

Screening of the use of benzodiazepines during COVID-19 pandemic in the general population

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Abstract

Benzodiazepines have been commonly prescribed for the treatment of anxiety and insomnia in the last few decades. There has been a rising concern regarding safety of benzodiazepines due to overdose related deaths, addictions and cognitive side effects. COVID-19 pandemic is expected to cause a mental health crisis. Several studies have shown an increase in anxiety and insomnia. The prescriptions of benzodiazepines could increase due to increase in anxiety and insomnia. The pandemic calls for a rapid adaptation of conventional medical practices to meet the evolving needs of such vulnerable patients. COVID-19 patients may frequently require treatment with psychotropic medications. This pandemic is leading to additional health problems such as stress, anxiety, depressive symptoms, insomnia, denial, anger and fear, globally.

The COVID-19 pandemic is a challenge to humanity. It is not only a health crisis but also a social crisis. The life is unlikely to be the same after we come out of the pandemic. There will be changes at the level of individuals, families, communities, states, nations, international relationships, and the way all of us will deal with a range of human and environmental situations. Disasters are always associated with increased rates of emotional health needs from distress to specific disorders, such as posttraumatic stress disorder. Past experiences have shown psychosocial interventions, ranging from self-care, psychological first aid, counseling, social support and formal psychiatric care can minimize the emotional health impact of disasters. These activities can be initiated by individuals and professionals.

Keywords: coronavirus, COVID-19, mental health, benzodiazepines

Introduction

The corona virus pandemic is a global health emergency calling for a rapid adaptation of conventional clinical practices in many medical areas, including psychiatry. Corona virus disease (COVID-19) is a systemic infection potentially targeting multiple organs and functions. Interstitial pneumonia is the landmark feature of this condition, leading to severe respiratory distress requiring intensive life support in about one out of twenty symptomatic cases (Grasselli et al., 2020; Wu and McGoogan, 2020). Old age and preexisting medical

comorbidities are associated with increased severity and mortality (Yang et al., 2020).

This epidemic leads to additional health problems such as: stress, anxiety, depressive symptoms, insomnia, denial, anger and fear, globally. Collective problems affect day-to-day behavior, cost-effectiveness and preventive decision-making strategies by health organizations and medical centers, which may weaken COVID-19 control strategies and lead to greater morbidity and global mental health needs (Torales et al., 2020).

Benzodiazepines have been around since the 1960s and they have been one of the most commonly prescribed medications worldwide. Over years, there has been a

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rising concern of the risk of overdose-related deaths, addiction, and long-term cognitive concerns with benzodiazepines. As per the Centers for Disease Control and Prevention (CDC), there were 67367 deaths in the United States due to overdose in 2018. Synthetic opiates were the main drugs involved in deaths. As per the National Institute on Drug Abuse (NIDA), benzodiazepines were involved in more than 30% of the opiates-related overdose-related deaths (CDC, 2020; NIDA, 2020; Torales et al., 2020).

Benzodiazepines are used to treat anxiety, sleep disorders and other conditions. Oral overdose with benzodiazepines, without co-ingestion, rarely results in significant morbidity or mortality. However, patients often do not take them as prescribed, use them in combination with other drugs or substances, or both. The U.S. Food and Drug Administration recently requested an update to the benzodiazepine warning to include the risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions. Prescription of benzodiazepines has increased dramatically over the past decade and during the COVID-19 pandemic. According to research, psychiatrists who prescribe benzodiazepines are at a sustainable level (29.6% vs. 30.2% now), but primary care physicians have increased (3.6% vs. 7.5%) (Agrawal, 2020; Agarwal and Landon, 2019). Primary health care prescribes about half of all benzodiazepine prescriptions. This growing pattern of benzodiazepine prescriptions is very worrying amid the COVID-19 pandemic.

The COVID-19 pandemic could cause a mental health crisis. Studies have shown an increase in anxiety and insomnia in health care providers, as well as in the general (Agarwal and Landon, 2008; Lai et al., 2020; Pappa et al., 2020). According to a survey conducted by the American Psychiatric Association in March 2020, 48% of the general population reported anxiety, 36% reported that the pandemic was severely affecting their mental health, and 19% reported insomnia. Pappa et al. (2020), during the pandemic showed a prevalence of 23.2% anxiety and 22.8% depression in health workers. In one study of health care providers treating patients with COVID-19 in China, 50.4% reported depression, 44.6% anxiety, 34% insomnia, and 71.5% distress (Lai et al., 2020). This increase in anxiety, insomnia and depression is alarming in both the general population and health professionals. Hence, it can be predicted that there will be an increase in the use of prescription benzodiazepines.

Social isolation and lack of ready access to support is another risk factor (Baldessarini, 2019). Pandemic social isolation measures can have a ripple effect on mental health as the support network may be disrupted for some people. There is a lot of fear of illness, death, finances, housing, unemployment, childcare due to a pandemic. The longer this pandemic lasts, the worse it will be for mental health. Stress can activate the hypothalamic-pituitary axis which really increases cortisol. Cortisol is a steroid

hormone that plays a role in the stress response and immunity along with other functions. Chronic stress can increase inflammatory conditions in the body, reduce immunity (Wolf et al., 2008). During this time of pandemic when we have no treatment for COVID-19, we need immunity to fight this infection.

Insomnia can be caused by acute stress and over time can become chronic. People who have a high sleep response are more prone to stress insomnia. Sleep reactivity is a trait that some people may have and is also associated with a risk of depression and anxiety (Kalmbach et al., 2018). There has been an increase in insomnia due to the pandemic and can be explained by cognitive impairments, survivors that some people may have at bedtime. Bed rest can increase anxiety and link sleep time to anxiety, so relaxation techniques, such as progressive muscle relaxation, can help us relax before bed and reduce sleep latency. A study by Palagini et al. (2018), of subjects with insomnia found that low elasticity was associated with a high sleep response associated with stress, emotional dysregulation, and hyperarousal.

Therefore, the main target of this research paper is investigation on the use of benzodiazepines during the COVID-19 pandemic in the general population.

Materials and methods

An analytical cross-sectional study was prepared in the period from 06.2020 to 12.2020. A questionnaire was used which was compiled and evaluated by the authors. 260 survey questionnaires were sent through Google forms. The response rate is 92% (240). The research was conducted in Strumica and Skopje.

The survey questionnaire consists of III parts. The first part consists of 6 demographic questions. The second part consists of the benzodiazepines taken and the third part the benzodiazepines taken in the last 6 months.

The respondents are persons over 18 years of age, who agreed to take part in the survey. In one part of the survey, questionnaire uses a Likert-type scale - a scale of attitudes, which consists of a series of statements, dedicated to different aspects of an attitude. It is given to the respondent with the task to express a degree of agreement or disagreement for each individual statement, as a rule on a five-point scale, from disagree at all, to agree completely. Each answer of the respondent is scored in the appropriate way and then, by adding the statements, the total score is obtained, which expresses the attitude of the respondent, to a certain extent positive or negative. With five answer options, we used this odd Likert scale question to gather information about a topic by including a neutral answer option for respondents to select if they don't wish to answer from the extreme choices. Standard statistical descriptive methods were used. Difference test, rates and central tendency (mean) were determined.

Results

A total number of 240 participants participated in the research. The participants in the survey are 82.9% females and 17.1% males. The percentage difference is statistically significant for $p < 0.05$ ($p = 0.0000$).

29.2% of the participants are aged from 40 to 49, followed by the age of 30-39 (27.5%), 60 to 69 (17.4%) etc. The percentage difference is statistically significant between the ages of 40-49 versus other age groups for $p < 0.05$ ($p = 0.0100$).

67.5% have higher education, Masters are 30 (11.9%), Doctors of Science are 12 (5%), and 30.4% have secondary education. The representation of higher education is significant compared to the others ($p = 0.0000$).

More than half of the respondents are married (58.3%), employed are 70.0%, and retired are 14.6%. Most live in the city - 91.0% (Table 1).

Table 1. Overview of the demographic characteristics of the study participants

Gender	N=240	%
Male	41	17.1
Female	199	82.9
Age		
<30	22	9.2
30-39	48	20.0
40-49	70	29.2
50-59	60	25.0
60-69	32	13.3
>69	8	3.3
Education level		
Primary	5	2.1
High	73	30.4
Faculty	120	50.0
Masters	30	11.9
PhD	12	5.0
Marital status		
Married	140	58.3
extramarital	16	6.7
Divorced	24	10.0
Widow	40	16.7
Without a permanent partner	20	8.3
Employment status		
Employee	168	70.0
Unemployed	27	11.2
Students	10	4.2
Pensioner	35	14.6
Place of residence		
Urban	218	90.8
Rural	22	9.2

To the first question "Have you ever been diagnosed with a psychiatric disorder", 33.3% of respondents

answered yes compared to 66.7% who did not. Most of the 60% are neurotic and stress-related disorders and somatoform disorders (anxiety disorders) and 40% are mood disorders (depression). Most of the respondents take alprazolam (Helex, Xanax) - 105 (43.75%), Diazepam take 24.6%, 11.7% take Lexilium, while 8.7% take Demetrin, etc. The percentage difference compared to taking Alprazolam versus other types of drugs is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2).

Benzodiazepines are mostly taken by the respondents due to anxiety (57.5%), insomnia (40%), tension (37.5%), restlessness (33.75%), fear (28.3%), high blood pressure (14.6%), etc. The percentage difference in taking Benzodiazepam due to anxiety versus the other modalities of the variables is statistically significant for $p < 0.05$ ($p = 0.0001$) (Table 2).

Now most of the surveyed, 65% take benzodiazepines due to anxiety, 41.7% take them due to tension, 45.8% due to insomnia, 36.7% due to fear and 42.5% due to restlessness (Table 2).

According to the dynamics index, the rate of increase in benzodiazepine intake due to anxiety increased by 13%, due to fear by 29.4%, due to insomnia by 14.6%, due to tension by 11.1%, due to restlessness by 25.9, etc. Generally, the use of benzodiazepines shows an increase rate of 20.9%.

The drug does not help to 18 (7.5%) of the respondents, moderately does not help to 28 (11.7%), moderately good helps to 51 (21.25%) of the respondents, helps well to 81 (33.75%) and helps very well at 61 (25.4%) of them. The percentage difference between those who are not helped by those who are helped by the drug (19.2% vs. 80.8%) is statistically significant for $p < 0.05$ ($p = 0.0000$) on average, the respondents indicate the help of the drug with 6.8 (Table 2).

Most of the respondents take benzodiazepines on the advice of a psychiatrist (32.5%), family doctor (26.25%), self-initiated (18.3%), and 14.2% take it on the advice of an internist. The percentage difference that benzodiazepines took on the advice of a psychiatrist and family doctor versus the other modalities is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2).

96.25% of respondents take prescription drugs, 75% of respondents tried to stop taking the drug, and 37.5% of respondents now need a higher dose of the drug.

75% of the respondents take the drug daily, very often take 13.3% and very rarely 11.7%. The percentage difference in relation to taking the drug daily versus the other modality of taking is statistically significant for $p < 0.05$ ($p = 0.0000$) (table 2).

The following answers refer to the drugs used in the last 6 months, these are views and claims. On the statement "Take a higher dose, otherwise I do not feel well" (P11), 70% of the respondents think that it is completely incorrect. The percentage difference in relation to the completely incorrect version of the other modality of the statement is statistically significant for

Table 2. Overview of the answers (part II and III)

question/Q	N=240	%	question/Q	N=240	%
Q1			Q11		
Yes	80	33.3	Completely incorrect	168	70.0
No	160	66.7	Partially incorrect	18	7.5
Q1a*			I am not sure	24	10.0
F 32-33	32	40.0	Partially true	26	10.8
F 41-43	48	60.0	Completely true	4	1.7
Q2			Q12		
Helex	67	27.9	Completely incorrect	145	60.4
Xanaks	38	15.8	Partially incorrect	35	14.6
Diazepam	59	24.6	I am not sure	16	6.7
Lexilium	28	11.7	Partially true	35	14.6
Demetrin	21	8.7	Completely true	9	3.75
Lorsilan, Lorazepam	11	4.6	Q13		
Aclonil	16	6.7	Completely incorrect	144	60.0
Q3			Partially incorrect	17	7.1
Anxiety	138	57.5	I am not sure	16	6.7
Fear	68	28.3	Partially true	31	12.9
Tension	90	37.5	Completely true	32	13.3
Insomnia	96	40.0	Q14		
Restlessness	81	33.75	Completely incorrect	185	77.1
High pressure	35	14.6	Partially incorrect	26	10.8
Other reasons	33	13.75	I am not sure	11	4.6
Q4			Partially true	9	3.75
Anxiety	156	65.0	Completely true	9	3.75
Habit	18	7.5	Q15		
High pressure	24	10.0	Completely incorrect	77	32.1
Insomnia	110	45.8	Partially incorrect	24	5.7
Tension	100	41.7	I am not sure	19	7.9
Fear	88	36.7	Partially true	41	17.1
Restlessness	102	42.5	Completely true		
Other reasons	36	15.0	Q16		
Q5			Completely incorrect	121	50.4
1	9	3.75	Partially incorrect	24	10.0
2	9	3.75	I am not sure	35	25.0
3	11	4.6	Partially true	42	17.5
4	17	7.1	Completely true	18	8.5
5	29	12.1	Q17		
6	22	9.2	Completely incorrect	44	18.3
7	26	10.8	Partially incorrect	26	10.8
8	55	23.0	I am not sure	11	4.6
9	21	8.75	Partially true	150	62.5
10	41	17.1	Completely true	9	3.75
Q6			Q18		
Family doctor	63	26.25	Completely incorrect	73	30.4
Psychiatrist	78	32.5	Partially incorrect	15	6.25
Internist	34	14.2	I am not sure	12	5.0
Self-initiated	44	18.3	Partially true	100	41.7
Pharmacist	3	1.25	Completely true	40	16.7
Friend/relative	10	4.2	Q19		
Another specialist	8	3.3	Completely incorrect	120	50.0
Q7			Partially incorrect	20	8.3
Yes	231	96.25	I am not sure	3	1.25
No	9	3.75	Partially true	17	7.1
Q8			Completely true	80	33.3
Yes	180	75.0	Q20		
No	60	25.0	Completely incorrect	42	17.5
Q9			Partially incorrect	23	9.6
Yes	90	37.5	I am not sure	5	2.1
No	150	62.5	Partially true	131	54.6
Q10			Completely true	39	16.3
Daily, regular	180	75.0	*one do not give an answer		
very often	32	13.3			
Very rare	28	11.7			

$p < 0.05$ ($p = 0.0000$) (Table 2). The average value of the answers among all respondents is 1.7, which means that the statement of the respondents is between completely and partially incorrect.

To the statement "I get nervous if the drugs are not available to me" (P12), 60.4% of the respondents think that it is completely incorrect. The percentage difference in relation to the completely incorrect version of the modality of the statement is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2). The average value of the answers is 1.9, which makes the claim of the respondents closer to partially incorrect.

On the statement "I was told to take a lower dose" (P13), 60% of the respondents think that it is completely incorrect. The percentage difference in relation to the completely incorrect version of the other modality of the statement is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2). The average value of the Likert scale is 2.2 with which the claim of the respondents is partially incorrect.

On the statement "I take more drugs than prescribed" (P14), 77.1% of the respondents consider it completely incorrect. The percentage difference compared to the completely incorrect version of the other modality of the statement is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2). The average value of the Likert scale is 1.5 with which the statement of all respondents is completely incorrect.

On the statement "I feel safe when I have medication with me" (Q15), the claim of the respondents is divided. Namely, 39.2% of the respondents think that it is completely incorrect, and 32.1% think that it is completely incorrect. The percentage difference in relation to completely incorrect and completely accurate version of the remaining modality of the statement is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2). The average value of the answers is 3.1, with which the statement of all the respondents is in the middle. There is an uncertainty in the answers.

On the statement "The effect of the drug is now weaker than at the beginning of taking" (P16), half of the respondents consider it to be completely incorrect (50.4%). The percentage difference compared to the completely incorrect version of the remaining modality of the statement is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2). The average value of the Likert scale is 1.9, with which the statement of all respondents is partially incorrect on average.

On the statement "I use drugs much faster now" (P17), half of the respondents think that it is partially true (62.5%). The percentage difference versus the other modality of the statement is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2). The average value of the answers is 3.1 with which claim the respondents are not sure.

To the statement "Immediately before taking the

drug, I only think about it" (P18), 41.7% of the respondents think that it is partially true, and 30.4% completely incorrect. The percentage difference between the partially correct version and the modality of the statement is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2). The average value of the answers is 3.1 with which claim the respondents are not sure.

On the statement "I take the prescription before the scheduled check" (P19), 50% of the respondents think that it is completely incorrect, and 33.3% completely correct. The percentage difference between the partially correct version and the modality of the statement is statistically significant for $p < 0.05$ ($p = 0.0002$) (Table 2). The average value of the answers is 2.7, which claim the respondents are not sure about.

On the statement "I take a large amount of medication" (P20), 54.6% of the respondents think that it is partially true. The percentage difference between the partially correct version and the modality of the statement is statistically significant for $p < 0.05$ ($p = 0.0000$) (Table 2). The average value of the answers is 3.7, with which statement the respondents are partially correct.

Discussion

The last 12 months have been the most difficult and traumatic period for humanity. The world, as we all know, is upside down (Srinivasa, 2020). Social structures and their functioning are under pressure. The health of the population is a victim of the current pandemic. There is a fear of death and anxiety about the future among all individuals around the world (Brooks, 2020; Clopton, 2020, Davis, 2020; Hackethal, 2020; Sunita, 2020; Vijayakumar and Thara, 2020). Medical care services are stretched and healthcare workers are at risk of serious illness. The opinion is that the world will not be the same as it was before COVID-19.

There is much debate about the use of benzodiazepines in the medical community. Some support the use as a result of immediate benefits, some are not because of addiction, tolerance, risk of cognitive decline, etc. Conflict studies make it difficult to make the right decision when patients are seen in clinics and hospitals. There are limited resources for psychotherapy and this makes it difficult for primary care physicians to treat anxiety and insomnia. In our research, 1/4 of the benzodiazepines were prescribed by a family doctor, 1/5 of the respondents took the drug on their own initiative without a doctor's advice. 4% of respondents took the drug without a prescription, although benzodiazepines are available only on prescription. 33% of the respondents have a psychiatric disorder. The rise of benzodiazepine prescriptions is very worrying amid the COVID-19 pandemic.

In general, there is no denying the fact that we see more deaths related to overdose, addiction problems, suicides in the world (NIDA, 2020; National Institute of Mental Health, 2020).

Due to the COVID-19 pandemic, a mental health crisis is expected and we will probably see an even greater increase in anxiety and insomnia. In the last 12 months, anxiety has been recorded in more than half of 65% and 48% of insomnia in our research. The findings coincide with the research done by the American Psychiatric Association in March 2020. 48% of the general population reported anxiety, 36% informed that the pandemic seriously affected their mental health and 19% reported insomnia (New Poll, 2020). A systematic examination and meta-analysis performed by Pappa et al. (2020), thirteen studies were included in the analysis with a combined total of 33,062 participants, anxiety was assessed in 12 studies, with a pooled prevalence of 23.2% and depression in 10 studies, with a prevalence rate of 22.8%.

In a study by Lai et al. (2020), in China, a cross-sectional study of 1257 respondents, it was found a high prevalence of mental health symptoms in healthcare professionals treating COVID-19 patients, overall, 50.4%, 44.6%, 34.0%, and 71.5% of all participants reported symptoms of depression, anxiety, insomnia, and anxiety, respectively. This increase in anxiety, insomnia and depression is alarming in both, the general population and health professionals. Benzodiazepines may be tempting at this time because of their "quick fix", but we know that because of this "quick fix", patients are unable to develop coping skills that can cope with stressors (Davydow et al., 2008; Gelpin et al., 1996; Guina and Merrill, 2018; Mellman et al., 1998). Patients become addicted to drugs and so long-term use becomes a problem of addiction. The first line of treatment for anxiety and insomnia is psychotherapy, so it should be used before switching to pharmacotherapy. There are several types of psychotherapy available, such as: Cognitive Behavioral Therapy for Anxiety, Insomnia, Supportive Therapy, Interpersonal Therapy, Trauma Focused Therapy, etc. Therapy can help develop rational thinking and help patients cope with their experiences and worries, and can help with anxiety and insomnia. Building a positive attitude with psychotherapy can take a long time and help develop the resilience to deal with all the stressful factors in life. Elasticity is a trait that shows how adaptable an individual is to stressful events. People with high elasticity can adapt and have a low risk of anxiety, insomnia and stress. Given that people with low elasticity are at high risk of insomnia and anxiety during stressful events such as the current pandemic. Low elasticity may increase anxiety and insomnia in some people with the current pandemic.

Prescription of benzodiazepines has increased dramatically over the past decade and during the COVID-19 pandemic. Overall in our research, the use of benzodiazepines shows an increase rate of 20.9%. Most

respondents use benzodiazepines because of anxiety, insomnia, restlessness and 47% said that the drug helps a lot (on a scale of 8 to 10).

Conclusion

This epidemic leads to additional health problems such as: stress, anxiety, depressive symptoms, insomnia, denial, anger and fear, globally. Collective problems affect the day-to-day behavior, cost-effectiveness, prevention and decision-making strategies of policy makers, health organizations and medical centers, which can weaken COVID-19 control strategies and lead to greater morbidity and global mental health needs.

The focus is on the transmission of COVID-19 infection worldwide, while distracting the public from the psychosocial consequences of the affected individuals and the general population. New mental health issues related to this global event, COVID-19 infection, can escalate into long-term health problems, isolation and stigma. Global health measures should be applied to psychosocial stressors, especially related to the use of isolation/quarantine, fear and vulnerability among the general population. Inclusive response around the world should include a focus on the impact on the mental health of patients and the general population.

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Резиме

Скрининг на употребата на бензодиазепини за време на КОВИД-19 пандемијата кај општата популација

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Клучни зборови: коронавирус, КОВИД-19, ментално здравје, бензодиазепини

Бензодиазепините се пропишуваат за третман на анксиозност и несоница во последните неколку децении. Постои зголемена загриженост за безбедноста на бензодиазепините поради смртни случаи поврзани со предозирање, зависности и когнитивни несакани ефекти. КОВИД-19 пандемијата се очекува да предизвика криза во менталното здравје. Неколку студии покажаа зголемување на анксиозноста и несоницата. Пропишувањето на бензодиазепини може да се зголеми како резултат на зголемување на анксиозноста и несоницата. Пандемијата бара брза адаптација на конвенционалните медицински практики за да се задоволат еволутивните потреби на ваквите ранливи пациенти. КОВИД-19 пациентите бараат третман со психотропни лекови. Пандемијата води кон дополнителни здравствени проблеми како што се: стрес, вознемиреност, депресивни симптоми, несоница, негирање, лутина и страв на глобално ниво.

Пандемијата КОВИД-19 е предизвик за човештвото. Таа истовремено е здравствена и социјална криза. Животот, веројатно нема да биде ист откако ќе излеземе од пандемијата. Има промени на ниво на поединци, семејства, заедници, држави, нации, меѓународни односи и начинот на кој сите ќе се справиме со низа човечки и еколошки ситуации. Катастрофите секогаш се поврзани со зголемени стапки на емоционалното здравје, од вознемиреност, до посттравматско стресно нарушување. Искуствата од минатото покажаа психосоцијалните интервенции, од грижа за себе, психолошка прва помош, советување, социјална поддршка и формална психијатриска нега можат да го минимизираат влијанието на емоционалното здравје од катастрофи. Овие активности можат да бидат иницирани од индивидуи и професионалци.