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Urinary Incontinence as a Significant Problem in Neurological Diseases

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Abstract

Background: *Urinary incontinence is a common problem among the general population. In patients with neurological diseases, this phenomenon is much more common; its diagnosis and treatment are often overlooked due to other symptoms that are easier to perceive. In neurological diseases, urinary incontinence can have various causes, related to brain damage as well as damage to the peripheral nerves or the spinal cord.*

Objectives: *The aim of this study is to draw attention to the often-overlooked problem of urinary incontinence among neurological patients.*

Material and Methods: *The data was analysed from the many articles available using Google Scholar and PubMed. The mechanisms have been discussed, so that the work is better understood and provides a complete analysis of the problem of urinary incontinence in neurological diseases.*

Results: *Urinary incontinence is an often-overlooked problem associated with neurological diseases. The various mechanisms that lead to urinary incontinence pose a challenge to effective treatment. There are many therapies used in treatment, including drug therapy, neurostimulation, surgery, but also behavioural therapy and treatment of the underlying disease.*

Conclusions: *Due to the various causes of urinary incontinence in patients with neurological diseases, more studies should be done to improve patients' quality of life.*

Key words: *urinary incontinence, neurology, multiple sclerosis, Alzheimer's disease, Parkinson's disease*

Introduction

Urinary incontinence [UI] is defined as the involuntary, uncontrolled leakage of urine from the urethra. Among patients with neurological diseases, this problem is quite common – a meta-analysis showed that the incidence of UI was 50.9% in patients with multiple sclerosis, 52.3% with spinal cord injury, 33.1% with Parkinson's disease and 23.6% with a stroke [1]. According to the International Continence Society (ICS), there are three main types of urinary incontinence: stress urinary incontinence, overactive bladder (or urge incontinence) and mixed incontinence. Stress urinary incontinence is associated with the weakening of the pelvic floor muscles, which do not properly clamp the urethra, while urgent incontinence is caused by abnormal and excessive bladder activity – there is, often a very strong, urgent need to urinate and it usually takes a few seconds to urinate outflow. In the mixed form, we observe both these mechanisms overlapping each other. UI can manifest as a constant leakage of urine, realizing a small amount of urine and a lack or less of an urge to urinate. Risk factors for urinary incontinence include female gender, Caucasian, age, obesity, smoking, pregnancy, natural childbirth, pelvic surgery, pelvic radiotherapy, and neurological diseases.

UI related to neurological causes may result from damage to the brain, peripheral nervous system, or spinal cord. This applies to people with diseases such as multiple sclerosis, Alzheimer's, Parkinson's disease, diabetes, tumours of the central nervous system and congenital spinal defects, or a history of spinal cord injury, spine surgery, stroke, or heavy metal poisoning such as mercury. Drugs used in neurological diseases also contribute to the development of UI (drug-related urinary incontinence) [2]. Urinary incontinence in the course of neurological diseases is often referred to as NLUTD – neurogenic dysfunction of the lower urinary tract (neurogenic bladder). Urine loss in these patients may also be due to factors that impede toilet use, including problems such as cognitive impairment, movement disorders, and deregulated micturition. Adequate diagnosis can be useful in finding the specific location of a neurological impairment [3].

Urinary incontinence is an important disease entity that is a complication of neurological diseases – it is not only a medical challenge, but also significantly worsens the patient's quality of life.

Multiple Sclerosis (MS)

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system that also affects the urinary system, leading to dysfunction of the lower urinary tract (LUT). It is estimated that 8 years after the diagnosis of MS, patients report symptoms of LUT dysfunction [4].

In the course of MS, the myelin sheaths of nerve fibres are lost, mainly in the white matter, manifested as injures (plaques). This process leads to multifocal (disseminated) damage to the brain and spinal cord, and thus to numerous neurological disorders. Clinical symptoms of MS include: paraesthesia, motor weakness, inflammation of the retrobulbar nerve, unsteady gait, dizziness, double vision and urination disorders [5]. The most common manifestation of urinary disorders is urinary incontinence (UI), which, as a factor causing inconvenience in everyday activities and limiting trips, often leads to a reduction in social life and a reduction in Quality of Life (QOL) [6]. In patients with MS, the main reason leading to UI is the lack of control over the muscles responsible for urinary incontinence and the detrusor hyperactivity [7]. It is an often overlooked problem which, if left untreated, may lead to recurrent urinary tract infections, repeated hospitalizations and, moreover, a deterioration of the patient's clinical condition, which is why proper management of these disorders is so important [8].

The selection of appropriate treatment should take into account the patient's mobility, disease phase, manual dexterity, comorbidities and the degree of urinary disorders [4].

Pelvic floor muscle training

Pelvic floor muscle training is of benefit only to patients with preserved pelvic floor muscle contraction. This training activates the reflex inhibiting the

activity of the detrusor muscle with voluntarily contracted pelvic floor muscles [9]. Research on the effectiveness of such treatment is ambiguous due to the small number of patients and the discussion of gender-specific methods [10].

Pharmacological treatment

The choice of pharmacological treatment depends on whether the patient has a problem with voiding or with urine storage [11].

In the treatment of problems with voiding, alpha-blockers are used, which, by inhibiting the action of the sympathetic system on the internal urethral sphincter and the smooth muscle of the bladder neck, reduce the degree of bladder obstruction [12]. In cases of resistance to pharmacological treatment, catheterization or neuromodulation may be proposed.

Antimuscarinic drugs and beta-3 agonists are used in the pharmacological treatment of urine storage problems. By blocking detrusor muscarinic receptors, antimuscarinic drugs inhibit its activation [13]. The use of oxybutynin and solifenacin in urine storage disorders in MS was tested in comparison with a placebo, and an improvement in urination frequency, urinary incontinence and an increase in QoL was demonstrated [14]. Unfortunately, antimuscarinic agents bind non-selectively, which is responsible for the side effects of these drugs: constipation, blurred vision and a dry mouth [15]. A representative of beta-3 receptor agonists is mirabegron, which significantly improves the frequency of urination and incontinence episodes [16].

In pharmacological treatment, desmopressin, Phosphodiesterase Type 5 Inhibitors and Cannabinoids may be considered [17–19]. In case of the ineffectiveness of pharmacological treatment, intravesical treatments may be considered. The most commonly used botulinum toxin inhibits detrusor activity and thus significantly improves QoL and reduces urinary incontinence episodes in MS patients [20]. The most common complications of the procedure were urinary retention and urinary tract infections [21].

The treatment of urinary system disorders in the course of MS includes neuromodulation (stimulation of the tibial nerve, stimulation of the sacral nerve), surgery and catheterization [22].

Alzheimer's disease

Lower urinary tract dysfunction is a common phenomenon in patients with dementia, often accompanied by multiple morbidity and multiple social and economic burdens.

Lower urinary tract symptoms lead to restricted activities of daily life and, consequently, a deterioration in the quality of life of the patients [23]. Urinary incontinence is common in the group of patients with Alzheimer's disease and may lead to numerous complications in the course of this disease [24]. Urinary incontinence in patients with dementia is not only the result of cognitive impairment, but may also result from urological disorders such as detrusor overactivity [23].

Despite the existence of international guidelines for the treatment of urinary incontinence, they often do not address the complex comorbidities of Alzheimer's patients and are rarely followed. Most dementia patients can be successfully treated with standard treatments, both pharmacological and non-pharmacological. The diagnosis of dementia does not exclude the treatment of urinary incontinence, but options may be narrowed in patients with advanced dementia who are unable to understand and remember the information given to them [25].

According to a study conducted by Hae Ri Na et al., the incidence of urinary incontinence in patients with Alzheimer's disease was 24.8%. The most common types of urinary incontinence were urgent urinary incontinence (44.3%) and functional incontinence (25.3%). Urinary incontinence in patients suffering from Alzheimer's disease was clearly correlated with the Barthel scale [26]. A study conducted by Robert L. Grant and colleagues also provided conclusive data; urinary incontinence is three times more common in patients with dementia than in non-demented primary care patients in the UK [27].

Treatment of urinary incontinence in patients with dementia is conditioned by factors such as comorbidities, the use of multi-drug therapy and other urological ailments. The first step of the treatment is behavioural therapy, but this will not be appropriate for all patients. Behavioural programmes such as timed voiding, habit training, and prompted voiding can reduce the

problem of urinary incontinence in cognitive-impaired elderly people. Electrostimulation, biofeedback and pelvic floor muscle exercises are reccomended elderly people without advanced cognitive and physical disorders [22]. Drug treatment should be considered when behavioural therapy is not producing the desired results. The type of treatment depends on whether the patient has problems with urination or storage. Anticholinergic drugs or mirabegron, a beta-3 receptor antagonist, are used to treat urinary incontinence [23]. The mechanism of action of antimuscarinic drugs is to inhibit bladder contraction, while mirabegron, by activating beta-3 adrenergic receptors in the detrusor muscle, results in bladder relaxation and an increase in its capacity [28]. Unfortunately, the use of antimuscarinic drugs in the geriatric population carries the risk of cognitive deterioration due to side effects with long-term use [23]. Cognitive decline is associated with a blockade of the M1 muscarinic receptor in dementia patients who initially have low levels of acetylcholine in the brain [29]. The disturbances resulting from the use of antimuscarinic drugs are reversible upon their withdrawal. However, there are reports that antimuscarinic drugs may lead to an increased risk of dementia [30].

In the case of patients with problems with urination, only alpha-blockers are currently used [22, 23].

Parkinson's disease

With over 6 million cases [31], the second most common neurodegenerative disorder after Alzheimer's belongs to Parkinson's disease (PD) [32]. It is a progressive disorder of the central nervous system that leads to the death of the patient [33]. It has been noticed that its incidence increases with age and is more common for men than women. The aetiology relates to the loss of dopaminergic neurons in the substancia nigra of the midbrain, the occurrence of Lewy bodies inside nerve cells and increased neuroinflammation. Moreover, cholinergic, GABAergic and noradrenergic cells can be damaged, such as the primary ones [34–36].

Diagnosing Parkinson's disease is about examining the patient and knowing the history of his illness because of the heterogeneous nature of this

disorder. Progression can be slow or very rapid depending on each patient [31]. There are typical symptoms of PD normally defined by motor perturbations and disease is typically diagnosed when the first one appears. Many of these include bradykinesia, rest tremor, rigidity of muscles or postural instability [35]. PD also has non-motor symptoms and one of them is urinary incontinence which may occur first, before traditional symptoms [37].

Urinary incontinence (UI) is an embarrassing problem for patients with Parkinson's disease, which significantly affects quality of life [36]. As a neurodegenerative disorder PD impacts the nerve function of the bladder which causes neurogenic bladder dysfunction [38]. Unfortunately this symptom does not always respond to treatment with levodopa which suggests the cause of this problem is complex [39]. Urinary problems also include frequent nocturnal urination, daytime pollakiuria, and urgency [40].

Thirty-eight to 71% of patients with PD complained because of lower urinary tract symptoms [41]. However, it is not possible to conclusively determine whether this problem is due to Parkinson's disease or some other cause. This symptom is also reported by patients with clinically silent cerebral ischemia, with benign prostatic hyperplasia and women with stress urinary incontinence [42, 43].

Videourodynamic examinations, pressure-flow analysis and electromyography have been used to diagnose bladder problems. Patients with PD have reduced bladder capacity with excessive detrusor activity, consisting of phasic and involuntary detrusor contraction, and unstoppable relaxation of the external sphincter due to the voluntary reduction of its electromyographic activity, which usually exists with excessive detrusor activity [43, 44]. The last one may therefore be the main factor of excessive bladder activity [45]. The pressure-flow analysis of the voiding phase in PD shows weak detrusor activity during voiding and a slightly decreased urethral patency [46, 47].

Regarding treatment, levodopa and other antiparkinsonian drugs may affect the way the bladder works. In research with apomorphine and levodopa a positive effect was obtained in the form of bladder enlargement and disturbing symptoms were much less frequent. In others studies switching bromocriptine with pergolide reduced nocturnal urination [48]. However,

the use of dopaminergic drugs can be unpredictable [49]. Parasympatholytics are generally used as the first line treatment of an overactive bladder. They should be taken carefully because too high a dose may cause urine retention [50, 51].

Studies on Studies on pharmacological treatment have also shown the positive effect of mirabegron (β3 adrenergic agonist) on patients with Parkinson's disease. Most of the respondents report improvement in treatment so this drug is safe and effective for them if they are resistant to anticholinergic medications [32].

It is not only drugs that can be used in the treatment of urinary incontinence. Research has shown that behavioural therapy can also have a positive effect. In a randomized study, it was proved that regular pelvic floor exercises, bladder training, and constipation and fluid control management improved the quality of life of patients [52]. In the treatment of urinary incontinence, you can also try deep brain stimulation. It involves stimulation of the globus pallidus pars interna or the nucleus of the hypothalamus. In a twelve-month study, a positive effect was found in urinary retention and the frequency of urination regardless of gender. Unfortunately, the stimulation showed no effect on nocturia and nocturnal urinary intrusion [53].

Brain stroke

Studies imply there is a significant correlation between urinary incontinence (UI) and being a post-stroke patient. Therefore, UI often causes long term disability and may lead to the institutionalization of these patients [54]. We can distinguish full, partial and no UI symptom states. During the acute stage of a stroke the proportions between those three is as follows: 41%, 12%, and 47%. We can observe the change in the 12 following months, where the percentage of full UI drops to 16%, partial UI moves to 16% and no UI grows to 68%. Worth mentioning is the fact that during those 12 months (following the stroke incident) 45% of patients that experienced full or partial UI were institutionalised compared to 5% of patients who developed no symptoms of UI. The logistic regression model shows that we can differentiate three

independent factors creating a higher risk of institutionalizing a patient during the 12 months after a stroke. Those factors are: severe disability at 12 months, age and urinary incontinence at day 7 [55].

These results are confirmed in data collected from a population of unselected stroke survivors, of whom more than 50% experience UI in the acute stage of a stroke. This number drops to one third in the next 12 months. In this case the risk of being institutionalised is also significantly higher for stroke survivors who were incontinent during the acute stage of a stroke [56].

The researchers of urodynamic studies agree that the main cause of post-stroke urinary incontinence is the overactivity of a detrusor. The exact number varies between 28% and 79% [57]. While diagnosing a type of UI it is crucial to conduct a physical exam and study the case history.

The numbers presented above are from one of the few studies from one of the few studies conducted in this field. The authors of those which exist emphasize the need for further investigation of post-stroke UI as well as the risks and symptoms [58]. Furthermore, there is still a lack of data showing the effects of pharmacologic and non-pharmacologic treatments in post-stroke UI patients. Pharmacological treatment includes beta adrenergic medications and antimuscarinics but its use is still experimental. There is also no hard proof of behavioural therapy being effective [59]. Obtaining such data could become crucial in creating treatment allowing post-stroke survivors to elevate their life comfort.

Urinary incontinence can become an issue reducing life quality causing further behavioural disorders. The lack of ability to control the urine flow can discourage a patient from participating in social activities. It may furthermore lead to social distancing and depression [60].

Existing research and collected data support the thesis that assessment of the severity and type of post-stroke urinary incontinence is significant for the patient [55]. Acknowledging the connection between occurrence of the UI in the acute stage of a stroke and the risks it brings should encourage stroke health professionals to study this field more thoroughly [38]. This could create an individually tailored treatment strategy to reduce the symptoms of urinary incontinence.

Discussion

The problem of urinary incontinence in neurological diseases occurs largely in poorly treatable or untreatable conditions. Another link can be seen; the diseases mentioned above have a strong correlation with the age of the patient, namely their incidence increases in increasingly older patients. The exception here may be multiple sclerosis, MS, which primarily affects young people, but also to some extent, stroke, as its occurrence is also associated with comorbidities such as hypertension, atherosclerosis, overweight/obesity. It can be concluded in this situation that stroke is predominantly influenced by an unhealthy diet and static human lifestyle, which can be related to age, although there is an increasing incidence in people in the group of 20–64 years [61, 62].

In developed countries, one can see ongoing social changes such as declining birth rates, increasing wealth, a focus on educating individuals, and increasing life expectancy due to rapid medical advances. The consequence of this is the increasing percentage of elderly people over 65 years old among the citizens of European countries [63]. It can be deduced that incontinence resulting from Alzheimer's, Parkinson's and stroke will increase and become a more and more common problem over the coming years.

In the aforementioned neurological conditions (Alzheimer's disease, Parkinson's disease, stroke and MS), a variety of pharmacological and physiotherapeutic treatments are tested and used. The results of the study are promising, but so far, no fully effective method has been found to eliminate urinary incontinence in seniors, and there are too few data on the effectiveness of treatment methods in the elderly and in people with neurological diseases. Surgical treatment is considered to be an effective method only in the case of stress urinary incontinence [64].

The lack of fully effective treatment methods and the consequent persistent incontinence may lead to episodes of urinary tract infections [65]. A population-based study of 157 men and 322 women aged 85–86 published in 2011 noted that urinary incontinence and cognitive impairment of daily living (ADL) were independent risk factors for urinary tract infection (UTI) in older

adults aged 85–86 years [66]. In addition, a history of urinary tract infections can lead to increased incontinence among women [67]. This is dangerous because, UTI can have a real impact on mortality in elderly people [65].

Reduced quality of life in these patients is also an important consideration. One of the most common conditions of old age, in addition to those mentioned above, is depression. Urinary incontinence can result in decreased life satisfaction, making it a risk factor for depression in seniors [68]. A 2018 study of 510 women with different types of incontinence found that increasing the severity of the condition, not the type of incontinence itself, increased stress, but also anxiety and depression [69]. Additionally, it was noted that in addition to incontinence, Parkinson's disease is also a common comorbidity with depression [70].

Seniors with Alzheimer's, Parkinson's, MS and stroke may have difficulty or be unable to perform activities of daily living, thus requiring additional assistance from others, often family members. Such a relationship can cause a sense of shame and lead to lower self-esteem, but it is also an additional risk factor for skin infections, largely due to poor hygiene of the genitourinary area [71].

The emerging consequences significantly underline the importance of finding and refining a fully effective treatment method that not only eliminates the problem of urinary incontinence, but also indirectly prevents the development and aggravation of other currently serious diseases of old age.

Conclusion

Incontinence is a common problem in patients with neurological diseases, affecting up to 50% of them. UI significantly deteriorates the patient's quality of life. Possible causes of this condition are brain damage caused by the disease, medications and other disorders associated with the disease.

In the course of MS, multifocal damage to the brain and spinal cord results, inter alia, in the lack of control over the muscles responsible for urinary incontinence and detrusor hyperactivity, leading to UI. Alpha-blockers, antimuscarinics, beta-3 agonists, desmopressin, phosphodiesterase type

5 inhibitors, and cannabinoids may be effective in MS patients. In the event of ineffectiveness of pharmacotherapy, neuromodulation, surgery or catheterization can also be used.

Patients with AD suffer from UI due to cognitive impairment and urological disorders such as detrusor overactivity. A problem in the treatment of urinary incontinence in AD patients may be a disturbance in remembering and understanding information. The first step in treatment will be behavioural therapy. In patients with preserved cognitive functions, electrostimulation, biofeedback and pelvic floor muscle exercises can be used. Drug treatment should be considered when behavioural therapy is not producing the desired results. Anticholinergic drugs or mirabegron, beta-3 receptor antagonists, are used in the pharmacotherapy of UI in patients with AD. It should be remembered that antimuscarinic drugs in the geriatric population may contribute to the deterioration of cognitive functions with long-term use.

UI in PD is caused by neurodegeneration affecting bladder function, resulting in neurogenic bladder dysfunction. Patients with PD have reduced bladder capacity with excessive detrusor activity. Treatment with levodopa and anti-Parkinsonian drugs, e.g. apomorphine, bromocriptine and pergolide, had a positive effect on reducing the frequency of disturbing symptoms. Parasympatholytic drugs used in the treatment of an overactive bladder and beta-3 adrenergic agonist mirabegron were also positive. Non-pharmacological treatments for UI include behavioural therapy and deep brain stimulation.

Stroke patients suffer from UI mainly due to detrusor overactivity as a result of brain damage. Pharmacological treatment includes adrenergic and antimuscarinic beta-drugs, but there is no evidence that such treatment is effective in patients after a stroke. There is also no unequivocal evidence of the effectiveness of behavioural therapy in stroke patients with UI.

Due to the high prevalence of the problem, more data should be obtained on possibly effective therapies that could improve the quality of life of neurological patients with UI, such as pharmacotherapy, behavioural therapy, pelvic floor muscle training and deep brain stimulation.

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