EVALUATION OF VESICOURETERAL REFLUX IN NEUROGENIC BLADDER DYSFUNCTION AND CHOICE OF TREATMENT STRATEGY

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Summary

The aim of the research is to enhance the treatment outcomes of vesicoureteral reflux (VUR) that arises in the context of neurogenic bladder dysfunction (NBD) by developing a systematically justified approach for selecting treatment strategies for patients and improving existing treatment methods accordingly.

Materials and methods. A clinical examination was conducted on 279 patients with vesicoureteral reflux (VUR) that occurred in the context of neurogenic bladder dysfunction (NBD). Out of these, 87 patients received conservative treatment. The study design employed was a longitudinal (prospective) case-control study. Randomization was not used. Inclusion criteria required the presence of VUR in patients concurrently with NBD. Patients with Grade V VUR were excluded from the study. Clinical and laboratory manifestations of VUR and its complications were studied and assessed. A comprehensive evaluation of the severity of VUR and treatment effectiveness was performed. Patients were divided into three groups based on the proposed system «Method for a Comprehensive Assessment of the Severity of Vesicoureteral Reflux Disease and Treatment Effectiveness.»

Results. Vesicoureteral reflux (VUR) was most frequently observed in patients between the ages of 6 and 10, constituting 44.4 % of the cases. VUR of Grade III-IV was more commonly diagnosed in patients under 5 years of age. Complaints related to urinary disorders tended to decrease or disappear with age (t= –0.1533; p=0.010). As patients grew older (after 7-8 years), the frequency of pyelonephritis exacerbations decreased (t= –0.1344; p=0.025). However, dilatation of the upper urinary tract (t=0.2157; p=0.001) and deterioration of kidney function (t=0.2354; p=0.001) were observed more frequently. Inflammation of the urinary tract occurred more frequently in women (t=0.1419; p=0.018), while renal function impairment due to VUR was more common in men (t=–0.1733; p=0.004).

Conclusions. Most clinical and laboratory manifestations of vesicoureteral reflux (VUR) do not correlate with its grade. A reverse correlation was found between the grade of VUR and age, and a direct correlation with leukocyturia. Urinary disorders, leukocyturia, and the frequency of pyelonephritis exacerbations are components of VUR’s clinical presentation that affect the quality of life and are among the first to change due to treatment, primarily through the normalization of bladder function. Clinical manifestations and complications of VUR negatively impact the quality of life in 66.2 % of patients. The assessment of treatment effectiveness takes into account the grade of VUR and the complex of main clinical manifestations and complications, which can be considered using the proposed system «Method for a Comprehensive Assessment of the Severity of Vesicoureteral Reflux Disease and Treatment Effectiveness.»

Keywords: vesicoureteral reflux, neurogenic bladder, neurogenic bladder dysfunction
the quality of life of individuals. [3] The main goals of neurogenic lower urinary tract dysfunction management are preventing upper urinary tract damage, improving continence, and quality of life [6]. Although some argue that vesicoureteral reflux is a «phenotype» that often resolves without intervention, others contend that untreated reflux has the potential to cause irreversible renal damage over time [4]. Opinions vary regarding the diagnosis and treatment of vesicoureteral reflux, and diagnostic procedures remain debatable. [5] There continues to be a need for high-quality studies that assess bladder-related Quality of life (QOL) before and after interventions in different urologery populations, and studies that elucidate changes in QOL during the course of neurologic diseases [7]. As a result of this approach, the treatment outcomes for VUR in the presence of NBD are not always satisfactory [8]. Furthermore, there is a lack of a comprehensive assessment system for VUR and its treatment outcomes, which complicates the objective evaluation when comparing different treatment methods and makes it challenging to justify the selection of a specific therapeutic approach. Treatment depends on the cause and severity [9].

The aim of the research is to enhance the treatment outcomes of vesicoureteral reflux (VUR) that arises in the context of neurogenic bladder dysfunction (NBD) by developing a systematically justified approach for selecting treatment strategies for patients and improving existing treatment methods accordingly.

This study is based on the results of comprehensive clinical examinations of 279 patients with vesicoureteral reflux (VUR) occurring in the context of neurogenic bladder dysfunction (NBD), and the conservative treatment of 87 patients. The research design employed a longitudinal approach (prospective case-control study). Randomization was not utilized. Inclusion criteria for the study were the presence of both vesicoureteral reflux and neurogenic bladder dysfunction in patients. Patients with Grade V VUR (according to the classification by P. E. Heikel and K. V. Parkkulainen), signs of infravesical obstruction, anatomical anomalies of the urogenital system, or central nervous system disorders were not included in the study.

We studied and evaluated the clinical and laboratory manifestations of vesicoureteral reflux (VUR) and its complications, as well as their changes following treatment. The age of the patients ranged from 1 year to 41 years, with 269 patients (96%) being under 20 years old. There were 32 male patients and 247 female patients. We analyzed patient complaints, medical and life history. Dynamic monitoring was conducted for up to 3 years.

All patients underwent comprehensive examinations using commonly accepted clinical, laboratory, and biochemical tests, which included clinical and biochemical analyses of urine and blood, bacteriological urine analysis. Diagnostic methods employed without exception included quality of life (QOL) scale testing, monitoring of the daily urinary rhythm, ultrasound examinations of the kidneys and urinary bladder, radiological studies (micturition cystography, excretory urography, radiosotope renography), urodynamic investigations (uroflowmetry, cystometry), and as indicated, cystoscopy and neurological assessments [2].

The treatment results at the initial stage were assessed based on radiological changes associated with vesicoureteral reflux (VUR). Subsequently, a comprehensive evaluation of the severity of VUR and treatment effectiveness was conducted using selected indicators that are crucial for assessing the severity of the condition, taking into account both objective and subjective manifestations of VUR. These indicators included patient complaints related to urinary disorders, the frequency of pyelonephritis exacerbations per year, changes in the general urine analysis (severity of leukocyturia), kidney function impairment, the degree of ureterohydronephrosis (UHN), and VUR.

The assessment of these six criteria was performed using a scoring system based on the severity of each of these features. Zero points were assigned when there were no changes, and 3 points were assigned in the case of maximum changes.

Based on the patient’s survey and the assessment of additional diagnostic methods, scores were assigned for all criteria, and the total score was calculated. The effectiveness of the treatment was determined by the change in the total score from the first visit to the last visit. If the total score at the last visit relative to the first visit did not change or decreased by 0-30%, the treatment effect was considered negative. If the total score decreased by 31%-66%, it was considered satisfactory; if the score decreased by more than 66%, it was considered good.

Patients were divided into three groups (Table 1) based on the total scores, according to the proposed system «Method for a Comprehensive Assessment of the Severity of Vesicoureteral Reflux Disease and Treatment Effectiveness» [1].

An algorithm for diagnosing and determining the treatment strategy for patients with vesicoureteral reflux (VUR) has been developed (Figure 1). The foundation of this algorithm is a differential treatment approach for patients with VUR, utilizing a comprehensive scoring system to assess the severity of the condition [1].

The algorithm consists of visits, the objectives of each visit, diagnostic measures, the selection of tactics, and treatment procedures. Each visit is associated with a specific objective, based on which diagnostic and treatment measures are carried out.
One of the significant advantages of the proposed algorithm is the clear rationale for indications and the selection of treatment tactics for vesicoureteral reflux (VUR), which is based on an objective scoring assessment of the patient’s condition and changes in the total scores due to treatment. This allows for clear criteria to decide whether to change the treatment approach or continue with the current one.

For the analysis of the obtained data, we employed statistical variation methods for data processing, including calculating correlation relationships, their strengths, the coefficient of rank correlation, statistical descriptive data for the entire sample, descriptive statistics for comparing two groups, t-test data (Student’s t-test), and the results of linear multifactorial regression of a general nature. The critical level of significance ‘p’ for testing statistical hypotheses in this study was set at 0.05. Data processing was carried out on IBM-compatible computers. Programs used for storing and processing results included Quatro Pro version 5.0, Microsoft Excel 2000, and the statistical processing program Statistika for Windows version 5.0 by Statsoft. Some of the material was processed using the statistical software SPSS version 7.0.1.

RESULTS OF THE RESEARCH AND DISCUSSION

Based on the examination of 279 patients with vesicoureteral reflux (VUR) that occurred against the background of neurogenic bladder dysfunction (NBD), the following findings were made:

- VUR Grade I was diagnosed in 93 (33.3 %) patients, VUR Grade II in 12 (4.3 %), and VUR Grade III-IV in 174 (62.4 %).
- Among the forms of NBD that cause urodynamic disturbances and the development of VUR, hyperreflexic bladder was observed in 230 (82.4 %) patients, normoreflexic bladder was diagnosed in 41 (14.7 %), and hyporeflexic bladder in 8 (2.9 %).
- Complaints of urological disorders (urge incontinence, imperative voiding, pain during urination, enuresis, nocturia) were present in 183 (65.6 %) patients.
- Exacerbations of chronic pyelonephritis within the last year were observed in 186 (66.7 %) patients.
- Leukocyturia was diagnosed in 185 (66.3 %) patients during laboratory tests.
- Ureterohydronephrosis was found in 60 (21.5 %) patients.
- Kidney function impairment was diagnosed in 11 (3.9 %) patients.

After analyzing the clinical manifestations and secondary changes in the urinary tract in patients with different grades of vesicoureteral reflux (VUR), we studied the dependence of their presentation on the severity of VUR, the age, and the gender of the patients.

Comparison of the severity of clinical manifestations and secondary changes among patients with different grades of VUR (Table 2).
In our statistical analysis, we found that as the grade of VUR increased, there was a more significant change in the general urine analysis due to an increase in the number of leukocytes \((t = 0.153; \ p = 0.010)\). Moreover, it was likely that leukocyturia was less frequent in patients with VUR I-II grade, while pronounced leukocyturia was observed less often in patients with VUR III-IV grade, where «t-Student’s t-test» and «p» level of significance were taken into account.

The research findings indicate that VUR is most commonly observed in the age group of 6 to 10 years, with 124 patients (44.4 %). In children under 5 years of age, VUR grade III-IV is more likely to be diagnosed \((t = 0.1157; \ p = 0.015)\). As patients age, the grade of VUR tends to decrease or even disappear \((t = –0.1492; \ p = 0.013)\). Similarly, complaints related to urinary disorders in patients with VUR tend to diminish or disappear with age \((t = –0.1533; \ p = 0.010)\).

As patients get older (after 7-8 years), the frequency of pyelonephritis exacerbations decreases \((t = –0.1344; \ p = 0.025)\). However, dilatation of the upper urinary tract \((t = 0.2157; \ p = 0.001)\) and deterioration of kidney function \((t = 0.2354; \ p = 0.001)\) are more commonly observed in older patients.

The majority of patients were female, accounting for 247 (88.5 %) of the total. The distribution of male and female patients by VUR grade was not uniform. In females, more severe VUR grades were almost twice as common as compared to the initial grades. In contrast, in males, the frequency of initial and severe VUR grades was nearly equal.

The severity of dysuric disorders was almost the same in men and women; however, inflammatory processes in the urinary tract were more common in women \((t=0.1419; \ p=0.018)\). In men, the likelihood of having ureterohydronephrosis (UHN) was significantly higher \((t = –0.1734; \ p=0.004)\), and kidney function impairment due to VUR was also more frequent \((t = –0.1733; \ p=0.004)\).

Based on the data obtained, a likely correlation was established between the grade of VUR and the patient’s age and the severity of leukocyturia. No correlation was found between the grade of VUR and gender, complaints of dysuric disorders, the frequency of pyelonephritis exacerbations, changes in kidney function or kidney, and the degree of UHN associated with VUR.

The clinical manifestations in patients with different degrees of VUR were practically the same. The obtained results do not confirm the commonly accepted belief that the severity of clinical manifestations increases with the degree of VUR.

The distribution of patients corresponds to the picture of clinical manifestations and reflects the individual assessment of the severity of the patient’s condition and the severity of VUR (Table 1).

When analyzing the groups and the results, it was found that there is a general tendency for the severity of VUR to increase with an increase in the total score according to the proposed system (Table 1). In the first group, there were more patients with VUR of grade I-II, while in the third group, there were more patients with VUR of grade III-IV.

Therefore, the proposed «Method for Comprehensive Assessment of the Severity of Vesicoureteral Reflux and the Effectiveness of Treatment» allows for a more objective assessment of clinical manifestations related to NDSM and VUR, and in the future, a more accurate analysis of the effectiveness of using various therapeutic methods.

The next step in our study was to identify primary factors that could predict changes in the degree of VUR after a course of treatment. We analyzed the selected clinical and laboratory signs as well as secondary changes associated with VUR. The severity of these signs was assessed based on the comprehensive assessment of the severity of VUR and treatment effectiveness. The treatment results in the initial stage were evaluated based on radiological changes in VUR.

The calculations revealed the following patterns: as the severity of UGN increases, the treatment results for VUR worsen \((t=0.3053; \ p=0.004)\). This suggests that in patients with pronounced UGN, it is possible to predict the absence of a reduction in VUR after conservative treatment. Conversely, in patients with mild or no UGN, a positive outcome of VUR treatment can be expected.

However, no statistically significant correlation was found between changes in the degree of VUR and the severity of urinary disorders, the frequency of pyelonephritis exacerbations, changes in urine analysis (severity of leukocyturia), or changes in kidney function. This indicates that the treatment results for VUR are similar regardless of the severity of these manifestations.

When analyzing the effectiveness of VUR treatment, you compared your evaluation system with the generally accepted one (Table 3). You found a direct correlation between the evaluation of treatment effectiveness using your methodology and changes in the degree of VUR according to the generally accepted methodology. However, in each group with different treatment effectiveness according to your system, there were patients who showed a significant reduction in the degree of VUR. This indicates that changes in VUR do not always correspond to changes in the clinical picture.
Table 3

<table>
<thead>
<tr>
<th>Groups of patients</th>
<th>Effectiveness of treatment according to the proposed method</th>
<th>Changes in VUR</th>
<th>Absent or minimal, (n)</th>
<th>Moderate, (n)</th>
<th>Reflux disappeared, (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Unsatisfactory (n = 26)</td>
<td></td>
<td>22</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>II</td>
<td>Satisfactory (n = 21)</td>
<td></td>
<td>18</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>Good (n = 40)</td>
<td></td>
<td>13</td>
<td>8</td>
<td>19</td>
</tr>
</tbody>
</table>

Note: n – number of patients.

It is worth noting that in Group I, despite the disappearance of reflux in 11% of patients, the treatment effect can be considered unsatisfactory because other indicators have not changed. Conversely, in Group III, one-third of patients did not have changes in reflux, although other manifestations of the disease significantly decreased. In this group, the treatment effect is traditionally considered absent, even though a comprehensive analysis of the patient’s condition indicates a significant improvement.

The next step was to compare changes in VUR and the quality of life of patients. For patients with VUR, a decline in quality of life is a significant problem, considering the widespread occurrence of voiding disorders and chronic urinary tract infections, especially among children (who make up the majority of VUR patients). Neglecting the impact of these clinical manifestations on the adaptation of children to their social environment is considered incorrect. We did not find any studies on this issue in the literature we reviewed. Given this, we decided to explore the relationship between changes in VUR following a course of treatment (which is traditionally used to assess the effectiveness of therapy in these patients) and changes in their quality of life (Table 4).

Table 4

<table>
<thead>
<tr>
<th>Groups of patients</th>
<th>Changes in vesicoureteral reflux</th>
<th>Improvement in quality of life</th>
<th>Absent, (n)</th>
<th>Moderate, (n)</th>
<th>Severe, (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Absence or minimal (n = 53)</td>
<td></td>
<td>9</td>
<td>11</td>
<td>33</td>
</tr>
<tr>
<td>II</td>
<td>Moderate (n = 11)</td>
<td></td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>III</td>
<td>Reflux disappeared (n = 23)</td>
<td></td>
<td>3</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>

Note: n – number of patients.

As we can see from the data provided, there is no correlation between the reduction of vesicoureteral reflux (VUR) degree and improvement in the quality of life. In 66.7% of patients, it is observed that changes in the VUR degree do not correspond to changes in the quality of life. For example, in 83.0% of patients in Group I, the quality of life improved or became good in the absence of changes in VUR. Conversely, in Group III, where VUR completely disappeared, 13.0% of patients did not report any changes in the quality of life. This suggests that the quality of life, which is an important indicator of the effectiveness of treatment in patients, often does not correlate with changes in the VUR degree.

Therefore, based on the analysis of changes in the main clinical manifestations and complications of vesicoureteral reflux (VUR) during treatment, the following findings were made:

– Changes or disappearance of many clinical manifestations accompanying VUR due to conservative treatment do not correspond to radiological changes in VUR in 39.1% of patients.

– Diuretic disorders and the activity of inflammatory processes in the kidneys are important factors that change or disappear primarily, reflecting the results of treatment in patients with VUR. In such cases, rapid changes in the patient’s condition indicate the normalization of bladder function, leading to an improvement in the quality of life, even though VUR itself may not change.

– The quality of life, which is an important indicator of the effectiveness of treatment in patients, does not correspond to changes in the degree of VUR in 66.7% of patients.

The conducted research has allowed us to develop and propose our own algorithm for the diagnosis and determination of treatment tactics for patients with vesicoureteral reflux (VUR) (Figure 1). The basis of the algorithm is the differential treatment strategy for patients with VUR using a comprehensive scoring system to assess the severity of the disease [1].
Fig. 1. Algorithm for the diagnosis and determination of treatment tactics for patients with vesicoureteral reflux.
CONCLUSIONS

Based on multifactorial statistical analysis, it has been demonstrated that most clinical and laboratory manifestations of vesicoureteral reflux (VUR) do not have a correlation with its degree. However, a reverse correlation was established between the degree of vesicoureteral reflux and age ($t = -0.1492; p = 0.013$), and a direct correlation was found with leukocyturia ($t = 0.153; p = 0.010$).

Dysuric disorders, leukocyturia, and the frequency of pyelonephritis exacerbations are components of the clinical picture of vesicoureteral reflux that affect the quality of life and are the first to change due to treatment, resulting in the normalization of bladder function.

Dysuric disorders, leukocyturia, and the frequency of pyelonephritis exacerbations are components of the clinical picture of vesicoureteral reflux (VUR) that affect the quality of life and are the first to change due to treatment, resulting in the normalization of bladder function.

Clinical manifestations and complications worsen the quality of life in 66.2% of patients. Therefore, improving the quality of life is just as important a goal of treatment as reducing reflux, and it should be taken into account when determining the treatment strategy and assessing its results.

Changes in the degree of vesicoureteral reflux as a result of treatment do not coincide with the reduction of clinical manifestations in 39.1% of patients and do not match the changes in the quality of life in 66.7% of cases. Therefore, evaluating the effectiveness of treatment in patients based solely on changes in the degree of VUR is insufficiently objective.

When assessing the condition of VUR patients and evaluating the effectiveness of their treatment, it is important to consider not only the degree of VUR but also the entire complex of main clinical manifestations and complications of the disease. This can be achieved by using the proposed system for a comprehensive assessment of the severity of vesicoureteral reflux and treatment effectiveness.

In the absence of direct indications for surgical intervention, the choice of a conservative treatment method for patients with vesicoureteral reflux (VUR) depends on the change in the total score over the course of treatment, which should be > 30%. If the change in the total score is < 30%, another treatment method is recommended.

COMPLIANCE WITH ETHICAL REQUIREMENTS

The study was conducted in accordance with the principles of the Helsinki Declaration of the World Medical Association «Ethical principles of medical research involving a person as an object of research». All study participants provided informed consent in writing to participate in the study.

FUNDING AND CONFLICT OF INTERESTS

The author declares that there is no conflict of interests. Source of funding – self-funded.
Резюме

ОЦІНКА МІХУРОВО-СЕЧОВІДНОГО РЕФЛЮКСУ ПРИ НЕЙРОГЕННИХ ДИСФУНКЦІЯХ СЕЧОВОГО МІХУРА ТА ВИБІР ТАКТИКИ ЛІКУВАННЯ

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Мета дослідження. Покращення результатів лікування міхурово-сецовідного рефлюксу (МСР), що виник на тлі нейрогенних дисфункцій сечового міхура (НДСМ), шляхом розробки об'єктивно обґрунтованої системи диференційованого підходу до вибору тактики лікування хворих та удосконалення на цій підставі існуючих методів лікування.

Матеріали та методи. Клінічно обстежено 279 хворих на МСР, який виник на тлі НДСМ. Отримали консервативне лікування 87 пацієнтів. Варіант дослідження: поздовжнє (проспективне дослідження, випадок- контroll). Відсутня рандомізація. Критеріями включення: наявність у пацієнта МСР одночасно з НДСМ. У дослідженні не ввійшли пацієнти з МСР V ступеня. Вивчали і оцінювали клініко-лабораторні прояви МСР та його ускладнення. Проводили комплексну оцінку важкості захворювання на МСР та ефективності лікування. Пацієнтів поділили на 3 групи за запропонованою системою «Спосіб комплексної оцінки тяжкості захворювання на міхурово-сецовідний рефлюкс та ефективності лікування».

Результати досліджень. Наїбільш часто МСР спостерігається у віці від 6 до 10 років – 44,4 % пацієнта. У віці до 5 років частіше діагностується МСР III-IV ст. Скарп на дисуричні розлади з віком зникають або зменшуються (t= –0,1533; p=0,010). Зі збільшенням віку хворих (після 7-8 років) частота загострень піелонефриту зменшується (t= –0,1344; p=0,025), але частіше спостерігається ділянчатне розширення верхніх сечовивідних шляхів (t=0,2157; p=0,001) та погіршення функції нирок (t=0,2354; p=0,001). Запальні процеси сечовивідних шляхів частіше виникають у жінок (t=0,1419; p=0,018). У чоловіків порушення функції нирки зі сторони МСР зустрічається частіше (t= –0,1733; p=0,004).

Висновки. Більшість клінічних та лабораторних проявів МСР не мають кореляційного зв’язку із його ступенем. Встановлена зворотна кореляційна залежність ступеня МСР з віком та пряма – з лейкоцитурією. Дизуричні розлади, лейкоцитурія, частота загострень піелонефриту є складовими клініки МСР, що впливають на якість життя та змінюються першими внаслідок лікування за рахунок нормалізації функції сечового міхура. Клінічні прояви та ускладнення МСР погіршують якість життя у 66,2 % хворих. Оцінка ефективності лікування хворих приймає до уваги ступінь МСР і комплекс головних клінічних проявів та ускладнень, що можливо при використанні запропонованої системою «Спосіб комплексної оцінки тяжкості захворювання на міхурово-сецовідний рефлюкс та ефективності лікування».

Ключові слова: міхурово-сецовідний рефлюкс, нейрогенный сечовий міхур, нейрогенна дисфункція сечового міхура