal circulation immediately after birth.

Results

80 patients received PCA with remifentanil for labor analgesia. Patients' characteristics are given in Table 1.

Table 1. *Patients' characteristics*

Age (years)	29.85±5.2
Weight (kg)	80.34±8.6
Level of education High Medium Basic	 37 (46.25%) 34 (42.5%) 9 (11.25%)
ASA classification ASA 1 ASA 2 Duration of analgesia (min) Delivery ended with sc	 61 (76.25%) 19 (23.75%) 165.22±63.1 13 (16.25%)

FHR-fetal heart rate

sc – cesarean section

FHR abnormalities were recorded in 12 patients. Loss of variability and early decelerations are nonpathological, benign changes, but 4 patients experienced serious disorders or pathological CTG records, and in those patients the babies were rapidly delivered. Type of the abnormalities is shown in Table 2.

Table 2. *FHR abnormalities*

FHR abnormalities	12 (15%)
Loss of variability and early decelerations	8
Deep variable decelerations	1
Late decelerations	1
Bradycardia	2

FHR-fetal heart rate

Distribution of the Apgar scores are shown in Table 3, while average Apgar scores are shown in Table 4. The most common Apgar score in the 1st minute was 8, in the 5th it was 9 and in the 10th minute it was 10. There was only 1 newborn with lower Apgar scores in the 1st and 5th minute, in women whose delivery was instrumental, with a vacuum extractor due to a pathological CTG record.

Table 3. *Distribution of Apgar scores in parturients vaginally delivered and delivered with cesarean section*

Apgar score	Vaginally delivered (67) N (%)			Delivered with s.c. (13) N (%)		
	1 min.	5 min.	10 min.	1 min.	5 min.	10 min.
3	1 (1.49)	0	0	0	0	0
5	0	1 (1.49)	0	0	0	0
6	1 (1.49)	0	0	0	0	0
7	3 (4.48)	0	0	2 (15.38)	0	0
8	47 (70.15)	5 (7.46)	1 (1.49)	10 (76.92)	2 (15.38)	1 (7.69)
9	15 (22.39)	47 (70.15)	13 (19.40)	1 (7.69)	10 (76.92)	3 (23.08)
10	0	14 (20.9)	53 (79.10)	0	1 (7.69)	9 (69.23)

sc – cesarean section

Table 4. *Average Apgar scores*

Apgar score	VD			SC		
	N	mean ± SD	min – max	N	mean ± SD	min – max
1st min	67	8.07 ± 0.8	3 – 9	13	7.85 ± 0.5	7 – 9
5th min	67	9.07 ± 0.7	5 – 10	13	8.85 ± 0.6	8 – 10
10th min	67	9.8 ± 0.4	8 – 10	13	9.77 ± 0.4	8 – 10

VD – vaginal delivery

SC – cesarean section

There was no need for naloxone in any neonate after birth, no need for neonatal resuscitation, only few of the infants required mild tactile stimulation.

Intermediate values of all parameters from the umbilical acid-base status of newborns in the current study are within normal limits. Only 2 newborns deviated from normal pH and BE values. In the first newborn, as a result of FHR abnormalities in the second period of birth, the delivery was performed instrumentally, with vacuum extractor, with pH 7.03 and BE-12.2, with Apgar 3/5/8; and the second newborn with a normal vaginal delivery, with the exclusion of remifentanil 15 minutes before delivery, with pH 7.09 and BE-10.8, with Apgar score 8/9/10. The acid-base status in the both neonates was rechecked 1 hour later and was normal in both newborns. Average neonatal acid base status is shown in Table 5.

Table 5. *Neonatal acid-base status*

Fetal acid-base status (UA)	mean ± SD	min-max
pH	7.28±0.15	7.03-7.32
pCO_2 (mmHg)	52.38±11.27	26.4-79
pO_2 (mmHg)	18.61±5.77	10.5-34.4
HCO_3 act (mmol/l)	22.33±2.13	16.5-26.9
HCO_3 std (mmol/l)	19.07±1.97	15.1-22.9
BE (mmol/l)	- 5.28±2.85	-12.2--1.0

UA-umbilical artery

Discussion

Many studies have shown that during labor, remifentanil offers hemodynamic stability with respiratory side effects for the mother, but the limited number of studies on newborns have shown that remifentanil during labor analgesia in general is safe for the neonates (3,4,5,6). However, during general anesthesia with remifentanil, 50% of newborns may require ventilatory assistance because of respiratory depression (7). Therefore, supervision and monitoring of both the mother and the infant are necessary.

In this study, the main cause of FHR abnormalities was the reduction of variability and early decelerations, which were assessed as benign changes and without the need for obstetric intervention. Loss of variability is a typical finding of opioid analgesia during labor, and it is also common both for during intravenous and epidural analgesia[8]. However, 4 patients from our study experienced serious disorders or pathological CTG records, and in those patients babies were rapidly delivered. Many studies are describing the changes in the CTG record during remifentanil analgesia and all of them describe the changes as short-lived and without the need for obstetric intervention (4,9). Compared to the other methods of anesthesia, in the large systemic review of Cochrane from 2017, analgesia with remifentanil has a lower risk of CTG irregularities compared to another opioid, and quite the same compared to epidural analgesia (10).

In this study, there was no need for naloxone in any neonate after birth, there was no need for neonatal resuscitation, only few infants required mild tactile stimulation. All of this correlates with many studies investigating remifentanil for labor analgesia (3,5,9,10). But there are some case reports that reported neonates requiring naloxone at birth, on very high remifentanil doses, during general anesthesia (11,12). One of these cases was associated with chest wall rigidity and in this case, the mother had received an infusion of remifentanil at a dose of 0.1 – 1.5 μg/kg/min which is the highest reported dose in an obstetric patient and suggests that neonatal effects should be expected in this dose range (12).

Few studies reported neonates requiring assisted ventilation at birth during general anesthesia with remifentanil. According to the review of Hill, neonatal respiratory depression is expected in approximately 50% of neonates, making the presence of an attending physician experienced in newborn resuscitation advisable (13).

Cardiovascular instability immediately after birth were noticed in some cases. In a pilot study, INSURE, with remifentanil 2 μg/kg infused over 60s, mean blood pressure decreased 5 minutes after remifentanil application, but is usually normalized within 20-30 minutes after remifentanil infusion (14). When using higher doses of remifentanil, increased risk of side effects is expected. Standing *et all, in a* study in infants undergoing cranioplasty concluded that remifentanil is effective in causing arterial hypotension (15).

The study of Konefal et all is the first published report on the biophysical monitoring of the heart rate, pulse oximetry and blood pressure during the first 24 hours after birth in neonates born to PCA remifentanil labor analgesia mothers. The authors did not find any differences in the heart rate, pulse oximetry, or systolic and diastolic blood pressure values between the group of newborns born to remifentanil PCA labor analgesia women and the group of newborns born to control women, except for non-significant hypotension (systolic blood pressure below 60 mm Hg in the remifentanil group) at 1 hour after delivery. Summarizing the above data, it is clear that hypotension in neonates after remifentanil infusion can occur, but further trials are needed to evaluate ideal dosing regimens of remifentanil in labor analgesia.

In our study, as well in all available studies, the Apgar scores of the neonates were in normal range after administration of remifentanil (3,4,5,6,10). However, the association between application of remifentanil and low Apgar scores is shown in a study of Noskova et all from 2015 (17). The study investigated remifentanil as an addition to general endotracheal anesthesia for caesarean section. In the study of 151 parturients, patients received a bolus of 1 μg/kg remifentanil 30 seconds before standard introduction into general anesthesia. 25% of newborns had an Apgar score less than 7 in the first minute, compared to 9.3% in the control group. Newborns only needed tactile stimulation and by the 5th minute, the Apgar scores were the same in both groups. One explanation is of course the short time (4 minutes) from the induction to the baby's extraction, as other studies with the same doses of remifentanil had better neonatal outcomes[18]. According to a systematic review of Cochrane, 5th-minute Apgar scores did not differ between different opioid analgetics for intravenous labor analgesia, as well as between epidural and remifentanil analgesia (10).

The median values of all parameters of the umbilical arterial acid-base status of neonates in the current study were within normal limits. The base deficit along with lactate levels is known to be a good indicator of neonatal outcome (19). All the parameters we examined were in normal range. Several studies examined the acid-base status of the newborn after analgesia with remifentanil, and the most of them (4,6,20) agree that remifentanil analgesia is completely safe for the newborn, which is probably the result of rapid metabolic remodeling or redistribution of remifentanil.

According to studies comparing analgesia with remifentanil with other intravenous opioids, the findings for umbilical pH do not differ between analgesia with remifentanil and meperidine-pethidine, but late side effects of pethidine (as a result of accumulation of its metabolite – norpethidine) on newborns are well known (21). Compared to epidural analgesia the results represent similar pH and BE (4,6,10). Although a major retrospective study[22] of Lin and collaborators from 2014 on 370 parturients, showed lower pH and significantly lower BE in patients with analgesia with remifentanil and suggests that despite the rapid and easy metabolism of remifentanil in the newborn, it still has an effect on the newborn and the resuscitation kit should be prepared at any time.

Conclusion

Remifentanil has a place in obstetric anesthesia and analgesia. Neonatal side effects during patient-controlled intravenous analgesia with remifentanil are minimal. One-to-one care, appropriate continuous monitoring of the parturient and neonate with available resuscitation kit are mandatory. The presence of an attending physician experienced in neonatal resuscitation is advisable.

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THE CORRELATION BETWEEN THE COMPONENTS OF EXECUTIVE FUNCTION AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN ADOLESCENTS

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ABSTRACT

Aim: The purpose of this research is to determine the interplay between dimension of executive functions (EF) and the attention deficit hyperactivity disorder (ADHD).

Introduction: Executive functions defined as neurocognitive processes are shown to be key factor in understanding the development of ADHD and related problems associated with it.

Methodology: It is a two-stage longitudinal study of children from 11 to 18 years old in Prishtina made with multiple stratifications. The first phase was the screening for ADHD symptoms and Global Executive Composite (GEC). Instruments used: demographic questionnaire, Youth Self Report/YSR 11-18 years old and BRIEF-2 (Behavior Rating Inventory of Executive Function), and identifying the four groups for further analysis-the experimental phase (Group 1-high risk for ADHD and high scores in (GEC), Group 2-high scores in ADHD low scores in GEC, Group 3-low ADHD and high GEC and Group 4-low ADHD and low GEC). In the second phase we used u two neuropsychological tests: Stroop Task and Go/NoGo Task.

Results: A significant correlation was found between ADHD and GEC ($r = .703$, $p < .001$). Children with high scores in ADHD have difficulties in one or more areas of executive function compare to the control group (Group 4-low ADHD and low GEC).

Conclusion: The result shows that three components of EF are important predictors for ADHD symptoms in adolescents. Our study emphasizes the importance of taking a developmental approach in investigating ADHD in adolescents in order to predict the disorder and make a comprehensive treatment for them.

Key words: ADHD, adolescent, children, executive function, GEC.

Introduction

Executive functions are defined as a summary of cognitive processes involving goal-oriented behaviors organized by activities within the prefrontal cortex (Olson & Luciana, 2008). Executive functions include a wide range of functionalities including the ability to stop an inappropriate behavior and thoughts, regulate attention and monitor actions, including self-monitoring, mental flexibility, self-regulation, planning and the future organism (Arnsten & Ming-Li, 2005). On other hand, ADHD is characterized by elevated and persistent levels of inattention and hyperactivity-impulsivity (six or more symptoms within at least one domain). ADHD is a neuropsychiatric disorder that is characterized by inattention, hyperactivity and impulse (Swanson, 2003).

Large number of researches indicate the role of executive functions in ADHD (Bierdman et al., 2004; Lowrence et al., 2004; Brown, 2009; Shoemaker et al., 2012), especially-the role of cognition, executive functions and behavioral control (Martel, Nicholas & Nigg, 2007).

Components of executive functions are curricular to the various aspects of hyperactive behavior, by Barkley (1997), pointing out that executive function components enable self-regulation, behavioral control of initial stimulus behaviors, and organization of different behaviors. The most consistent findings are that these executive deficits then create deficiencies in motor control-fluency-syntax or the control of motor behavior by internally represented information (Barkley, 1997).

Deficits in executive functions appear to be a complex component in ADHD (Willcutt et al., 2005). The way executive functions affect ADHD are given in different alternatives from researchers who emphasize that ADHD-specific specifics have a primary source in executive functions in domains that relate to inhibition responses, work memory, or even general weaknesses in executive control (Castellanos & Tannock, 2002).

Although we have extensive evidence of the association of Executive Functions with ADHD, there are major dilemmas about the nature of this relationship. In general, studies that analyzed this relationship have used executive functions as one component. The current study uses a comprehensive assessment to assess heterogeneity in all three components of executive functions: Behavior Regulation, Emotion Regulation, and Cognitive Regulation in ADHD.

Methods

Procedure:

After receiving permission from the Ministry of Education Science and Technology, respectively from the Department of Pre-University Education for the right to conduct research, and approval from the Ethics Commission at the Faculty of Medicine Prishtina, approval from the Department of Education in the Municipality of Prishtina, I received list of 43 elementary and high schools from Prishtina and the villages of Prishtina. We made a selection randomly of three primary schools, three high schools and three schools from the rural areas in the municipality of Prishtina. The selection of classes has been randomized as every first and last class. The inclusion criteria (the subject of the research) were students from all classes except students with

IQ <80 and, students who were absent that day at school. There were no students who refused to participate in the research.

Instruments:

Youth Self Report (YSR) 11-18 years old (Thomas M. Achenbah, 1991, 2001): The YSR was translated into Albanian (Shahini M., 2011). In the 2001 problem scales for the YSR were computed from the 112 problem items. It is self-administered, with youth responding to the items on a three-point scale: 0 (not true), 1 (sometimes true), 2 (very true); and it takes about 30 minutes to complete. There are three broad-band scales (Internalizing, Externalizing, and Total Problems); eight empirically based syndromes (Anxious/ Depressed, Withdrawn/ Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-Breaking Behavior, and Aggressive Behavior). We used the Attention Deficit/Hyperactivity Problems Scale.

The BDEFS-CA is a rating scale designed to evaluate the major components of executive functioning in daily living activities of children ages 6 – 17, as self-report. The questionnaires take 10 minutes to administer with youth responding to the items on a four-point scale: 1 (not true), 2 (sometimes true), 3 (often), 4 (very often); and it takes about 30 minutes to complete. The BRIEF-2 uses 10 clinical scales and separates self-monitoring from task monitoring: Inhibit; Self-Monitor; Shift; Emotional Control; Initiate; Task Completion; Working Memory; Plan/ Organize; Task-Monitor; Organization of Materials. Based on T-scores, percentiles, and 90% confidence intervals for four developmental age groups, by gender, three broad indexes are calculated (Behavior Regulation, Emotion Regulation, and Cognitive Regulation)

Including and Excluding Criteria:

The study included pupils with IQ > 80 (the IQ test is performed from the school psychologist), pupils with previous psychiatry history on ADHD. We excluded pupils with IQ < 80 from the study, which means children with special needs, children with readings problems.

Results

We had 1260 participants in total, 46.8% were male and 53.2% were female. The mean age was 14.23 years (SD=2.24). Most of the parents had a median income of 76.2% (N=960), 3.2% (N=40) did not state in which category, while 0.9% (N=12) have poor income. Participants reported that 2.2% (N=28) had any illness at the time of the interview and 8.3% (N=105) had left-handed writing. The number of family members was an average of M=5.5 (Sd=1.7), while the average number of children was M=3.1, (Sd=1.2)

Regression Analysis

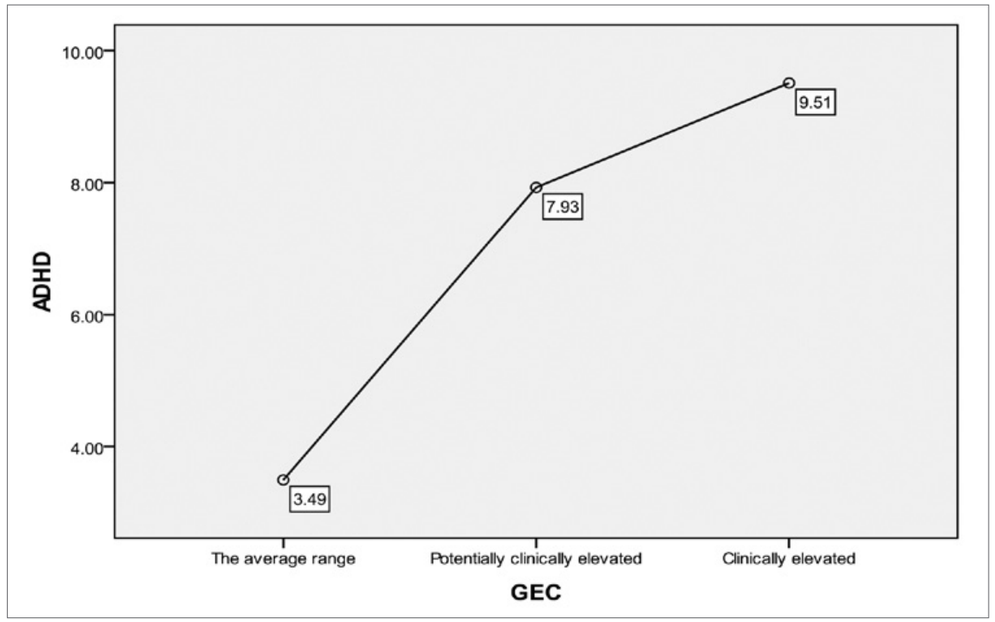
The results showed that there was a positive, very good and significant relationship between ADHD and Global executive composite (GEC), (r=. 703, p<.001). The most of the symptoms of

ADHD are associated with dysfunction at the global scale of executive functions. The regression coefficient R2=0.494 indicating that 49.4% of the variance of ADHD is explained by executive functions. Multiple regression was used for the three separate scales and it was found that all three were statistically significant predictors p<0.001.

The analysis of multiple regression has reported that Behavior Regulation Index is a strong predictor of ADHD in children F (1, 1259)=822.0, R^2 =.395, p<.001, explaining 39.5% of the variance of ADHD. At the same time, reported results show that emotional regulation is a significant predictor of ADHD (F (1, 1259)=823.6, R^2 =.396, p<.001). Furthermore Cognitive regulation was the strongest predictor of problem manifestations in ADHD, F (1, 1259)=446.5, R^2=.448, p<.001 and as well global executive components are significant predictors of variance of ADHD in children, F (1, 1259)=543.2, R^2=.494, p<.001. The analysis of one way ANOVAs is used to show the difference between groups in global executive composite (GEC), where the difference is reported between groups in EF F (2, 1259), R^2=165.9, p<.001.

ADHD has a significant effect on groups of GEC, (F (2)=251.7, p<.001, η^2=0.286). The group with clinical elevated scores in GEC had higher scores in ADHD. Bonferoni analysis showed that the group with average range in GEC had significantly lower scores in ADHD compared to the other groups. Children with high scores in ADHD have difficulties in one or more areas of executive function.

Figure 1. *ANOVA results for ADHD scale with GEC categories*



ANOVA is used to test the effect of ADHD on categories of GEC (Group 1-average range; Group 2-Potentially clinical elevated and Group 3-Clinically elevated). Results showed that

Two way ANOVA is used to see if an interaction effect between ADHD and GEC is affected according to two groups of age (Group 1 11-15 years old, Group 2 16-18 years old). Results showed that there was no difference on the interaction effect between ADHD and GEC when comparing the age groups.

Differences on EF and ADHD according to Demographic Variables

T-test analysis was used to analyze whether the mean distribution of ADHD and GEC rates is gender-influenced. The findings indicate that there were no statistically significant differences in the mean distribution for ADHD by gender (t (1258)=-.58, p=.560). Significant statistical difference was found with age (t (1258)=-5.05, p=.001). Children aged 16-18 years had higher mean ADHD (M=4.78, SD=3.36) compared to the age group 11-15 years (M=3.83, SD=3.19). Participants from the city reported a higher average than those from the village and the difference was significant (t (1258)=-3.71, p=.001). It is worth noting that participants who had a health problem had no difference in reporting a mean ADHD rate compared to those who did not have a health problem. There was also no difference in regard to the hand dominance. Fathers' education was found to affect the rate of ADHD, participants who had a fathers with elementary school reported lower rates of ADHD compared to those with more educated fathers like completed secondary and higher education. Mothers' education has not affected the results reported on this scale.

Table 1. *T test results for ADHD and GEC scale according to place of living.*

	Place of living	M	SD	t	P
ADHD	Urban	4.44	3.29	- 3.71	.001
	Rural	3.67	3.25		
GEC	Urban	91.37	22.71	- 3.63	.001
	Rural	86.14	23.92		

There were no statistically significant differences in mean distribution for EF, (t (1258)=1.1.48, p=.139) by gender. Significant statistical difference in GEC scores was found only for the Emotional Regulation Index (t (1258)=-6.18, p=.001), with girls reporting higher mean value (M=27.1, SD=7.2) than boys (M=24.6, SD=6.8). According to the findings, a significant statistical difference was found with age (t (1258)=-5.05, p=.001), on the Behavior Regulation Index (BRI) scale for 16-18 years old (M=22.8, SD=6.22) compared to those aged 11-15 years (M=21.42, SD=6.45). The same trend holds for the Emotion Regulation Index (ERI): (t (1258)=-6.02, p=.001), and the Cognitive Regulation Index (CRI): (t (1258)=-2.96, p=.003). Significant differences were found in relation to place of residence, with city children reporting higher average values than village children (t (1258)=-3.63, p=.001), as well as those who were ill had a higher mean values than those without disease (t (1258)=1.95, p=.05). GEC reporting has not been found to be influenced by the participants' hand dominance, neither by parents' education

nor by family income. As to the family members, the higher the number of family members was, the higher the reporting average value was and this influence was significant F (16.1529)=2.51, p=.001, as well as the number of children in the family F (9.1259)=2.31, p=.014.

Discussion

The aim of the current study was to create a better understanding of the role of the executive functions in ADHD, as new clinical alternative in the ADHD treatment.

This study has shown that there was a positive correlation between component of executive function and ADHD in children. In many studies regarding the association between executive functions and ADHD, it is supported the view that ADHD is associated with impairment in some EFs, but not all EF processes (Barkley & Murphy, 2010; Pennington & Ozonoff, 1996; Alderson et al., 2015). Regarding gender, the study showed that there were no significant differences in relation to ADHD. While significant and positive correlation was found between negative affect and the risk for ADHD in the male gender, the opposite was reported for female gender (Cole, et al., 1994). Children living in the urban area present higher average of ADHD compared to the children living in rural area. In regard to findings dealing with child residence, it has been seen that children from rural areas may not have easy access to health care, compared to the children living in urban areas and thus may be less likely to be prescribed medication to treat ADHD or undergo inpatient treatment for ADHD (Knopf, et al., 2012). Behavior Regulation Index is a strong predictor of ADHD in children presented in this study. Research done suggests that the development of executive control over emotion regulation processes (e.g., Emotional Control) initiates early, in terms of maturity, may lag behind others, such as executive control associated to abstract resolution of problems (i.e., problem solving; Zelazo & Carlson, 2012). Cognitive regulation is a strong predictor of problem with ADHD presented in this study. While another study conducted in adolescents and adults with ADHD also failed to demonstrate cognitive inhibition problems compared to controls (Engelhardt, et al., 2008). Children with high score of ADHD present difficulties in one or more area of EF. The same data reported that children with ADHD presented deficits in EF domains of inhibition and response execution, alertness, working memory, placement and flexibility, and task / cognitive task planning (Toplak, et al., 2008; Willcutt et al., 2005).

Conclusion

The results showed that Global Executive Components have an important influence in ADHD, but are not the only elements. This study supports theories that include ADHD connectivity and underlying EF deficits as essential for social development and child interaction, by suggesting further research to analyze the depth of this relationship.

Conflict of Interest: Authors deny any conflict of interest.

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CASE REPORT UDK: 616.231-035.7-089.5

SURGICAL TREATMENT OF IATROGENIC LESION OF TRACHEA USING "COR MATRIX" PATCH

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ABSTRACT

Injuries of trachea are rare but life-threatening conditions that need urgent and accurate diagnosis and prompt treatment.

We present a case of a 29-years old female patient who had two surgical interventions under general anesthesia within a period of four months, in which after the second intervention, subcutaneous emphysema on the neck was detected that was enlarging during the afternoon and therefore an injury of trachea was suspected. CT scan of the neck and thorax was performed that confirmed the subcutaneous emphysema and emphysema in the mediastinum and a suspected lesion of the trachea. Afterword, a bronchoscopy was conducted and a 3 cm long linear lesion of the trachea was visualized 3 cm from the vocal cords and 3,5 cm from the tracheal carina. Then a surgical intervention was performed in general anesthesia, with an approach from the basis of the neck, that led to the dorsal wall of the trachea that was injured, using with PDS suture 000, a part of the lesion was closed, and on the rest part a "cor matrix" patch was placed, which also wrapped the trachea. The patient was extubated the third day after surgery and on the control bronchoscopy the trachea was normal.

Early and accurate diagnosis, as well as prompt surgical reparation of tracheal injury provides great morphological and functional results, and prevents further complication.

Key words: cor matrix, iatrogenic lesion of trachea, surgical treatment.

Introduction

Iatrogenic injuries of trachea are rare but life-threatening conditions. Depending on the size, they are manifesting with subcutaneous emphysema of the neck, in the mediastinum, and rarely with pneumothorax and global respiratory dysfunction (1, 5, 7, 8, 10, 11).

Early and exact diagnosis (native radiograph of the thorax, bronchoscopy and a computerized tomography) are necessary to plan the treatment (1, 2, 7, 8).

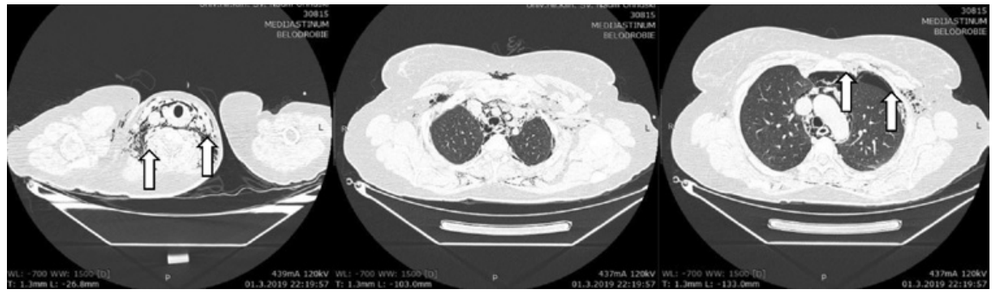
Surgical treatment with reparation of the tracheal wall is a method of choice for treatment, especially for larger lesions (2, 4, 5, 10).

In this article, we report a case of a female patient with iatrogenic lesion of the trachea, aiming to present the diagnostic approach in these patients and their treatment.

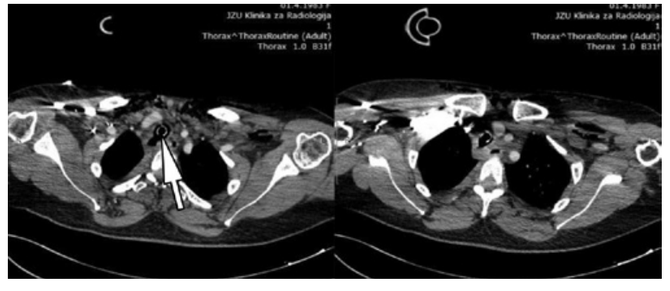
Case Report

A 29-year old female patient was referred at our department with subcutaneous emphysema on the upper parts of the thorax and the neck and an emphysema of the mediastinum that occurred after she had two surgical interventions of varicose veins on both extremities, with general endotracheal anesthesia. The first intervention was before 4 months, and the second one on the same day before she was presented at our department. Introduction to anesthesia and intubation was usual, with no difficulties as well as the extubation. Subcutaneous emphysema was noticed in the afternoon after the surgery and it was increasing within the next hours. Therefore the first CT scan of the neck and the thorax was performed and a tracheal lesion was suspected. Then using a bronchoscopy, a 3 cm long large lesion of the posterior wall of the trachea was visualized, at a distance of 3 cm from the laryngeal cords. The bronchoscopy didn't show an active bleeding. With second CT scan and with reconstructions a lesion with diameter of 3×2cm, 3.5 cm from the tracheal carina was confirmed, located on the lower part of the cervical part of the trachea. The impression was that it was an old lesion that was actualized with the recent intubation. After the diagnosis was made, the patient was intubated, with bridge over of the lesion and she was placed on mechanical ventilation. Due to the pneumothorax, also a thoracic drain was placed in the left hemi thorax.

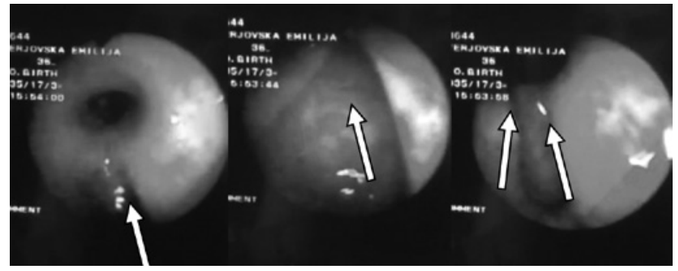
Surgical intervention was made with cervical approach (from the basis of the neck) that led to the trachea. The thyroid gland was mobilized, its two lobes were split and the trachea was approached. The esophagus was also mobilized and lateralized on the left. The trachea was mobilized and the posterior wall was approached were the lesion was detected. With separate stitches with PDS 000, a part of the lesion was closed. In addition, a "cor matrix" patch 7×4cm, was sewn on the posterior wall of the trachea, where the lesion was, and then it was fixed around the whole trachea on the part where the lesion was.



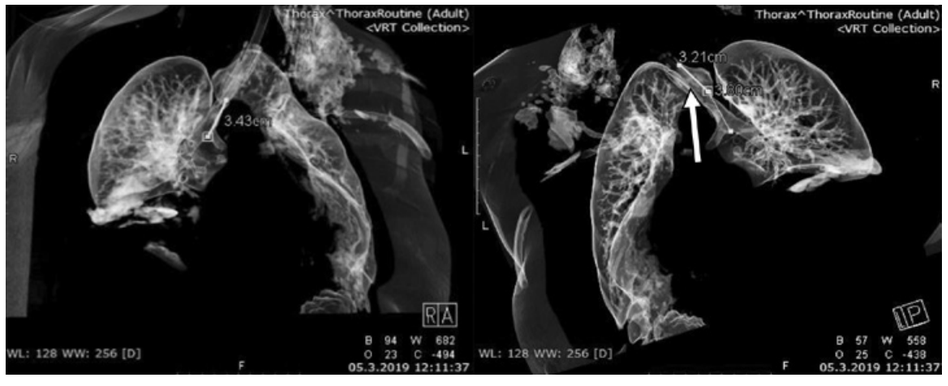
CT scans of the neck and thorax before the surgery that show existence of the emphysema in the mediastinum and a small pneumothorax on the left hemithorax.



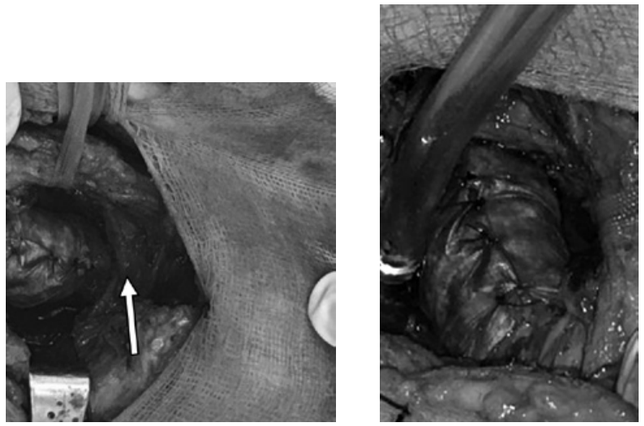
CT scans of the neck and thorax before the surgery that present the location of the tracheal lesion.



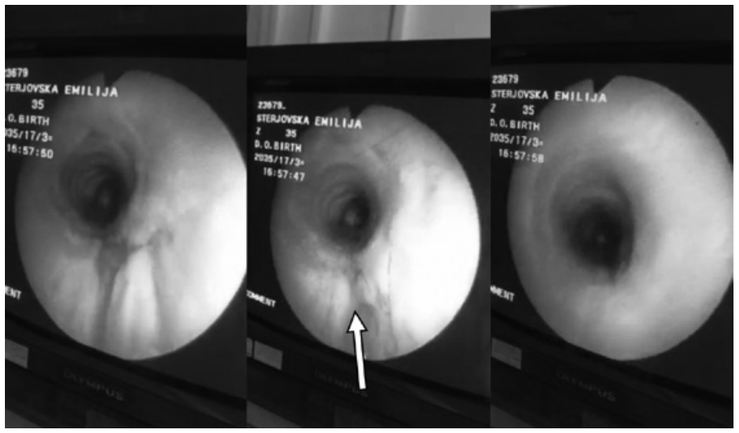
Bronchoscopy before surgery that clearly shows a large lesion of the posterior wall of the trachea (bottom to top).



CT scans of the neck and thorax with reconstruction before the surgery that present the lesion of the posterior wall of the trachea



Intraoperative closure of the lesion on the posterior wall of the trachea with placement of cor matrix on the lesion and around trachea



Postsurgical control bronchoscopy that shows healing of the tracheal lesion

The third day after the surgery, the patient was extubated, a control bronchoscopy was performed on the fifth day that showed normal tracheal finding, and the sixth day after the surgery, the patient was discharged from the hospital.

Discussion

Lesions of the trachea might occur either as a result of trauma or an iatrogenic injury during the intubation. Their frequency according to the literature is very low, between 0,005 and 0,035% (1, 5, 7, 8, 9, 10, 11).

Iatrogenic lesions of the trachea are more common in females, with short trachea, with tracheal stenosis, regardless if it is due to the weakness of the wall or outside pressure, during the intubation with two-luminal tube, performance of dilative tracheostomy etc. In these cases, the percentage of iatrogenic lesions might increase up to 1% (5, 7, 8).

Clinical manifestations of tracheal lesions are evident subcutaneous emphysema of the neck, irritating cough or respiratory dysfunction with hypoxia in larger lesions. This occurs due to the leak of the inhaled air from the trachea to the mediastinal space of the neck. Manifestation of the symptoms depends on the size of the tracheal lesion. In the later stage, symptoms of mediastinitis and sepsis might occur (1, 2, 3, 7, 9, 10).

In the light of all stated above for the importance of clinical manifestation of the tracheal lesions, it is necessary correct and prompt diagnosis to be made as soon as possible, so the appropriate treatment measures can be taken. An early and accurate diagnosis initially is made with computerized tomography (CT scan) of the neck region and the thorax. CT scan will confirm the suspected tracheal lesion, eventual subcutaneous or emphysema in the mediastinum, and can even predict the location of the tracheal lesion. However, the correct and final diagnosis of tracheal lesion is made with bronchoscopy. It will show if there is a lesion, on which part of the wall it is located, if there is active bleeding of tracheal wall, or there is presence of other structures over the lesion (1, 2, 7, 8, 9, 10, 11).

According to the results of these two examinations, a treatment approach will be decided, that might be either conservative or surgical (4, 7, 8, 11).

If the lesions are punctiform, they might be healed with rest, antibiotics and follow up. If the lesions are larger, but no more than 2 cm, a conservative treatment is also an option. In tracheal lesions, conservative treatment includes provision of antibiotics, inhalation of aerosols, antitussive medications, placement of thoracic drain, if there is a pneumothorax, placement of endotracheal tube that will bridge the lesion and will allow forming of fibrosis on the place of the lesion can be solution. During this period, the patient nutrition should be given by nasogastric tube (2, 5, 7, 8). Bridging the tracheal lesion might be performed also with placement of endotracheal stent (7, 8). If there is a larger tracheal lesion, a surgical intervention must be undertaken. Depending on the location of the lesion, the surgical intervention might be performed with transcervical approach, transsternal approach or with right-sided thoracotomy. Rarely, a combined approach is needed, mainly in large extensive lesions (2, 4, 9, 10).

Transcervical approach, which is less harmful, enables approach to the upper part of the trachea. It allows direct access to the trachea, and the thyroid gland is mobilized. Access to the posterior wall, where the lesions are the most common, might be with mobilization of the trachea itself, or with an opening of the anterior cartilaginous wall and access the posterior wall from the lumen of the trachea 94, 5, 9, 10).

Transthoracic approach is performed by right high thoracotomy in which the esophagus is mobilized backwards, the trachea forward, the lesion is visualized and is closing. If there are extensive lesions that affect both trachea and main bronchi, when there is doubt for safe intubation, an ECMO (extracorporeal membrane oxygenation) also might be used (2, 4, 5, 9, 10, 11).

If there is a large defect on the posterior wall, a direct suture might cause stenosis of the lumen of the trachea. Therefore, a patch (graft) can be used that might be synthetic or biological. In our

case, we use a biological graft – cor-matrix, which is acellular segment of the submucous part of the small intestine, graft that is highly rich with collagen which physically covers the defect, but also stimulates the surrounding area to colonize with epithelial cells from the trachea. This graft is used mainly in cardio-surgery, but it proved to be great patch also in other surgical areas.[6]

If a tracheal lesion is suspected, a precise and definite diagnosis should be made as soon as possible, so the prompt and adequate treatment can be performed. It will disable further loss of the air while breathing and possible disorder of the respiratory function as well as it will prevent spread of an infection into the mediastinum and mediastinitis.

If subcutaneous emphysema of the neck occurs after surgical intervention where endotracheal anesthesia was provided, a possible lesion of the trachea should always be suspected and appropriate diagnostic and therapeutic measures need to be taken as soon as possible in order to prevent further complications (5).

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OUR INITIAL EXPERIENCE WITH LAPAROSCOPIC RADICAL CYSTECTOMY

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ABSTRACT

Background and objectives: In this era of minimally invasive surgeries, at the University Clinic for Urologic Surgery in Skopje, the laparoscopic radical cystectomy (LRS) was performed in 11 patients for the first time. In this paper, we have evaluated and summarized the anesthesia management, features and complications of LRC.

Material and method: In a retrospective manner, we evaluated all patents who underwent LRC at our Clinic over a one-year period. We noted and analyzed the following parameters: patients' demographic data, preoperatively and postoperatively, laboratory data, intraoperative fluid volume, estimated blood loss, allogeneic transfusion requirements. Respiratory parameters including arterial blood gas data, anesthesia time, surgical time, time of oral intake, admission to ICU, hospital stay and any adverse events during the whole period of hospitalization were also analyzed.

Results: This evaluation included 11 patients who were successfully operated and their data were analyzed. Patients had similar demographic characteristics. Estimated intraoperative blood loss was 472 ml and decreased transfusion requirement was noticed. Due to prolonged surgical time and CO_2 pneumoperitoneum, hypercarbia was observed in few patients. Patients had shorter period of bowel dysfunction and rapid oral intake, shorter hospital stay and fewer complications.

Conclusion: We believe that these data from our initial experience with newly performed minimally invasive radical cystectomy will reflect to our daily routine practice in radical cystectomy surgery towards laparoscopy. However, some larger prospective evaluation is to be made for summarizing the overall conclusions.

Key words: anesthesia consideration, laparoscopy, radical cystectomy.

Introduction

Bladder cancer control depends on the aggressiveness of the resection, and hence, usually this procedure is done with open surgery (1-5). Today's minimally invasive laparoscopic surgery is a choice for management of urologic diseases. This approach is mainly reserved for kidney and prostatic conditions (6-8), although recent literature data support the feasibility of laparoscopic radical cystectomy (LRC) for patients with bladder cancer (9-12).

Open radical cystectomy (ORC) is mainly associated with a high morbidity. Alternative benefits from laparoscopy are well known. They include avoiding big incisions and thus decreasing pain, discomfort and blood loss, faster recovery, shorter hospital stay, and fewer complications.

In our hospital, laparoscopic radical cystectomy has not yet been established as a standard treatment for patients with bladder cancer. In the literature there are debates regarding results associated with ORC and LRC for the potential benefits of the perioperative and postoperative complications. Regarding anesthesiologists' point of view, patients presented for LRC experience longer surgical time, increased intra-abdominal pressure and carbon dioxide (CO_2) insufflation, expressive Trendelenburg position and all consequences associated with all the above mentioned. Therefore, the aim of our study was to evaluate and summarize the anesthesia management, features and complications of LRC.

Material and Methods

In the period **from December** 2018 until December 2019, 52 consecutive patients were treated for radical cystectomy. Out of these patients, 11 underwent LRC, performed by a team of three surgeons. In every patient radical lymphadenectomy was performed. All patients with confirmed metastasis by computer tomography or magnetic resonance did not undergo surgery. Carcinoma stage was determined by the histopathological report from transurethral biopsy and TNM classification, CT scans and MR images. The American Society of Anesthesiologist (ASA) score was assessed in all patients. We noted and analyzed the following parameters: patients' demographic data, preoperatively and postoperatively, laboratory data, intraoperative fluid volume, estimated blood loss, allogeneic transfusion requirements. Respiratory parameters (end-tidal carbon dioxide-EtCO_2 and respiratory rate), arterial blood gas data (pH, partial pressure of oxygen and carbon dioxide PaO_2/ $PaCO_2$), anesthesia time, surgical time, time of oral intake, admission to ICU, hospital stay and any adverse events during the whole period of hospitalization were also analyzed.

Statistical analysis was performed with SPSS program. Categorical variables were expressed as percentage and data were reported as median and ranges.

Results

Over a one-year period, 11 patients underwent successful LRC. Demographic characteristics of the patients and characteristics of the surgery are shown in Table 1.

Table 1. *Demographic characteristics and characteristics of the surgery*

Variables		LRC (n=11)
Gender (Male/Female)		11 / 1
Age (years)		64.4 ± 9.6
BMI	(normal 18.5-24.9%)	9
	(overweight 25-29.9%)	2
Smoking status (yes/no)		10/1
ASA (II/ III)		3/8
Duration of anesthesia (min)		450.90 ± 27.37
Duration of surgery (min)		346.36 ± 24.60

Data presented as mean and SD.

Postoperative pathohistological findings revealed stage IIC in one patient; stage IIB in 7 patients and IIA in 3 patients. Preoperative laboratory data findings demonstrated lower level of Hb in five patients. Intraoperative volume was maintained with crystalloids and natural colloids (albumen and FFP) 750 to 1000 ml per hour. Intraoperative blood loss was 472.72 ± 87.64 and transfusion requirement to maintain blood volume was as follows: patients with preoperative anemia were transfused with 2 units of RBC, 4 patients received one unit of RBC and 2 patients did not receive any transfusion. Respiratory parameters and arterial blood gas analyses were investigated at two time points: T0 before preoxygenation and induction in anesthesia and the second time point T1 was one hour after CO_2 insufflation. Respiratory parameters and arterial blood gas analysis are presented in Table 2.

Table 2. *Arterial blood gas analyses*

Variables	Investigated times	LRC (n=11)
SaO_2%	T0	95.1 ± 2.54
	T1	97.2 ± 1.27
PaO_2 (mmHg)	T0	91.4 ± 9.1
	T1	165.3 ± 34
$PaCO_2$ (mmHg)	T0	36.4 ± 6.1
	T1	46.7 ± 9.8
Ph	T0	7.42 ± 0.04
	T1	7.30 ± 0.07

Data presented as mean and SD, SaO_2% – oxygen saturation, PaO_2 – partial pressure of oxygen, $PaCO_2$ – partial pressure of carbon dioxide.

$PaCO_2$ was managed with mechanical ventilation parameters. $PaCO_2$ higher than 55 mmHg in the arterial blood gas were noticed in 2 patients. Hemodynamic data of the patients are shown in Table 3.

Table 3. *Hemodynamic parameters*

Variables	Investigated times	LRC (n=11)
HR	T0	85 ± 20.4
	T1	69 ± 11.5
MAP (mmHg)	T0	79 ± 10.2
	T1	74 ± 9.5
IAP (mmHg)	T1	12 ± 2.8
APP (mmg)	T1	64 ± 6.5

Data presented as mean and SD, LRC – laparoscopic radical cystectomy, HR – heart rate, MAP meddle artery pressure, IAP – intra-abdominal pressure, APP – abdominal perfusion pressure.

Abdominal perfusion pressure was maintained normal (above 60 mmHg) in each patient ensuring adequate tissue perfusion and oxygenation. Postoperative hospital stay was 6.9 ± 2.5 days and only one patient was postoperatively admitted to ICU. Conversion to open surgery was not performed in any patient. The second postoperative day oral intake was started in all patients and no bowl dysfunction was noticed. The observed postoperative complications included infection in one patient and subcutaneous emphysema in another patient.

Discussion

This study presents our initial experience with minimally invasive laparoscopic radical cystectomy. Our findings appeared comparable with those found in the literature (9-14). We noticed lower estimated blood loss, resumption of bowel activity, early mobilization and shorter length of hospital stay in our group of patients, which is similar to the results presented in the meta-analysis (9-11). On one hand, there were notable alterations in arterial, blood gases analyses towards hypercarbia, which was expected due to the prolonged surgical time and CO_2 insufflation in laparoscopy. On the other hand, Trendelenburg position is well tolerated, but it may have impact on ventilation and oxygenation especially if patients have respiratory comorbidities. Another study of Gavrilovska and coauthors showed similar alteration in arterial blood gasses and mechanical ventilation in patients with increased intra-abdominal pressure (15,16). In this evaluation, patients were managed with appropriate ventilation and did not have any prolonged adverse events or encountered any mental or neurological disorders. We had two cases when hyperventilation showed no improvement; the intra-abdominal pressure was then reduced to less than 15 mmHg, and the condition improved. Metabolic acidosis occurred in 2 patients and sodium bicarbonate was administered.

Closhen et al. in their study showed decreased cerebral oxygen saturation over 4 hours with Trendelenburg position and CO_2 pneumoperitoneum in patients who had undergone robotic surgery (17). Similarly, decreased cerebral oxygen saturation was shown in the study of Kuzmanovska et al. (18) Collins et al. reported that when more experienced team accomplished the procedure, improved performance and decreased surgical time was noticed (19). The reported surgical time in their study was 441 minutes, 368 minutes, 307 minutes in 30 cases, 30-50 cases

and in more than 50 cases, respectively. In our 11 cases we had median surgical time of 450 minutes. These are our initial results and our surgery team has to gain more experience in order to shorten the duration of surgery.

LRC is a technically challenging procedure. It offers advantages compared to the classic open radical cystectomy despite longer surgical time. Results presented in the literature showed benefits of LRC over ORC. Laparoscopy as minimally invasive procedure and hence it is the main reason for minimal blood loss and hemorrhage, which makes it safer surgery, and leads to less adverse events. Estimated blood loss in our group was 472 ml and we noticed decreased transfusion requirement. Novara et al. reported 375 ml estimated blood loss and lower transfusion rate in LRC compared to ORC group (11). On the other hand, Khan et al. did not find significance in blood loss and transfusion requirement between LRC and robotic surgery. Similar results were reported in the meta-analysis and systematic review of Fonseka (9).

In only few of the 11 evaluated patients complications were observed. One patient had subcutaneous emphysema and one patient had infection, which means in total 18%. Our results are similar to those presented in the literature. Massumoto et al. in their randomized trial included 10 patients with LRC and found adverse events in only 3 of them. A systematic review and meta-analysis comparing complications among robotic, LRC and ORC showed rates of 28%, 72%, and 47%, respectively (9). In another review, complication rates of 8% and 42% between LRC and ORC were reported (20).

Our data demonstrated that although LRC did not show severe complications in the small number of analyzed patients, in the literature taking precaution is advised for patients undergoing ORC. This is because these patients usually have a history of abdominal surgery prior to radical cystectomy.

Conclusion

In this new minimally invasive surgery era, laparoscopy provides effective cancer control with minimal impact on the quality of life. We believe that these data from our initial experience with minimally invasive radical cystectomy will reflect our daily routine practice in radical cystectomy surgery. We can advocate LRC over ORC. However, some larger prospective evaluation is to be made for summarizing the overall conclusions. LRC is a technically challenging procedure, but it can have excellent results performed by an experienced team.

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CASE REPORT UDK : 616.5-004-053.9:617.541-089.5

ANESTHETIC MANAGEMENT OF PATIENT WITH SYSTEMIC SCLERODERMA SCHEDULED FOR RIGHT LOWER LOBE RESECTION OF THE LUNG

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ABSTRACT

Progressive systemic sclerosis (PSS) or scleroderma is rare progressive fibrotic disorder of the connective tissue. Together with the connective tissue changes, atrophy of the skin, the involvement of various internal visceral organs may be present in these patients, as well. Not rarely, involvement of the alimentary tract, lungs, heart, kidney, CNS, the presence of the autoantibodies, collagen deposition on different body parts, together with the possible profound vascular hypersensitivity, are reported separately and in combination as possible anesthesiology challenges, sometimes even reported with detrimental outcome. We present a case of a successful anesthesiology management of a patient with PSS undergoing thoracic surgery and we discuss facts from the literature about this disease's issues and anesthesia.

Case Report

The case is reported after inform consent.

We present 63-years-old man, 178 cm tall and 72 kg weighted, with progressive scleroderma, referred to the Clinic for Thoracic Surgery in Skopje, for right lower lobectomy (due to lung malignancy).

During the pre-anesthetic assessment in this patient, we found normal laboratory tests of total blood cell count, arterial blood gas analysis, hemostasis, liver enzymes and kidney function tests. Vital signs were normal (blood pressure: 130/90 mmHg; pulse rate: 80bpm) as well as electro-cartographically (ECG) and echocardiography characteristic. X-ray showed pulmonary fibrosis, and on auscultation normal vesicular breathing sounds on the upper chest were heard with discrete fine bilateral crackles on the lung bases, more evident on the right side. Despite this, pulmonary functional tests showed slightly decrease in pulmonary function from restrictive type.

Physically, patient had typical scleroderma features, with thickness and over tightness of the skin especially dominant on the head, (neck and face) as well as on the hands. When talking for face features, patient's face was without wrinkles, smooth and tender. Fingers where sausage-like and shortened with present non-pitting oedema in his forearms and flexion contractures that leaded to limited movements. Patient had positive Raynaud's phenomenon and was chronically treated with Sulfasalazine 500 mg and Prednisolone 5 mg for several years. Apart from this, patient had history of controlled hypertension regularly treated with Nifedipine 20 mg.

Airway examination showed limited mouth opening of 2.5 cm, Mallampati grade 3, thyromental distance <6.5cm, restricted neck mobility and severely impaired neck extension.

After all tests, consultations and examinations were done, the patient was scheduled for right lower lobe resection in general anesthesia.

On the day of the surgery in the operating theatre, the patient underwent standard procedure. Peripheral intravenous access was obtained with difficulty, on the dorsal part of the arm with 20G cannula. Standard 5 lead ECG was attached together with intermittent non-invasive blood pressure cuff and pulse oximetry.

The initial vital signs were stable (heart rate was 80 bpm in regular sinus rhythm and blood pressure was 120 mmHg over 70 mmHg). However, the measurement of the SpO_2 was impaired and difficult (tried on every single finger, due to the thickness and vasospasm present). We have removed the pulse oximetry before induction from arms to his ear and it was 95%. Vital parameters were monitored continuously during the surgery and noted on every 5 minutes.

Patient received O_2 as pre-oxygenation for 5 minutes. A metroclopramide was given before induction. For the induction in anesthesia patient received 2 mg midazolam, 200 μg fenatnyl, 150 mg propofol, and after mask ventilation was obtained 50 mg Rocuronium was given. An ENT surgeon for tracheostomy was kept ready.

Laryngoscopy showed Cormack-Lehane grade 2 and left double lumen tube number 39 was inserted. The position of the tube was confirmed with auscultation. Patient was set on respirator on

Pressure Control Volume Guaranteed mode (PCVG) with tidal volumes 4-6 ml to achieve $EtCO_2$ 35-40 mmHg. Anesthesia was maintained with propofol continuous infusion 20 ml/h, fentanyl and rocuronium as needed. Before the incision one more intravenous line of 18G was placed.

Patient was carefully placed in lateral position; hot air circulators blankets and warmed intravenous fluids were given. Vital parameters remained stable all the time during the surgery. No surgical incidents and bleeding occurred as well as no drastic hemodynamic changes. The surgery was finished after 2 hours and 45 minutes and patient was extubated in the operating theater.

The only thing that was more pronounced on the emergency from the anesthesia was the evidence of the Raynaud's phenomenon on the hands. Postoperative course went uneventful.

Discussion

Progressive systemic sclerosis (PSS) or scleroderma is rare progressive fibrotic disorder of the connective tissue. Together with the connective tissue changes, atrophy of the skin and as well as involvement of various internal visceral organs may be present in these patients. Not rarely, involvement of the alimentary tract, lungs, heart, kidney, CNS, the presence of the autoantibodies, collagen deposition on different body parts, together with the possible profound vascular hypersensitivity are reported separately and in combination as possible anesthesiology challenges, sometimes even reported with detrimental outcome (1,2).

Simplified, systemic forms of scleroderma (SS) mainly occur in adults and involve internal organs, blood vessels, and skin. The progressive connective tissue fibrosis that affects the internal organs, especially lungs fibrosis, accompanied by interstitial lung disease, are reported as the leading cause of death in these patients (1).

Hereby, we present a case of a patient with SS undergoing anesthesia for thoracic surgery and discuss anesthetic concerns that should be considered for such patients in the perioperative management.

Firstly, the importance of the preoperative assessment should be emphasized.

Staging and the degree of the systemic involvement is the most important for the future anesthetic plans. Standard and widened preoperative tests are needed in these patients such as pulmonary functional tests (to find out the severity of pulmonary involvement), hemostasis (collagen is the factor that in these patients is deposed on different body parts and its involvement in coagulation may lead to different types of coagulation disorders), evaluation of the cardio-circulatory system (due to the known vascular hypersensitivity) as well as addition and evaluation of other diseases. This is the starting position for successful anesthesia plan (1,2). For our patient, preoperative wide screening was done and the decision for surgery was done after careful evaluation.

Mostly implied thing for anesthesia in such patients, as reported is the potential difficult airway management due to several factors. Microstomia, poor mouth opening, skin tightening of the head region, fibrosis of the temporomandibular joint, limited neck mobility may lead to

difficulties with mask ventilation and intubation. Additionally, presence of nasal or oral telangiectasias may cause occult bleeding during airway management (2,3).

In our patient the most of the typical features and the most of the predictors for difficult airway management and intubation were present. Therefore, our plan was to give the patient midazolam, fentanyl and propofol in order to see how the ventilation goes and if it is gentle and satisfactory to go for muscle relaxant. However, we considered the fact of difficult intubation and ENT specialist and fiber-optic video-laryngoscope was on standby. When the ventilation went uneventful and inspection showed good visualization, we gave muscular relaxant in order to facilitate double lumen tube intubation. Luckily, in our patient double lumen tube was easily and correctly placed.

However, anesthesiologist should always be aware that an awake fiber-optic intubation may be the most appropriate technique in these patients as well as an awake tracheostomy should be performed if intubation is failed (4).

Other issue commonly discussed for these patients is intravenous access. Difficulties in obtaining intravenous access may be due to dermal thickening and flexion contractures. Sometimes SS can be so progressive and the restricted blood flow can permanently damage the tissue at the fingertips, causing pits or skin sores (1,5,6). We had a problem with obtaining iv line for the patient. We managed to insert smaller cannula on the dorsal side of the arm and later on a larger one.

The standard monitoring with ECG, non-invasive blood pressure measurement and pulse oximetry might be a challenge if pits and skin sores are present. Modified putting of the monitoring with suppurative pads is recommended (5).

In our case ECG and blood pressure measurements were easily put, but due to non-pitting oedema in patient forearms, fingers oedema and flexion contractures, pulse oximetry was a problem. Our patient had Reynold syndrome on his hands, so the reading for the SpO_2 from the fingers was not taken into account. We changed the position of the pulse oximetry on regular time from one ear to other.

Literature reveals that patients with scleroderma often have esophageal motility disorders. Therefore, the risk of aspiration is present due to the hypotonic lower esophageal sphincter. Sometimes in these patients development of interstitial lung disease might be due to the repeated aspiration (4). We gave metroclopramid to our patient before induction of anesthesia in order to lower the incidence of silent aspiration.

Another important thing in patients with scleroderma is hypothermia that may lead to vasoconstriction and profound vascular crisis. Recommendations are the operating room temperature to be kept above 21 °C and administration of warmed intravenous fluids (5,6). In our case we put the warming blankets and administrated warmed intravenous fluids, but despite of this on the emergency from anesthesia peripheral vasoconstriction was pronounced and the Raynaud's phenomenon was emphasized. After awakening the patient subjective feeling was that he feels very cold.

Overall talking, literature does not give any special recommendation for what type of anesthesia to be used in such patients. When choosing the type of anesthesia, careful analysis of organ dysfunction and involvement should be considered.

Anesthesiologist should take consideration of all the pathophysiological changes in patients with scleroderma, should be well introduced to them and their impact on the surgical and anesthesia management in order to lower the risk for morbidity and mortality in such patients during the perioperative period.

Conclusion: Scleroderma is a multisystem disease that can have impact on every aspect of the anesthetic care. Proper knowledge of the pathophysiological changes, proper assessment and identifying of all the risks in these patients are detrimental for patients' perioperative and postoperative outcomes.

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Dag Stat. Mackinnon A. Available from: http//www.mhri.cdu.au/biostats.Accessed May 5th 2006.

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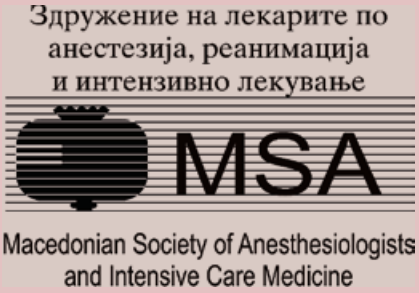
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