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ORIGINAL ARTICLE

Childhood nocturnal enuresis and clinical course of overactive bladder in women

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Abstract

Background. Overactive bladder (OAB) and nocturnal enuresis are among the most common causes of urinary dysfunction in adults and children, respectively. The pathogenesis factors of OAB and nocturnal enuresis largely coincide. Among adults with OAB, a large proportion of patients have a history of nocturnal enuresis.

Aim. To study the features of the clinical course of OAB in women with childhood nocturnal enuresis.

Materials and methods. The study included 212 women with OAB (mean age 54.1±0.8 years), who were divided into two groups depending on the presence of the history of childhood nocturnal enuresis. Group 1 included 41 (19.3%) patients with childhood nocturnal enuresis, group 2 included 171 (80.7%) women without a history of childhood nocturnal enuresis. All patients underwent a comprehensive urodynamic study.

Results. The severity of clinical symptoms of OAB did not differ between patients of groups 1 and 2. Predictors of a more severe clinical course of OAB and a greater likelihood of developing urge incontinence were the presence of a non-monosymptomatic form of enuresis and an age of cessation of enuresis of 10 years or older. Women from group 1 also showed a higher incidence of detrusor overactivity compared to group 2 (29.3% vs 10.5%).

Conclusion. The results of the study indicate a connection between childhood nocturnal enuresis and the clinical course of OAB in adult women.

Keywords: overactive bladder, detrusor overactivity, nocturnal enuresis, urge incontinence

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ОРИГИНАЛЬНАЯ СТАТЬЯ

Энурез в детстве и клиническое течение гиперактивного мочевого пузыря у женщин

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Аннотация

Обоснование. Гиперактивный мочевой пузырь (ГМП) и энурез – одни из самых частых причин нарушения мочеиспускания соответственно у взрослых и детей. Факторы патогенеза ГМП и энуреза во многом совпадают. Среди взрослых с ГМП большая доля пациентов с энурезом в анамнезе.

Цель. Изучить особенности клинического течения ГМП у женщин с энурезом в детстве.

Материалы и методы. В исследование включены 212 женщин с ГМП (средний возраст 54,1±0,8 года), которые в зависимости от наличия энуреза в детстве были разделены на 2 группы. В 1-ю группу включена 41 (19,3%) больная с энурезом в детстве, во 2-ю группу – 171 (80,7%) женщина без энуреза в анамнезе. Всем больным выполняли комплексное уродинамические исследование.

Результаты. Выраженность клинических симптомов ГМП не различалась у больных 1 и 2-й групп. Предикторами более тяжелого клинического течения ГМП и большей вероятности развития ургентного недержания мочи были наличие немоносимптомной формы энуреза и возраст прекращения энуреза 10 лет и старше. У женщин из 1-й группы также отмечена большая частота выявления детрузорной гиперактивности по сравнению со 2-й группой (29,3% vs 10,5%).

Заключение. Результаты проведенного исследования свидетельствуют о наличии связи между энурезом в детстве и клиническим течением ГМП у взрослых женщин.

Ключевые слова: гиперактивный мочевой пузырь, детрузорная гиперактивность, энурез, ургентное недержание мочи

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Introduction

Hyperactive bladder (HAB) is a disorder of the reservoir function of the bladder, manifested by imperative urges to urinate with or without urgent urinary incontinence (UI) and most often accom-panied by increased urination in the absence of infectious and other evident bladder disorders [1]. In contrast to detrusor hyperactivity, which is detected during urodynamic examination, HAB is diag-nosed based on clinical presentation. The prevalence of HAB is high, ranging from 15% to 28% in adult females, by various estimates, exceeding that in males [2].

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HAB and urinary tract infections are the two most common causes of urinary disorders in women [3]. HAB symptoms negatively im-pact almost all aspects of patients' quality of life.

The onset of HAB symptoms may be due to various neurological diseases, and in their absence, this condition is considered idiopathic. Many studies investigated the causes of this type of HAB, but no complete clarity on this issue has yet been achieved. It is clear that HAB has a pathogenetic diversity. Metabolic syndrome, emotional and affective disorders, deficiency of sex hormones, chang-es in the urine microbiota, and subclinical dysfunctions of the autonomic nervous system are consid-ered relevant factors in the HAB pathogenesis in females [4].

In the HAB development, the role of hereditary factors in the pathogenesis of another condition—enuresis, is not excluded [5]. Enuresis referred to UI during night sleep at the age when control over urinary tract function should be established, i.e., older than 5 years [6, 7]. The prevalence of enuresis in the general population of 5-year-old children is 15–20% and decreases by about 15% per year; the prevalence of enuresis in adults is estimated at 0.5-1.5% [7–9]. The main causes of enuresis are de-layed maturation of the central nervous system, bladder dysfunction, in particular, a decrease in its capacity and an increase in contractile activity, sleep and awakening disorders, an abnormal circadi-an rhythm of antidiuretic hormone secretion, and all these factors can be combined and be genetical-ly determined [7, 10].

Many factors in the pathogenesis of enuresis and HAB in adults overlap. Therefore, studying the association between enuresis and the clinical course of HAB in adults is relevant.

The objective of the study is to investigate the features of the clinical course of HAB in adult fe-males with a history of enuresis in childhood.

Materials and methods

The study included 212 females with HAB (mean age 54.1±0.8 years), 136 (64.1%) of whom had urgent UI. The mean age of onset of HAB symptoms was 47.0±0.9 years, and the mean duration at baseline was 6.9±0.4 years. In this study, we used the definition of HAB recommended by the International Continence Society (ICS) [1] and included only those patients who could accurately answer questions about the presence or absence of enuresis in childhood. Non-inclusion criteria were acute or exacerbation of recurrent lower urinary tract infections, impaired outflow of urine from the blad-der, stress UI, neurogenic urinary dysfunction, chronic pelvic pain syndrome, history of botulinum therapy and pelvic surgery, receiving of drugs affecting the function of the lower urinary tract less than 2 weeks before the assessment, and polyuria.

All patients had a comprehensive urological examination to exclude any other conditions that could affect the function of the lower urinary tract. When taking a medical history, special attention was paid to the presence of enuresis in childhood and the age of its ending. The severity of symp-toms was assessed based on the assessment of urination diaries completed by patients for 3 consecutive days. The frequency of urination, urgency, and episodes of UI were recorded in these diaries. All patients had a comprehensive urodynamic assessment following the recommendations of the ICS Standardization Committee [11].

Patients were divided into two groups depending on the presence of enuresis in childhood. Group 1 (n=41, 19.3%) included HAB patients with a history of enuresis at the age of 5 years and older, and group 2 (n=171, 80.7%) included HAB patients without a history of enuresis.

Statistical analysis of the data obtained was performed using specialized software packages Excel and Statistics 12.0. The results of the calculations are presented as M±m for numerical indicators and n (%) for frequency values. The parametric Student's test was used to assess the significance of the difference in the mean values. The statistical significance of the frequency difference was as-sessed using the χ^2 test. The statistical null hypothesis of no differences and correlations was rejected at $p<0.05$.

Table 1. Severity of HAB symptoms in women depending on a history of enuresis in child-hood, M±m (n=212)

Parameter	Group 1 (n=41)	Group 2 (n=171)
The number of urinations for 3 days	36.2±1.8	36.6±1.0
The number of imperative urges for urination for 3 days	8.1±1.2	9.9±0.7
The number of urgent UI episodes for 3 days	3.4±0.9	3.3±0.4

Note. For all pairs of features, the differences are statistically insignificant ($p>0.1$).

Results

At the time of the assessment, enuresis symptoms were observed only in 3 (7.3%) patients of group 1. In the remaining 38 (92.7%) patients, enuresis stopped at the age of 6 to 16 and in 25 (65.8%) at the age of 10 or younger.

The clinical manifestations of HAB (frequent urination and imperative urge to urinate with or without urgent UI) since childhood, from at least 5 years of age, were reported in 36 (17.0%) of 212 female patients with HAB: 21 of 41 (51.2%) in group 1 and 15 of 171 (8.8%) in group 2, the dif-ference was statistically significant ($\chi^2=42.27$; $p<0.001$). The presence of other symptoms, in addi-tion to nocturnal UI, indicates a non-monosymptomatic form of enuresis. Nineteen (90.5%) of 21 such patients in adulthood had urgent UI, whereas only 9 (60%) of 15 patients with monosymp-tomatic enuresis had urgent UI ($\chi^2=4.7$; $p=0.031$). The data presented shows an association between the form of enuresis in childhood and the clinical course of HAB in adults.

However, the enuresis itself in childhood did not affect the frequency of urgent UI in adult women with HAB. Enuresis in childhood was reported by 27 (19.8%) of 136 patients with HAB with urgent UI and 14 (18.4%) of 76 patients with HAB without urgent UI ($p>0.1$). Also, there were no differ-ences in the severity of the main clinical symptoms of HAB: the frequency of urination, imperative urges, and episodes of urgent UI. These conclusions are supported by the data of urination diaries presented in Table 1.

The study compared the results of urodynamic tests in women with HAB depending on a history of enuresis in childhood (Table 2).

The values of cystometric parameters characterizing the bladder sensitivity (bladder capacity at the time of the appearance of the first, normal, and strong urge to urinate and maximum cystometric capacity) did not differ significantly in patients of groups 1 and 2. However, differences in parame-ters related to the detrusor's involuntary activity were found. More Group 1 patients than Group 2 had detrusor hyperactivity and a higher detrusor pressure during the first involuntary detrusor con-traction (IDC). There were no differences between the two groups in the remaining IDC parameters.

The next stage of the study was to analyze the effect of the age of enuresis ending in childhood on the clinical course of HAB. Of 41 HAB patients with childhood enuresis, 38 (92.7%) had nocturnal UI stopped between 6 and 16 years of age, and only in 3 (7.3%) subjects did it persist during adult-hood. The age of the enuresis ending in the 38 patients was 9.9±1.2 years. Of these 38 patients, ur-gent UI was observed in 26 (68.4%), and HAB without urgent UI was reported in 12 (31.6%). De-pending on the presence or absence of urgent UI in adulthood, these patients were divided into two subgroups, 1A and 1B, respectively. Figure 1 presents data on the age of the enuresis

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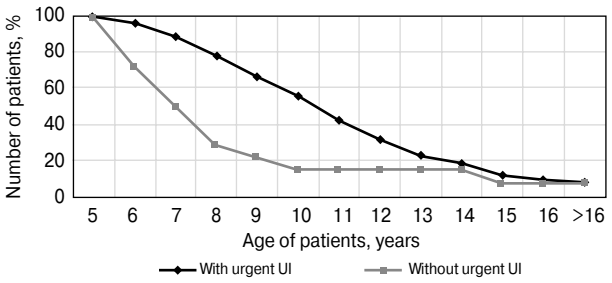
Table 2. Results of urodynamic tests in women with HAB of groups 1 and 2, M±m

Parameter	Group 1 (n=41)	Group 2 (n=171)	*p*
Bladder sensitivity indicators (n=212)			
Bladder volume at the first urge to uri-nate, mL	68.5±5.3	69.0±3.0	>0.1
Bladder volume at the normal urge to urinate, mL	102.3±5.7	104.9±3.4	>0.1
Bladder volume at the strong urge to urinate, mL	148.6±7.9	155.0±4.3	>0.1
Maximum cystomet-ric capacity of the bladder, mL	203.4±8.8	205.6±4.5	>0.1
Indicators of detrusor contractile activity during the filling phase (n=30)			
Detrusor hyperactivi-ty, n (%)	12 (29.3)	18 (10.5)	χ^2=9.56; *p*=0.002
Bladder filling vol-ume at the first IDC, mL	69.1±5.9	72.3±6.1	>0.1
Bladder filling vol-ume at maximum IDC, mL	147.5±6.2	150.8±6.0	>0.1
Detrusor pressure at the first IDC, cm H_2O	47.2±3.5	36.6±3.8	*t*=2.05; *p*=0.045
Detrusor pressure at maximum ICD, cm H_2O	52.2±4.0	43.4±3.9	>0.1

Fig. 1. The number of patients with enuresis in different age periods, depending on the presence (1A) or absence (1B) of urgent UI subsequently (n=38).



ending in these two subgroups. Fifteen (57.7%) of the 26 patients in subgroup 1A had enuresis stopped before the age of 10 versus 10 (83.3%) of the 12 patients in subgroup 1B. Thus, we noted the following pattern: the later the enuresis stopped in childhood, the higher the probability of urgent UI as a symptom of HAB. The later age of the enuresis ending was also associated with a more severe urgent UI. It was evidenced by the results of the correlation analysis, which showed a positive correlation between the age of the enuresis ending and the frequency of urgent UI in adult females with HAB (r=0.38; $p<0.05$).

Discussion

Many studies investigated the association between functional disorders of the lower urinary tract in children, including enuresis, and urinary disorders in adults. Most of them addressed the effect of enuresis on the risk of nocturia in adults. The relationship between these two conditions can be con-sidered proven [12, 13]. Bladder dysfunctions and nocturnal polyuria are considered possible causes of nocturia in adults with a history of enuresis [14, 15]. Many studies have also investigated the as-sociation between enuresis and the development of HAB in adults. Most studies clearly indicate the presence of this association [16–18]. M. Fitzgerald et al. (2006), in an extensive study involving 2,109 women aged 40 to 69 years, showed a higher incidence of HAB in adults with a history of enu-resis in childhood [17]. Similar data were reported by A. Foldspang et al. (1994), who interviewed 2,613 respondents and found a greater probability of urgent UI in women with enuresis in childhood [16]. However, other authors do not link the very fact of the presence of enuresis in childhood with the occurrence of HAB symptoms in adults, indicating a more complex relationship between these two conditions [19]. Our study did not analyze the probability of HAB in patients with enuresis in childhood. However, we investigated the features of HAB clinical courses in those with and without a history of nocturnal UI in childhood. Although in our study, the prevalence of enuresis in patients with HAB was 19.3%, which is higher than in the general population, we did not find evidence of the effect of the history of enuresis itself on the clinical course of HAB. The prevalence of enuresis in females with HAB with and without urgent UI was almost the same: 19.8% and 18.4%, respec-tively. Also, there were no differences in the severity of HAB symptoms (frequency of urination, imperative urge to urinate, and episodes of urgent UI), depending on the history of enuresis. Howev-er, we identified the characteristics of enuresis, which can be considered predictors of a more severe course of HAB in women. Firstly, it is non-monosymptomatic enuresis. It was shown that in this type of enuresis, the probability of urgent UI in women with HAB is significantly higher than in the mon-osymptomatic type: 90.5% and 60%, respectively. The second important factor was the age at which enuresis ended. Thus, urgent UI complicated the clinical course of HAB in 57.7% of women if the enuresis stopped before the age of 10 versus 83.3% if it stopped at the age of 10 or older. We also found a significant positive correlation between the age of the enuresis ending and the frequency of urgent UI.

Our results are similar to those reported by S. Akashi et al. (2014). On a large clinical sample (2,555 subjects), the authors showed that the risk of HAB and the severity of its clinical manifesta-tions increase if enuresis did not stop before the age of 12 [20]. According to D. Kuh et al. (1999), an important predictor of the HAB is the severity of enuresis. The authors showed that women who, at the age of 6 years, had nocturnal enuresis episodes several times a week were more likely to develop urgent UI than patients who had only rare episodes of nocturnal urine leakage in childhood [21].

We obtained interesting data when analyzing the results of urodynamic tests in HAB patients with and without enuresis in childhood. On the one hand, the bladder sensitivity was almost the same in patients of these two groups; however, in women with a history of enuresis, there was a significantly higher frequency of detrusor hyperactivity compared to those without enuresis: 29.3% and 10.5%, respectively. On the other hand, enuresis in childhood was reported in 40% of women with detrusor hyperactivity and only in 10.1% of those without it. In addition, the IDC amplitude was higher in patients with enuresis. Our data on the association between increased contractile activity of the de-trusor in women with HAB and enuresis in childhood aligns with the results previously reported in other studies. Thus, K. Moore et al. (1991) found that 38% of women with urodynamically proven detrusor hyperactivity had enuresis in childhood [22]. According to S. Gong et al. (2021), detrusor hyperactivity in patients with enuresis in childhood is a consequence of bladder function dysregula-tion, which is congenital and persists throughout life [13]. A. Foldspang et al. (1994) reported a simi-lar point of view and associated bladder dysfunctions in adults with a history of enuresis with a de-trusor inhibition deficiency [16].

Some authors consider the higher incidence of HAB in adults with enuresis in childhood a conse-quence not only of congenital disorders but also of greater susceptibility of the urinary tract to vari-ous pathological factors associated with aging. The most significant include bladder wall ischemia, chronic inflammation, and age-related hormonal changes [23–

26]. In this regard, one cannot but agree with the opinion of A. Goessaert et al. (2014) that ending childhood enuresis does not mean eliminating abnormalities that contributed to its development [18].

Therefore, based on our results, it can be assumed that a history of enuresis in childhood is a risk factor for the increased detrusor contractile activity manifested by detrusor hyperactivity. Given the fact that enuresis is a genetically determined condition, it is likely that the involuntary detrusor ac-tivity is also genetically determined, at least in some patients. The connection between the age of enuresis ending and the occurrence of urgent UI can be explained by the fact that the basis for de-veloping enuresis and HAB are fundamentally the same mechanisms—a dysregulation of the blad-der functional activity in the filling phase. In addition, the more severe this disorder, the later the urinary reflex normalizes and enuresis stops. However, such patients remain predisposed to HAB in adulthood. In addition to the greater risk of HAB in patients with enuresis in childhood, the disease is more severe and more often associated with urgent UI.

Conclusion

The study results show an association between childhood enuresis and HAB's clinical course in adult women. Urgent UI, which determines the more severe HAB symptoms, more often develops in patients with non-monosymptomatic enuresis and with a later ending of nocturnal UI. The data ob-tained contribute to a more complete understanding of the HAB pathogenesis. Further research is needed, particularly the study of the effectiveness of various methods of HAB treatment, depending on the history of enuresis.

Disclosure of interest. The authors declare that they have no competing interests.

Раскрытие интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Authors' contribution. The authors declare the compliance of their authorship according to the international ICMJE criteria. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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Ethics approval. The study was approved by the local ethics committee. The approval and procedure for the protocol were obtained in accordance with the principles of the Declaration of Helsinki.

Соответствие принципам этики. Протокол исследования был одобрен локальным этическим комитетом. Одобрение и процедуру проведения протокола получали по принципам Хельсинкской декларации.

Consent for publication. Written consent was obtained from the patients for publication of relevant medical information and all of accompanying images within the manuscript.

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