EFFICACY OF VARIOUS MODES OF THERAPY OF THE URGE URINARY INCONTINENCE IN WOMEN

The estimation of the efficacy of monotherapy with M-cholinolytics and combined therapy of M-cholinolytics with α1-adrenoblockers in the urge urinary incontinence (UI) in women was performed in this study. It was established that the results achieved during 3 months of follow-up were comparable in the both modes of therapy. Inclusion of α1-adrenoblockers into the scheme of therapy did not trigger intensity of the urine, and, however, allowed to achieve increase in period of remission in this disease in comparison with monotherapy.

ASILBEK GAYBULLAEV, ABDUMALIK ABDURIZAEV, FARRUH SARIMOV
Department of Urology, Tashkent Institute of Postgraduate Medical Education, Uzbekistan

Keywords: Incontinence, female, medicaments therapy

UDC: 616.62-008.22-085

Introduction

The urge urinary incontinence is world-wide and at the same time unresolved problem. According to the data of SIFO Group Survey 16% of population at the age above 40 years have symptoms of the hyperactive detrusor muscle function including 5% at the age 40-45 years, and 75% at the age above 75 years (Abrams, Cardozo, Khoury, and Wein, 2009). The urge urinary incontinence is the frequent state among the patients of all age and social groups. Development of disease results in significant worsening of the quality of life and so this problem has not only medical but also social context (Romikh, Apolihiina and Andikyan, 2004; Danilov, Volnyh, Abdullaeva, and Danilova, 2004).

The leading place in the medicamentous treatment of the urge urinary incontinence belongs to M-cholinolytics (Mazo and Krivoborodov, 2004; Schröder, Abrams, Andersson, Artibani et al., 2009). However, during use of anticholinergic preparations in some patients the adverse effects were noted, that requires stopping of treatment. It should be taking into consideration that there are occurred not seldom forms of urinary incontinence without response to the use of common medicamentous therapy and as a result - the disease has become a long chronic pathology. The main trend, characterizing modern approach to using of M-cholinolytics, is a change the dosage and dose mode for the reason reductions amount side effect (Lai, Boone and Appell, 2002).

Vishnevskiy and Danilov (2005) suggest the help to these patients could be more adequate if some preparations having good tolerability and efficacy would be presented for treatment of the urge urinary incontinence. Recently, the suggestion was brought forth about abilities of α1-adrenoblockers to act upon touch bladder neurons (Sellers and McKay, 2007).

It is of interest of efficiency of the complex treatment with preparations, influencing upon parasympathetic activity of the bladder. Will lead this to reinforcement their clinical effect?

In this connection the purpose of this study was to assess efficacy of various modes of medicamentous therapy concluded in monotherapy with M-cholinolytics and combined therapy of M-cholinolytics with α1-adrenoblockers in the urge urinary incontinence.
Material and methods

We have performed open comparative clinical study of the efficacy of monotherapy with M-cholinolytics and combined therapy including M-cholinolytics and α1-adrenoblockers for urge urinary incontinence in women under outpatient observation.

The patients were divided into 2 groups in relation to the method of treatment. Group 1 included 20 women with urge urinary incontinence, which was prescribed monotherapy with Driptan. Group 2 receiving combined therapy comprised 20 women with identical diagnosis.

The drug Driptan (oxybutynin hydrochloride) was chosen as M-cholinolytic preparation. And we used Focusin (tamsulosin), uroselective blocker of alpha-IA and alpha-ID adrenoreceptors, as α1-adrenoblocker.

Monotherapy with Driptan was performed in dose 5 mg 3 times a day for 3 months. In the combined therapy Driptan was prescribed in dose 5 mg 3 times a day, and Focusin was used in single dose 0.4 mg a day. The duration of therapy was also 3 months in group 2.

Beside patient comprised of study was received information consent.

Diagnosis of urinary incontinence in women was made according to the algorithm of the primary management of the women with urinary incontinence of the European Association of the Urologists (Guidelines EAU, 2009). The health state of the patients was evaluated before onset of therapy, after receiving of preparation and 3 months later the finishing of treatment.

The clinical picture of urinary incontinence was estimated with use of standard questionnaire ICIQ-SF proposed by European Association of Urologists. The patients had the diary of urination as well as they were performed urodynamic examinations at each stage of investigation. For exclusion of diseases which may stimulate the urge urinary incontinence the patients were also performed microscopic investigation of 1 ml sediment of urine middle portion, ultrasound scanning of the urinary tract, physical examination of the external genitalia, blood examination for sugar.

Statistical interpretation of the results obtained was performed for purposes to treat.

Results and discussion

Analysis of the results of tests performed before the beginning of therapy showed that in the comparable groups there was not achieved statistical significance in any studied parameters. (P>0.05). Thus, analysis of answers obtained for questionnaire ICIQ-SF revealed that frequency of the episodes of urinary incontinence in the first group was 3.1±0.2 and in the second - 3.9±0.1 times a day. The volume of urine being lost in group 1 was 2.8±0.2 and in group 2 -3.2±0.3. The assessment of the effect of urine incontinence on the quality of life by ten-point system showed that before treatment this parameter in the first group was, on the average, 6.5±0.3 and in the second group - 7.2±0.5 points.

Study of the data obtained from recordings in the dairy of urination before beginning of therapy revealed that the number of urinations a day in the patients receiving monotherapy with Driptan, on the average, was 14.0±0.5 times, and in the group of patients receiving combined therapy, 13.0±0.6 times. The episodes of urinary incontinence according to the data of dairy of urination was, on the average, 9.9±2.5 times in group 1, and 7.5±1.5 times in group 2. The mean minimal volume of the urine loss in urination in group 1 was 23.0±1.5 ml and 23.0±1.7 ml in group 2. Maximum volume of urine loss in group 1 was, on the average 191.0±9 ml, and in group 2 - 190±8.1 ml.

Urodynamic examinations showed, that mean velocity of urination before treatment in the compared groups had no reliable differences and was 14.1±1.6 ml/sec and 14.3±1.7 ml/sec, respectively, in group 1 and 2.
The parameters of cystometry in the compared groups were also not differed before treatment. Thus, the first urge to void urine occurred in administration of fluid, on the average, 34.7±2.0 ml into the bladder in the group receiving the further monotherapy with Driptan, and 34.2±1.9 ml of fluid in group of combined therapy. The strong urge to void urine occurred in 212.3±12.6 ml and 216.6±12.7 ml in the both groups, respectively.

After finishing of the course of therapy in the patients of the both groups there was noted significant improvement of the state in comparison with initial data. Thus, the frequency of episodes of urinary incontinence in group of patients receiving monotherapy with Driptan, decreased by 45.1%, the value of volume of urine loss reduced by 46.4%, detrimental effect of urinary incontinence on the quality of life attenuated by 45.8% (P<0.05). The urinary incontinence after treatment was fully cured in 4 patients, and the mixed urinary incontinence was still preserved, but of less degree, in 16 women.

Significant positive dynamics was noted in analysis of the findings from dairy of urinations. For example, the mean number of urinations decreased by 30%, episodes of urinary incontinence - by 72.7%. The mean parameter of minimal volume of urine loss increased twice as much and was 70±7.4 ml, and parameter of the maximum volume of urine loss also increased, but of less degree, and, on the average, was 328.0±27.0 ml (P<0.05).

The mean velocity of the urination after 3 months of therapy in the group of patients receiving monotherapy with Driptan decreased to 13.7±1.3 ml/sec and had no statistically significant difference with initial parameter. However, the findings of cystometry at the end of therapy showed statistically significant difference in comparison with initial parameters (P<0.05). Thus, the volume of fluid inducing the first urge for urination increased by 88.4% and that is 65.4±1.5 ml. The volume of fluid, inducing the strong urge to void urine, became increased - by 50.8%, and, on the average, achieved 320.2±12.8 ml.

In the group of patients who were performed combined therapy the frequency of episodes of urinary incontinence reduced by 69.2% and had statistically significant difference (P>0.05). The volume of urine loss decreased by 62.5%, and degree of negative influence of urinary incontinence on the quality of life in combined therapy decreased by 78.2% (P>0.05). After treatment the urinary incontinence was cured in 5 patients and preserved as urge urinary incontinence in 15 women.

As in the compared group in this period of observation the analysis of dairy parameters of urination demonstrated favourable dynamics. The mean numbers of urinations decreased by 40.7%, episodes of urinary incontinence - by 78.6%. The mean indicator of minimal volume of the urine loss increased to 78.0±8.5 ml, the mean value of maximum volume of the urine loss grew up to 383.0±23 ml. These changes had statistically reliable difference in comparison with the initial characteristics (P<0.05).

The urodynamic changes in the group of patients receiving combined therapy were analogue the characteristics in group of women receiving monotherapy.

The mean velocity of urination after 3 months of therapy in the group of patients having combined therapy decreased to 14.1±1.3 ml/sec, and had no statistically significant difference with initial parameter. The findings of cystometry at the end of therapy as in the first group, showed statistically significant difference in comparison with the initial characteristics. Thus, the volume of fluid inducing the first urge to void urine increased in two and became equal, on the average, 70.1±1.6 ml. The volume of fluid inducing strong increased by 64.4%, and, on the average, was 355.2±14.8 ml.

The assessed parameters in the compared groups were significantly differed 3 months after therapy.

The frequency of episodes of the urinary incontinence in the group of patients having monotherapy with Driptan returned to the initial value and was, on the average, 3.1±0.2 points, the volume of the urine loss increased to 2.5±0.2 points, effect of urinary incontinence on the quality of life increased to 6.7±0.3 points.
These parameters had no statistically significant difference in comparison with the initial values (P>0.05), and, on the contrary, reliably differed from parameters obtained immediately after ending of the therapy (P<0.05). In all the patients the episodes of the urge urinary incontinence were noted again.

Analysis of the dairy of the urinations in this period showed that the mean number of urinations and episodes of urinary incontinence increased in comparison with findings at the moment of the ending of therapy, and was 13.0±0.5 and 5.6±1.0, respectively. These values had no statistically significant difference with initial parameters (P>0.05). The mean parameters of minimal and maximum volumes of the urine discharged were not differed from the initial findings.

The same situation observed among the findings of cystometry. Thus, the first urge to void urine occurred at administration, on the average, of 37.7±1.3 ml of fluid, and the strong urge to void urine occurred in the mean volume of fluid administered 200.3±12.1 ml. The mean velocity of urination after 3 months of therapy in the group of patients receiving monotherapy with Driptan was 14.0±1.3 ml/sec and had no statistically significant difference with the initial parameter.

The other picture was noted in group of patients receiving combined therapy. In this group of women the analysis of results of interviews according to ICIQ-SF revealed absence of statistically significant difference with parameters obtained at the end of 3-month course of therapy (P>0.05). The frequency of the episodes of urinary incontinence preserved at the level 1.6±0.3, and the volume of urine loss – 1.8±0.3 ml. The negative effect of the urinary incontinence on the quality of life continued to stay at the level achieved at the end of therapy and, on the average, was 2.8±0.6 points. After 3 months of finishing therapy 4 patients continued to stay “dry”, and in 16 women the urge urinary incontinence preserved.

The study of the records in the voiding diary showed that after 3 months of therapy ending in the patients receiving combined therapy the mean number of voiding and episodes of urinary incontinence had no statistically reliable changes in comparison with data obtained at the moment of the ending of therapy and were 8.8±0.5 and 3.5±1.8, respectively (P>0.05). The mean values of minimal and maximum volumes of urine loss were also without changes in comparison with characteristics obtained at the finishing of 3-month course therapy.

The mean velocity of urination after 3 months of therapy in the group of patients having combined therapy, on the average, was 13.9±1.3 ml/sec, and had no statistically reliable difference in comparison both with initial parameters and parameters obtained at the end of therapy (P>0.05). The findings of cystometry at this period of observation did not differ from the measurements at the end of therapy (P>0.05). Thus, the first urge to void urine occurred during administration of fluid 65.3±1.4 ml, and the strong urge to void urine appeared at the mean volume of fluid administered 328.6±14.0 ml.

The examinations performed showed that the 3-month courses as monotherapy with M-cholinolytics, so as combined therapy including M-cholinolytics and α1-adrenoblockers, in women with the urge urinary incontinence did not differ in relation to efficacy. Particularly, results obtained during answering the questionnaires by patients of the compared groups after therapy finishing showed that practically there were no statistic reliable differences between all parameters. However, it was interesting that in combined therapy including prescription of α1-adrenoblockers, there were not found increase in episodes of the urge urinary incontinence. That is α1-adrenoblockers did not result in aggravation of the patients’ health state. Urodynamic findings and characteristics, obtained from the data of voiding diary, had no statistically reliable difference, too.

However, even 3 months after finishing of therapy the results of compared groups had statistically significant differences between them. And the women receiving combined therapy had more favorable condition. Comparative analysis of the results obtained during this period of observation showed that in group 1 all measured findings were closed to the
initial data. That is, three months after ending of monotherapy effect of the treatment was absent and the patients had recurrence of disease. On the contrary, in group 2 even three months after ending of monotherapy the measured values were at the level of data obtained at the end of therapy. Therefore, the use of combined therapy allowed increase of the period of remission in these patients.

**Conclusion**

Thus, on the basis of the results obtained we may conclude about efficacy of the both comparable modes of therapy in imperative urinary incontinence. However, combined therapy including M-cholinolytics in combination with α1-adrenoblockers provided double increase the period of remission in women with imperative urinary incontinence after ending of the course of therapy. This can be useful for patients, which cannot get the long treatment M-cholinolytics because of their side effect. Additional studies need for determination of optimum length of the treatment and dose mode for achievement of the best result.

**References**


