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КЛИНИЧЕСКАЯ МЕДИЦИНА, КЛИНИЧЕСКАЯ ФАРМАКОЛОГИЯ И ФАРМАКОТЕРАПИЯ

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METABOLIC HOMEOSTASIS AND QUALITY OF LIFE OUTCOMES IN PATIENTS AFTER CYSTECTOMY

ABSTRACT

The retrospective study in the work presented results of the treatment outcomes of 78 patients who underwent radical cystectomy (RCE) and were a core group of our observation. Urinary diversion with the Studer orthotopic ileal neobladder was performed in 45 (57.7%) patients after RCE and urinary diversion with Bricker ileal loop – in 33 (42.3%) patients. The aim of study was to assess the metabolic changes and the quality of life in patients with orthotopic ileocystoplasty by Studer and heterotopic noncontinent urinary diversion by Bricker. Patients were hospitalized at the clinical base of the Chair of Urology and Nephrology of Odessa National Medical University, Departments of Urology No.1 and No.2 of Odessa City Clinical Hospital #10, and oncourologic department of Odessa Regional Oncology Center. Age of the patients was on average 62.5 ± 8.5 years and ranged from 38 to 79 years. The number of men was 62 (79.5%), women - 16 (20.5%). The control group consisted of 28 patients with bladder cancer of comparable age, which have not underwent surgery and received the conservative treatment. We have used quality of life assessment by use of questionnaire "Medical Outcomes Study - Short Form" (SF-36), for the purpose of objectification and standardization of assessment of quality of life in patients who have undergone reconstructive surgery on the lower urinary tract. Objective assessment in patients who underwent recently ileocystoplasty have proved the presence of clinically significant hyperchloraemic acidosis in 16 patients (20.5%). Moreover, in 14 cases this complication observed after orthotopic ileocystoplasty by Studer and only in two cases after noncontinent urinary diversion by Bricker. A study was conducted in 21 days after orthotopic urinary diversion in 43 (95.6%) patients and after 12 months in 33 (73.3%) patients. It has been noted the shortage of buffer bases (BB) twice (p <0.05) and chlorine decrease after 21 days compared with the same parameter after 12 months. Study of quality of life showed the best long-term outcomes in patients with neobladder by Studer in comparison with ileocystoplasty by Bricker in social functioning by 18%, mental health and vitality by 19% and 25%, respectively.

Key words: metabolic homeostasis, quality of life, radical cystectomy, ileocystoplasty, neobladder.

Bladder cancer (BC) remains an important and urgent problem due to the steady increase in both morbidity and mortality. In Ukraine BC accounts for nearly 5 thousand new cases and 2.3 thousand deaths from this disease annually [1]. Bladder cancer is the most common malignancy of the urinary tract, with peak incidence in adults and the elderly [2]. Approximately 90% of all bladder tumors is urothelial carcinoma, also called transitional cell carcinoma (TCC) [3].

It is diagnosed a tumor invading the muscular bladder layer according to various reports in 25-30% of patients with primary BC [5]. The main option of treatment of muscular-invasive bladder cancer (MIBC) is radical cystectomy (RCE) in various versions [4,16,17,18]. Indications for cystectomy include invasive bladder cancer T_{2a} - T_{4a} , N_0 - N_x , M_0 , T_1G_3 , superficial high-risk, high-grade and reccurent tumors, cancer in situ, BC resistant to BCG therapy, as well as advanced papillary tumors that cannot be controlled with the help of transurethral resection and intravesical therapy. Radical cystectomy with orthotopic ileocystoplasty is the "gold standard" of treatment of MIBC and urinary diversion with have more than 60 proposed methods of conduit forming [13,14].

The results of the 10-year follow-up of treatment outcomes in patients after cystectomy show that the surgery alone cures most patients with MIBC pT_2N_0 stage, about 50% of patients with extravesical tumor spread ($pT_{3-4}N_0$ stage) and not more than 30% of patients with positive pelvic lymphatic nodes [6].

The main objective when choosing a type of intestinal urinary diversion after RCE is a local management of bladder cancer with the preservation of normal renal function and an improve in quality of life of operated patients. Psychological aspects of urinary diversion are still insufficiently studied.

Active development of medical science, the emergence of new technologies and the improvement of old techniques, new anesthetic drugs and medications have led to the rapid development of reconstructive surgery in urology, significantly increasing the age limit for performing surgical procedures. One of the best methods of urine derivation after RCE in elderly and with contraindications to orthotopic urinary diversion is non-continent ileal urinary diversion by Bricker [7.8]. The improving the quality of life of these patients remains one of the most important tasks of modern medicine [9,10,11].

It is well known that the graft of the ileum has the properties of resorption of urinary components with the development of hyperchloraemic acidosis, disorders of urodynamics of the upper urinary tract (UUT) and the progression of chronic renal failure (CRF), which significantly complicates the postoperative period in patients with advancing age and comorbidities [12]. Metabolic acidosis develops in 15% of patients with created conduit, in 50% of patients with iliac reservoir and in 80-100% with the colon urinary diversion [20]. The mechanism of development of hyperchloraemic acidosis is characterized by the fact that the intestinal epithelium, bathed in urine, rapidly absorbs ammonium ions and after them - chlorine ions. Anatomical and functional features of the formed urine reservoir have leaded us to outline the goals and objectives of the study.

An aim: to study the metabolic changes and quality of life in patients with orthotopic ileocystoplasty by Studer and heterotopic noncontinent urinary diversion by Bricker

Materials and methods: A retrospective study of treatment of 78 patients who underwent radical cystectomy was a core group of our observation. For the sake of urinary diversion in 45 (57.7%) patients after RCE it was performed an orthotopic ileocystoplasty by Studer and in 33 (42.3%) patients -noncontinent urinary diversion by Bricker. Patients were hospitalized at the clinical base of the Chair of Urology and Nephrology of Odessa National Medical University, Departments of Urology No.1 and No.2 of Odessa City Clinical Hospital #10, and oncourologic department of Odessa Regional Oncology Center. Age of the patients was on average 62.5 ± 8.5 years and ranged from 38 to 79 years. The number of men was 62 (79.5%), women - 16 (20.5%). All surgeries were performed according to standard operation procedures with the mobilization and extirpation of the bladder; mobilization and removal of portion of the ileum from the digestive tract, and the formation of ileoconduit and several anastomoses, lymphadenectomy [19]. The control group consisted of 28 patients with bladder cancer of comparable age, which have not underwent surgery and received the conservative treatment.

All patients before surgery were classified according to the scale of the American Association of Anesthesiologists (ASA), most of them included in II category, and patients with chronic obstructive

pulmonary disease (COPD) - III category. There was a fairly high incidence of concomitant diseases: coronary heart disease - 50%, obesity - 25%, diabetes - 9%, hypertension - 78%, COPD - 13%.

The pre-operative investigations included clinical and instrumental methods of investigation: ultrasound examination of the upper urinary tract and abdomen, multi-helical computed tomography of pelvis and lungs with contrast enhancement. Electrolytes, acid-base parameters and blood gases were studied in the early postoperative period (21 days) and at follow-up examination in 12 months.

We have used quality of life assessment by use of questionnaire "Medical Outcomes Study - Short Form" (SF-36) for the purpose of objectification and standardization of assessment of quality of life in patients who have undergone reconstructive surgery on the lower urinary tract.

Statistical processing of the results was performed using the methods of parametric and non-parametric statistics using Statistica for Windows software v 5.0

Results. Infiltrative growth of bladder cancer not only leads to loss of the reservoir and the accumulation functions of bladder but also to the gradual deterioration of upper urinary tract urodynamics, ureterohydronephrosis and in the future - the development of CRF. Patients have underwent percutaneous nephrostomy to decompress upper urinary tract and prepare the patient to RCE as a first stage of operative treatment due to the high frequency of ureterohydronephrosis - 20 cases, including 3 of them with bilateral lesion, 16 (20.5%).

Objective assessment of patients immediately after ileocystoplasty showed the presence of clinically significant hyperchloraemic acidosis in 16 patients (20.5%). Moreover, this complication observed after orthotopic ileocystoplasty by Studer in 14 cases and only in two cases after noncontinent urinary diversion by Bricker. It is noted that the symptoms of metabolic acidosis often develop on the background of chronic renal failure, acute pyelonephritis, or obstructive urine outflow from the upper urinary tract due to ureteroileal anastomoses stenosis. These complications were manifested with fatigue, nausea and vomiting in 14 (87.5%) patients, anorexia - in 3 (18.8%), confusion up to stupor - in 1 (6.3%). Patients were treated in all cases with hydration and alkalizing therapy with good clinical effect. The ureteral reimplantation to intestinal conduit was performed in case of blockage of the urine outflow from upper urinary tract.

Indicators of electrolyte and acid-base composition of the blood in the early postoperative period after ileocystoplasy by Studer are presented in Table #1. The study was conducted in 21 days in 43 (95.6%) patients and after 12 months in 33 (73.3%) patients. It has been noted according to the presented data that after 21 days the level of buffer bases (BB) and chlorine is twice less (p <0.05) than the same parameters after 12 months. The value of BB is one of the most informative indicators of metabolic disorders of the acid-base status thanks to the sign (+ or -) in front of a numeric expression. Some authors explain the development of this complication in patients after ileocystoplasty with a great length autograft and recommend its shortening, for the prevention of metabolic acidosis [15].

Table 1 - Results of acid-base status and gas composition in patients with neobladder by Studer

Parameter	Results after 21	Results after 12 months	Control group (n=28)
	days (n=43)	(n=33)	
K ⁺ (mmol/l)	4,2±0,30	3,9±0,24	4,01±0,12
Na ⁺ (mmol/l)	139±0,34	138±0,73	138±0,32
Cl ⁻ (mmol/l)	110±0,32*	108±0,76*	108±0,88
Ca ²⁺ (mmol/l)	2,2±0,43	2,1±0,86	2,1±0,92
pН	7,36±0,003	7,36±0,001	7,36±0,002
BE	-5,1±0,51*	-2,46±0,20*	-2,4±0,13
pC02 (mm)	35,1±0,21	35,7±0,41	35±0,32

Note: * - the difference between the indices is statistically significant $\ p < 0.05$

Results of the study of acid-base and electrolyte composition of the blood in patients after urinary diversion by Bricker presented in Table #2. The study was conducted in 21 days in 97%, after 12 months in 70.0% of patients, 10 patients died within 1 year after RCE due to the underlying pathology. There was a slight shortage of serum bases in the postoperative period, which in our opinion is due to the absence of prolonged contact of intestinal transplant with urine, but more severe physical complications

and higher incidence of chronic renal failure in this category of patients. Despite this opinion, CRF was rarely met, mainly in patients with large intestinal urinary reservoir, in creating anastaltic loops, stoma stenosis or stenosis of the ureteroileal anastomosis.

Table 2 - Results of acid-base status and gas composition in patients with ileoconduit by Bricker.

Parameter	Results after 21 days	Results after 12 months	Control group (n=28)
	(n=43)	(n=33)	
K ⁺ (mmol/l)	4,1±0,3	3,9±0,18	4,01±0,12
Na ⁺ (mmol/l)	139±0,14	138±0,54	138±0,32
Cl ⁻ (mmol/l)	103±0,15	102±0,54	108±0,88
Ca ²⁺ (mmol/l)	2,2±0,26	2,3±0,23	2,1±0,92
pН	7,36±0,04	7,36±0,02	7,36±0,002
BE	-3,1±0,54*	-3,2±0,21*	-2,4±0,13
pC02 (mm)	35,3±0,11	35,2±0,412	35±0,32

Note: * - the difference between the indices is statistically significant p < 0.05

The problem of rehabilitation of patients after radical cystectomy remains urgent today; according to various authors, the best indicators of quality of life can be obtained after orthotopic and heterotopic ileocystoplasty [21]. There is no universal definition of "quality of life" in patients undergoing RCE as different groups of patients may be different cultures, countries, research teams, depend on the instruments of the study (telephone survey, self-questioning), insufficient number of subjects, and their not quite successful grouping. We have assessed the quality of life of BC patients after RCE and urinary diversion using the SF-36 according to the type of surgery and diversion. Control group were presented with healthy individuals of corresponded age – 20 people listed in the table #3. Quality of life was possible to estimate in 33 (73.3%) patients after ileocystoplasty by Studer and 23 (70.0%) by Bricker.

Table 3 - Quality of life in patients after the RCE

Parameter	Patients after ileocysto-	Patients after ileocystoplasty	Control group
	plasty by Studer (n=33)	by Bricker (n=23)	(n=20)
GH	58,4±4,2	55,2±3,8	70,1±2,5
MH	76,1±4,6*	61,3±4,1	79,5±3,5
RP	62,1±3,1	61,4±2,7	80,6±4,1
RE	60,2±2,8	58,6±1,1	77,4±2,9
VT	68,7±3,3*	51,5±4,7	83,1±2,1
SF	63,7±4,1*	52,3±2,6	87,5±4,1

Note: * - the difference between the indices is statistically significant p < 0.05

The study conducted in a year after RCE has found out no cardinal, significant differences in the parameters of general health (GH) in patients with ileocystoplasty by Studer (58.4 ± 4.2) and by Bricker (55.2 ± 3.8) , but showed significant differences in comparison with the group of healthy volunteers (70.1 ± 2.5) . It should be noted that in the postoperative period, the overall health indicator was higher in patients with heterotopic plastics that can be caused by a large number of complications after orthotopic plastics, but the indicators were balanced in a year.

Index of Mental Health (MH), characterizing the presence of depression and general positive emotions and an indicator of vitality (VT) in both groups were significantly higher in patients after forming neobladder. These parameters characterize continent urinary diversion as more effective for both psychological and emotional components of the quality of life.

Neither role-emotional functioning (RE) nor role-physical condition (Role-Physical Functioning - RP) did not differ significantly in the first and the second group.

In turn, the index of social functioning (SF), which is responsible for social activity was significantly higher in the group of patients after ileocystoplasty by Studer (p < 0.05), which characterize

those patients as more socially-adaptable.

The study of quality of life for this group of patients is still causing a lot of controversy, most authors believe that the difference in quality of life indicators is practically absent, some noticed Studer neobladder advantages in both social and physical activities, compared with patients after ileocystoplasty by Bricker [22].

Conclusions.

Symptoms of metabolic acidosis occurs in 20.5% of patients after radical cystectomy, and most of them (18%) were after formation of neobladder by Studer and only 2.5% after ileocystoplasty by Bricker. Almost all episodes of metabolic homeostasis disorders develop on the background of chronic renal failure with narrowing of ureteroileal anastomoses in patients with orthotopic ileocystoplasty. We recommend preventing of this complication by adequate selection of candidates for ortho- and heterotopic ileocystoplasty, patients of impaired renal function should undergo Bricker conduit surgery. In the onset of symptoms of the metabolic acidosis, it is required to conduct infusion therapy with hydration, alkalizing solutions and rigorous control of adequate drainage of conduit and upper urinary tract.

Long-term study of metabolic changes in these patients is of interest, particularly metabolism of vitamin B12 deficiency, which leads to severe anemia, as well as bone demineralization control and vitamin deficiencies of vitamin D.

Watching a group of patients undergoing radical cystectomy with urinary diversion must be lifelong, not only due to the cancer alertness, but also in terms of metabolic control.

Study of quality of life showed the best performance in a year after RCE in patients with neobladder by Studer in comparison with ileocystoplasty by Bricker in social functioning by 18%, mental health and vitality by 19% and 25%, respectively.

Cultural features, insufficient number of social programs and available consumables for urostomy patients are lead to more complex social adaptation of patients after ileocystoplasty by Bricker and require further research.

These results indicate that the perception in patients with neobladder and continent urinary diversion is more physiological and gives an opportunity to the maximum socio-clinical rehabilitation and adaptation of the working-age group of patients.

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ТҮЙІН

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ЗАТ АЛМАСУ ГОМЕОСТАЗЫ ЖӘНЕ ЦИСТЭКТОМИЯНЫ БАСЫНАН КЕШІРГЕН НАУҚАСТАРДЫҢ ӨМІР САПАСЫ

Жұмыс барысында түбегейлі цистэктомияны (ТЦЭ) басынан кешірген 78 емделушіге ретроспективті зерттеу жүргізілді және олар біздің бақылаудың негізгі тобын құрады. ТЦЭ-дан кейін, Штудер бойынша 45 (57,7 %) науқаста, Бриккер бойынша зәрді деривациялау – 33 (42,3%) науқаста зәрді бөліп алу үшін қуық қалбыршағының ортопедиялық ұйымдыстыруы орындалды. Максаты - Штрудер бойынша ортопедиялык илеоцистіпластикамен және Бриккет бойынша гетеротопикамен наукастардың өмір сапасын және зат алмасуда өзгерістеді зерттеу. Барлық науқастар ОҰМУ-нің урология және нефрология кафедрасының клиникалық базасында, Одесса облыстық онкологиялқ диспансері №1 және №2 урология бөлімдерінде, ҰБ «№10 Қалалық клиникалық ауруханасында», сонымен қатар Одесса облыстық онкологиялық диспансерінің станционарлық емделуде болды. Науқастардың жасы шамамен 62,5 ± 8,5 жасты құрады және құрады және 38-ден 79 жасқа дейінгі аралықта болады. Ер адамдар саны 62 (79,5%), әйел адамдар - 16 (20,5%). Бақылау тобын ҚҚҚІ ота жасалмаған, кертартпа емделуде жүрген, жастарына сәйкес 28 науқас құрады. Төменгі қуық жолдарында ұйымдастырылған оперативті араласуды бастарынан өткерген науқастарда өмір сапасын стандарттау және нысандандыру мақсатымен, "Medical Outcomes Study Short Form" (SF-36) анкета-сауалнамалық негізіндегі зерттеумен социоклиникалық әдіс қолданылды. илеоцистіпластикадан кейін жақын

жасалғандарға әділ бағалау 16 науқаста (20,5%) клиникалық маңызды гиперхлоремикалық ацидоз белгілердің бар екендігін көрсетті. Оның ішінде осы асқынулар Штудер бойынша илеоцистопластикадан кейін 14 жағдайда және Бриккер бойынша зәр деривациясынан кейін тек қана екі жағдайда тіркелген. Науқастарда ортопедиялық илеоцистіпластикадан кейін зерттеу емделушілердің 43 (95,6%)-да 21 күннен кейін, 33 (73,3%) емделушіде 12 айдан кейін жүргізілді. Осының деректері бойынша буферлік негіздемелер (ВЕ) екі есе (р<0,05) және хлордың 21 күннен кейін 12 айдан кейінгі көрсеткіш деректерімен салыстырғанда жетіспеушілігін белгілеуге болады. Өмір сапасын социоклиникалық зерттеу Штрудер бойынша неоцистпен науқастарда, Бриккер бойынша илеопластикаға қарағанда әлеуметтік жұмыс істеуде 18%-ға, өмірлік белсенділікте 19% -ға, 25% сәйкестікте ең жақсы ұзақ мерзімді көрсеткіштерді көрсетті.

Кілт сөздер: зат алмасу гомеостазы, өмір сапасы, радикалды цистэктомия, илеоцистіпластика.

Аннотация

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МЕТАБОЛИЧЕСКИЙ ГОМЕОСТАЗ И КАЧЕСТВО ЖИЗНИ БОЛЬНЫХ ПЕРЕНЕСШИХ ЦИСТЭКТОМИЮ

В работе проведёно ретроспективное исследование лечения 78 пациентов перенёсших радикальную цистэктомию (РЦЭ) и составило основную группу нашего наблюдения. Для отведения мочи после РЦЭ была выполнена ортотопическая реконструкция мочевого пузыря по Штудеру у 45 (57,7 %) больных, деривация мочи по Бриккеру – 33 (42,3%) пациентов. Целью являлось изучение метаболических изменений и качества жизни у больных с ортотопической илеоцистопластикой по Штудеру и гетеротопической по Бриккеру. Все пациенты находились на стационарном лечении на клинической базе кафедры урологии и нефрологии ОНМУ отделениях урологии №1 и№2 КУ «Городская клиническая больница №10, а также отделения онкоурологии Одесского областного онкологического диспансера. Возраст пациентов составил в среднем 62,5 ± 8,5 года и находился в диапазоне от 38 до 79 лет. Число мужчин составило 62 (79,5%), женщин – 16 (20,5%). Контрольную группу составили 28 больных РМП не оперированных, находящихся на консервативном лечении, сопоставимых по возрасту. С целью объективизации и стандартизации оценки качества жизни у больных, претерпевших реконструктивное оперативное вмешательство на нижних мочевых путях, использован социоклинический метод исследования на основании анкет-опросников "Medical Outcomes Study - Short Form" (SF-36). Объективная оценка оперированных в ближайшем после илеоцистопластики периоде показала наличие симптомов клинически значимого гиперхлоремического ацидоза у 16-ти больных (20,5%). Причем в 14 случаях данное осложнение отмечено после илеоцистопластики по Штудеру и только в двух случаях после деривации мочи по Бриккеру. У больных после ортотопической илеоцистопластики исследование проводилось через 21 день у 43 (95,6%) пациентов, через 12 месяцев у 33 (73,3%) больных. По данным которого можно отметить дефицит буферных оснований (ВЕ) в два раза (p<0,05) и хлора через 21 день по сравнению с данным показателем через 12 месяцев. Социоклиническое исследование качества жизни продемонстрировало лучшие долгосрочные показатели у пациентов с неоцистом по Штудеру, в отличии от илеопластики по Бриккеру в социальном функционировании на 18%, психическом здоровье и жизненной активности на 19% и 25% соответственно.

Ключевые слова: метаболический гомеостаз, качество жизни, радикальная цистэктомия, илеоцистопластика.