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Conference Paper · June 2017

DOI: 10.23919/ConTEL.2017.8000041

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ICT-Assisted Personalized Therapy and Rehabilitation in Urinary Incontinence

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***Abstract*— Urinary incontinence is uncontrolled leakage of urine. Its incidence is increasing and its treatment is expensive, however often not efficient. The paper reviews existing findings of genetic effects, effects of environment and lifestyle on occurrence of urinary incontinence. The development of personalized medicine assisted by information and communication technology is of great importance for the assessment of risk of developing urinary incontinence, as well as achieving better health. There are already smartphone applications that are focusing on some segments of personalized therapy and rehabilitation, such as tracking condition or providing exercising support. In this paper we are proposing the digital support framework that tackles all addressed issues under control of the user. The introduced connected health model of a new mobile application has gathered the most helpful functionalities that are supported by medical evidence.**

Keywords—urinary incontinence; personalized medicine; gene therapy; connected health; smartphone applications

I. INTRODUCTION

Urinary incontinence is defined as loss of bladder control with subsequent unintentional leakage of urine. It is common problem, which leads to negative impact on quality of life [1]. Women are affected twice as likely as men, which is due to weakening of pelvic floor muscles after vaginal childbirth [4]. Urinary incontinence can affect women and men of all ages; however, it is more common among elder women. Since life expectancy has increased in developed countries, there is a proportional increase of prevalence of continence problems in women [2]. It is estimated that one in every three women over the age of 60 has problems in control of her bladder [3]. Other known risk factors for development of urinary incontinence are advanced age, parity, low estrogen levels at menopause and other physical and mental disabilities, use of medications, surgical procedures or cerebrovascular insults, which can cause lower pelvic muscle tone or nerve damage and as such lead to urinary incontinence [5].

Urinary incontinence is divided into four subtypes. Urgency incontinence is due to an overactive bladder. People with overactive bladder syndrome present with urinary urgency, which is frequently accompanied with frequency and nocturia in absence of urinary tract infection. Stress incontinence is due to poor closure of bladder because of damage to pelvic support structures. It is defined as loss of urine associated with physical exertion, coughing, sneezing or any other activity that increases intra-abdominal pressure. Mixed urinary incontinence contains both, the causes of stress and urgency urinary incontinence [6] [7]. Another type of urinary incontinence is overflow incontinence, which can be caused either by urethral blockage or by poor bladder contraction. The most common types of urinary incontinence are stress and urgency incontinence. The severity ranges from occasional leakage of urine to having an urge to urinate that is so sudden that patients do not manage to get to a toilet in time.

In the diagnosis of urinary incontinence, a detailed medical history is very helpful. Taking medical history with special focus on the pattern of urine loss can help us define type of incontinence. Other important points include straining, use of medications, recent surgeries or other illnesses. To test incontinence we use stress tests, urodynamics, cystoscopy, ultrasonography assessment of kidneys, bladder and urethra as well as urinalysis to rule out the infection and blood tests.

There are several treatment options for urinary incontinence. Treatment options range from conservative treatment to medications and surgery [8] [9]. Conservative treatment consists of behavioral training, such as prompted voiding, bladder training, weight reduction (in obese patients) and pelvic muscle rehabilitation by means of pelvic floor exercises. In addition to behavioral training conservative treatment includes neuromuscular electrical stimulation (NMES), catheterization and use of absorbent pads [10]. To treat incontinence a number of medications exist. They are recommended in patients with urgency incontinence, who are

not showing improvement with conservative methods of treatment. However, many medications appear to have limited benefit on improving urinary incontinence [11] [12]. Among the most common surgical procedures in the treatment of stress incontinence are abdominal slings, bladder neck suspension and the most frequently used tension-free vaginal tapes [13].

The success of treatment depends on the accuracy of diagnosis and selection of the most appropriate method of treatment. To do so, we have to take into account the specificities and needs of the individual, and thus accommodate the most optimal way of treatment and rehabilitation to each individual. With personalized medicine we can ensure the achievement of these objectives.

II. Personalized Medicine

The term "personalized medicine" is widely in use nowadays, however it is often interpreted in different ways. In our article we define it as an innovative approach to disease prevention and treatment, which creates more unified ways of treatment of individuals [14]. Redekop and Mladsi have defined personalized medicine as the use of combined knowledge – genetic or otherwise – about person to predict disease susceptibility, disease progression or treatment response and thereby improving that person's health [15]. Despite the genetic impact, personalized medicine takes into account also differences in lifestyle and environment.

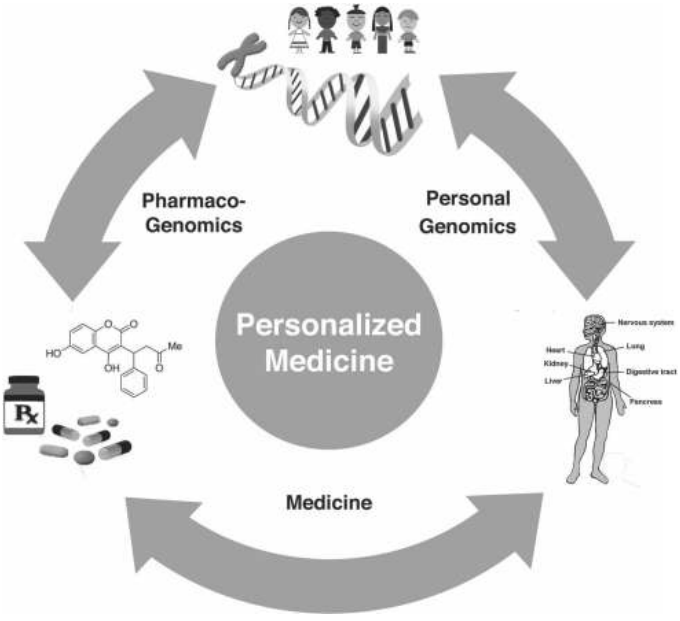

Fig. 1. The wheel of personalized medicine [15]

Personalized medicine deals with the prediction of individual risk for developing certain diseases, based on one or more genes. This allows early preventive action before the actual onset of illness [16]. It can also provide earlier intervention once the disease has already developed and allow more efficient drug therapies [17]. Advances in personalized medicine have led to progress in the development of medications that are tailored to the specific characteristics of the individual or genetic profile of tumor.

III. The Methodology

The study used a qualitative methodological approach to research and analyze the subject matter. An extensive analysis of existing relevant national and international resources concerning the existing mobile applications tackling the problem of urinary incompetence was done. It has enabled finding a common ground in all the app, in order to develop the novelty approach adding few new functionalities, using the personalized medicine approach.

IV. Related Work

A. Genetic Influences

Relationship between hereditary risk factors and the occurrence of pelvic floor disorders and subsequent urinary incontinence is known for more than 150 years [18]. A positive family history is associated with earlier onset and more rapid progression of urinary incontinence [19]. In first-degree relatives, the risk of incontinence and prolapse is two to three times higher [20] [21]. Numerous studies have examined twins to quantify heritability of lower urinary tract symptoms. A sample of 16,886 Swedish twins aged more than 50, showed a heritability of 41% for stress incontinence [22]. In a cohort of 2,336 women enrolled in the Danish register of twins, heritability ranged between 42-49% for urgency incontinence, 39% for stress and 27-55% for mixed urinary incontinence [23].

Abnormalities in the expression of extracellular matrix proteins can lead to structural changes in the matrix. Genes encoding these proteins and their inhibitors or inducers are thought to lead to the formation of stress incontinence. There is also increasing evidence that presence or absence of estrogen and progesterone may influence expression of these genes [24].

Meta-analyzes showed several DNA loci that may be associated with the risk of urgency urinary incontinence, including loci within the ZFP521, ADAMTS16 and CIT genes. Moreover, links between the occurrence of urgency urinary incontinence and wound healing pathways have also been proven [25].

ZFP521 gene is involved in the control of blood, bone and neural stem cells [26]. It is also important for the development of striatonigral part of the brain and its dysfunction leads to degeneration of striatonigral projections, which is manifested by Parkinson's disease. In patients with Parkinson's disease bladder detrusor hyperactivity is known, causing problems with continence [27] [28].

The role of the ADAMTS16 and CIT gene is less clear. CIT gene encoding Rho interacting serine and threonine protein kinase that is associated with cell division. Rho kinase influences the contraction of the bladder. Inhibition of Rho kinase may inhibit the hyperactivity of the bladder [29].

Further identification of genetic risk factors would allow clinical risk assessment, assessment of prognosis and response to a particular type of treatment. Moreover, such findings can contribute to the understanding of the pathogenesis of this complex disease, which would certainly affect new drug treatments and preventive strategies [30].

B. Lifestyle Influences

Urinary incontinence has a significant negative impact on quality of life. It can be mitigated by the various changes in lifestyle. The modifiers of lifestyle are elimination of dietary bladder irritants, adjustment of fluid intake, weight control, or weight reduction in case of obesity and smoking cessation [31]. Even caffeine was proven an important stimulant of bladder activity, due to its diuretic properties. It supposedly raises detrusor pressure and excitability of the detrusor muscle [32]. It is therefore advisable to reduce caffeine intake, in order to improve continence [33].

Excessive fluid intake can exacerbate the symptoms of urinary incontinence. As greater physical stress, which occurs in larger volumes of bladder, increase likelihood of unwanted leakage of urine. On the other hand, the extreme restrictions on liquid produces more concentrated urine, which irritates the bladder and leads to more frequent episodes of urgency incontinence and urinary tract infections [34]. Optimal daily intake of fluids should be limited to 30 mL / kg body weight per 24 hours [35].

Obesity is an independent risk factor for developing urinary incontinence, because it increases intra-abdominal pressure, which causes chronic stress on the pelvic floor [36]. The increase in body weight of 5 to 10 kg by the age of 18, increases the risk for development of urgency urinary incontinence up to 44% [37]. Physical activity affects the body weight reduction and increases the volume of the pelvic floor muscles, which has a positive effect on the reduction of incontinence. Nevertheless, excessive physical activity can also have negative impacts, as forces during exercise increase intra-abdominal pressure [38].

The long-term smoking increases the likelihood of chronic cough, which also increases intra-abdominal pressure. It is expected that nicotine and other toxins that are excreted in the urine irritate the bladder and thus further promote leakage of urine. The medical guidelines encourage smoking cessation, as this reduces episodes of coughing in smokers with urinary incontinence; furthermore, it reduces risk of developing bladder cancer [39].

Damage to the pelvic floor, which often occurs during vaginal delivery, can serve as a trigger factor for the occurrence of urinary incontinence. Especially vulnerable are women with abnormalities in wound healing or tissue remodeling [25].

C. Environmental Influences

The environmental factors that cause urinary incontinence include medications, location of toilets, appropriateness of the toilet facilities and type of clothing [40].

Diuretic, sedative hypnotics, anticholinergic medications, narcotics, antihistamines and antispasmodics have a major impact on incontinence among the drugs. Fast-acting diuretics increase urine volume and frequency of voiding. In combination with impaired mobility, they may affect the involuntary loss of urine before reaching the toilet. Sedative hypnotics delay conscious awareness of the need to void.

Similar effect on conscious awareness of need to void has alcohol. Furthermore, alcohol consumption can lead to mobility impairment and has diuretic effect, producing larger volume of urine. All mentioned causes could increase urinary incontinence. Anticholinergic medications and antihistamines contribute to retention of urine, leading to overflow incontinence [40].

We must also emphasis early treatment and prevention of disease progression. Particular attention should be paid to vulnerable groups [41].

New medications that are nowadays used to treat urinary incontinence are significantly better than those that were used 20 years ago. However, new forms of anticholinergic agents (tolterodine, controlled-release oxybutynin) are at the upper limit of capacity, so it is difficult to expect further success of treatment with these drugs.

Further successful treatment can be expected with the development of drugs based on targeting the afferent nerves that control the bladder. With the development of personalized medicine special attention is also focused on the development of gene therapy and delivery of drugs directly to the site of action (into the bladder), thus avoiding many side effects [42].

In the course of research is the use of herpes simplex virus (HSV) as vectors to implement gene therapy for the treatment of nervous system of certain organ. HSV is a virus that spreads along nerves and can remain in a latent form in dorsal root ganglia. Researchers are trying to ascertain whether HSV can infiltrate nerves, which innervate the bladder. Researches were done with special non-replicating HSV virus that is capable of expressing nerve growth factor (NGF) for at least 3 months.

After intrathecal NGF injection the bladder became overactive. After injection of HSV with NGF bladder remained hyperactive for up to 3 months. Since NGF stimulates the growth of nerves it can be expected to be of great importance in the treatment of certain conditions, such as diabetic neurogenic bladder, in which due to peripheral neuropathy there is deficiency of neurotrophic factors [42].

Incontinence can also be associated with inaccessible toilets and physical deficits, which impair person's ability to use toilet independently. In the elderly, incontinence can also be associated with fear of falling, so without appropriate assistance they refuse to use the toilet. Nighttime incontinence can occur, if the bed is too high for elderly person to get up without assistance. In addition, the lack of privacy in nursing homes can lead to rejection of the use of toilets [40].

Clothing items, which are more difficult to undress, require more time, which can lead to involuntary leakage of urine. Furthermore tight undergarments increase pressure on the bladder and promote incontinence [40].

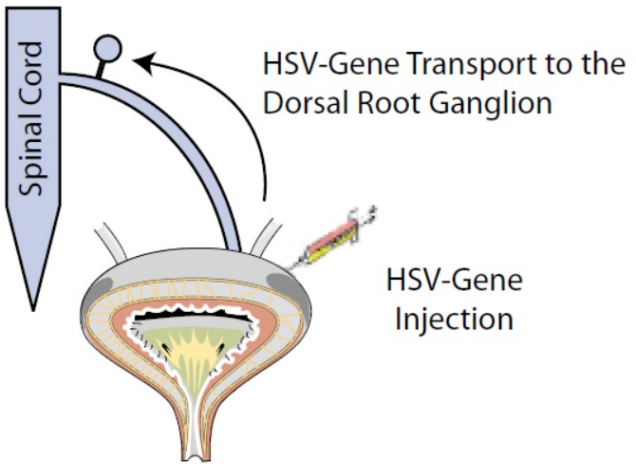

Fig. 2. Use of HSV as vector in treatment of Bladder dysfunction (42)

D. 2.4. *Smartphone Applications for Urinary Incontinence*

In regulating urinary incontinence, patients may already benefit from usage of existing smartphone applications, such as iDry, which identifies factors that affect individual's urinary incontinence, such as exercise, diet, drugs and behavior, furthermore it tracks progress, shares it with doctors and predict future success[1].

Another application is LeakFreeMe, which focuses on stress incontinence and provide education and guidance of each individual's stress incontinence[2]. BladderPal application was created to help patients suffering from urinary incontinence regain bladder health in conjunction with their doctors. It is used to track fluid intake and output[3].

Application SitOrSquat is used to make travel planning easier. It is so called Restroom Finder, which provides information about location of public toilets located in the vicinity of the user[4]. Kegel Kat and Kegel Nation are two applications, which promote an implementation of Kegel exercises, the later even allows monitoring the frequency of urgency sensation, frequency of incontinence events and bathroom using, as well as number of used urinary pads[5].

Above mentioned apps are designed for both sexes. On the other hand Squeezy Men, which is another application of this kind is and is particularly aimed at men who want to strengthen their pelvic floor muscles to avoid urinary incontinence, erectile dysfunction or premature ejaculation. The program reminds you when to do exercises and maintains a record of the number of completed exercises [43].

Brief comparison of before mentioned and other similar smartphone applications is provided in Table 1.

[1] https://sensortower.com/ios/nl/three-ten-llc/app/idry/545087250/

[2] https://itunes.apple.com/us/app/leakfreeme/id881278706?mt=8

[3] https://itunes.apple.com/us/app/bladder-pal-2/id771198956?mt=8

[4] https://play.google.com/store/apps/details?id=com.charmin.sitorsquat&hl=sl

[5] https://play.google.com/store/apps/details?id=com.bitty.kegelkatfree&hl=sl

TABLE I. COMPARISON OF SMARTPHONE APPLICATIONS

No.	*Application name*	*Features*	*Operating system(s)*
1.	iDry	Tracker, exercises monitoring	Android
2.	LeakFreeMe	Diary, reminders, tracker, exercises monitoring	iOS
3.	BladderPal	Tracker, questionnaire, diary, e-mail export	iOS, Android
4.	SitOrSquat	Maps, search, bookmarks, ratings, Facebook Connect	iOS, Android
5.	Kegel Kat	Diary, audio guide, reminders, instructions	iOS, Android
6.	Kegel Nation	Monitoring (biofeedback), tracker, graph, video guide	iOS
7.	Squeezy Men	Tracker, video and audio guide, diary, tips & tricks	iOS, Android
8.	Prostate Pal 2	Diary, questionnaire, tracker, e-mail export	Android
9.	Bedwetting Tracker	Diary, graph, send e-mail, how-to guide	Android
10.	Senior Incontinence	Quiz	iOS

Smartphone applications allows patients to actively participate in their treatment process, which gives them greater sense of security and control of their health and provides faster and more accurate information about their illness. Furthermore, self-monitoring by using smartphone applications keeps health changes under constant supervision also between doctor appointments, which tremendously reduce the number of needed appointments, lowering travel costs for patients and workload for health care workers [44].

Although mobile technology has many potential advantages, it also has some limitations. The greatest policy concerns of smartphone applications used in broader medical purposes are quality, privacy and safety of gathered data. Another problem, which limit usage of smartphone apps in clinical practice, is information overload. Other drawback is the fact that majority of mobile apps are non-evidence based apps. In some cases there is also access limitations. Mainly elder people are the ones who are facing with urinary incontinence and many of them do not own a smartphone or they cannot consistently use them. This can be a major obstacle to the introduction of mobile applications in clinical practice, since the greatest dropout rate is in the population that is most frequently encounters with urinary incontinence [45].

Even though mentioned apps seem to have a potential to assist in self-monitoring, there are no studies, which would already evaluate and prove their usefulness. This is important aspect for future work.

V. PROPOSED WORK

The incidence of urinary incontinence is increasing proportionally with increasing age of population. It is associated with multiple factors. For primary prevention of urinary incontinence, it is important to identify most prevalent risk factors and strategies, which would help individuals to alter the modifiable risk factors [41].

As seen in previous section, there are applications that are focusing on some segments of personalized therapy and rehabilitation, such as tracking condition or providing exercising support. In this paper we are proposing the digital support framework that addresses all mentioned issues under control of the user. The idea is to monitor different parameters with biosensors using smartphone application and provide the best treatment or preventive measures.

The design and development: the smartphone application will contain three modules:

1. Sensing,
2. Recommendation and
3. Training and Life Alterations.

The sensing module will collect data related to the patient's lifestyle and environment, such as the amount of movement, feet temperature, smoking, ambient temperature and humidity. First, the data will be collected from the smartphone sensors, as well as from commercial sensors, which are worn by the user (e.g. a smart bracelet) or placed in the living area. Secondly, weather data will be collected from the Internet. Thirdly, features that cannot be measured will be inputted manually.

The training module would provide guidance on conservative training techniques. This module will support bladder re-training. We will also implement techniques to control and suppress urgency: relaxation techniques (e.g. slow deep breathing exercises to relax the bladder, distraction techniques in which the patient needs to solve tasks requiring mental concentration, such as Sudoku). The application would monitor the improvement of strength and durability of pelvic floor muscles.

The recommendation module will warn the patient of the negative impact of current factors on incontinence. For example, if cold feet were detected, the patient will be warned that urgency is often associated with cold feet and he/she will be instructed to put on warm shoes.

Also, the recommendation module will give a signal to the user about the time of the liquid last intake in the current day, so the probability of nightly wetting is lessen by far.

All the important data will be sent to the doctor and the modification of the treatment could be done according to the data collected. It is important to detect new patterns that influence urinary incontinence in each individual [46].

The goal is to use the proposed treatment as a part of the regular clinical practice. Assuming the clinical trials adequately demonstrate the efficacy of the treatment and the treatment is taken up by the clinicians who recommend it to their patients, a sizable fraction of the patients could be reached in a relatively short time. A contributing factor to the attractiveness of the proposed treatment is that it is very easy to implement – it requires minimum investment in time and equipment, which would quickly be recouped by the lower cost of treatment.

VI. Conclusion

Urinary incontinence is a medical condition, which is affected by many genetic, lifestyle and environmental factors. Studies of twins have convincingly shown a genetic predisposition for urinary incontinence. The incidence of urinary incontinence is increasing and its severe negative impacts on quality of life, has led to development of different methods of treatment. Today, wide ranges of conservative, pharmacological and surgical treatments are available.

It is very important that the right patient gets the right treatment. Nevertheless, due to individual variations in the causes and extent of disease among individuals, the treatment is often poorly effective and expensive. With the development of personalized medicine, it can be expected that new methods of treatment based on gene therapy will develop. This would make treatments more suitable for each individual, thus allowing better efficacy and limit the progression of the disease. Important part of the personalized medicine is the use of IT tools, especially the mobile applications. The introduced connected health model of a new mobile application has gathered the most helpful functionalities that are supported by medical evidence.

Acknowledgment

This work was supported by TD COST Action TD1405 – "European Network for the Joint Evaluation of Connected Health Technologies" (ENJECT). The authors are thankful to Ms. Alina Morano for proof-reading the paper.

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