

КЛІНІЧНА ЕНДОКРИНОЛОГІЯ

**PATHOGENIC THERAPY OF DIABETIC CYSTOPATHY
WITH ALPHA LIPOIC ACID AND GROUP B VITAMINS
IN TYPES 1 AND 2 DIABETES MELLITUS PATIENTS***

Kravchun N. A.¹, Tkachuk E. Yu.²

¹ *SI «V. Danilevskiy Institute for Endocrine Pathology Problems of NAMS of Ukraine», Kharkiv;*

² *Regional Clinical Hospital — Center for Emergency Medical Aid and Medicine of Catastrophes, Kharkiv
allen-tkachuk@yandex.ua*

Disordered urination act is a serious complication caused by various diseases, which produces extremely negative impact on life quality (LQ) of the patients. Frequently, symptoms of the disordered urination (DU) present clinical manifestations of the main disease. The problem of the disordered urination act is especially topical in diabetes mellitus (DM) as it manifests urogenital form of diabetic autonomic neuropathy (DAN) [1, 2]. There are no specific assessment criteria for diabetic neuropathy (DN), but it is considered that 50 % of DM patients develop somatic neuropathy, and 75–100 % of them consequently develop neurogenic dysfunction of lower urinary tract. According to the data presented by European Association of Urologists (EAU), 43–87 % of insulin dependent DM patients, regardless of

age and gender, develop the so-called «diabetic cystopathy» [3].

Up-to-date assessment of DU degree and character in cases of the above mentioned nosology entities is performed, firstly, on the base of detailed and thorough questioning of the patient. Various, especially designed, scales are used to assess the symptoms pertaining to the disordered urination act [4–6].

Short Form Medical Outcomes Study (SF-36) questionnaire which determines total values of physical (Physical Health PH) and mental (Mental Health MH) components of health [7] is one of the most commonly used tools for LQ assessment.

It is generally recognized that the main pathogenically reasonable and clinically confirmed method to prevent and correct diabetic

* This work was completed in concordance with the target Research and development program of the department of Pharmacotherapy of Endocrine diseases of State Institution «V. Danilevskiy Institute for Endocrine Pathology Problems of NAMS of Ukraine» «To determine special features of hormonal metabolic and immunology disorders in the patients with type 2 diabetes mellitus and obesity with non-alcoholic fatty liver disease» (State registration number 0114U001205).

Institution, which financed the research: NAMS of Ukraine

The authors assume responsibility for the published work.

The authors guarantee absence of competing interests and their own financial interest when carrying out the research and writing the article.

The manuscript was received by the editorial staff 21.09.2017.

polyneuropathy is attainment and maintenance of optimal glycemic control ($HbA_{1c} \leq 7\%$). Progressing character of the disease determines the steady growth of incidence of DM comorbid chronic complications, therefore, the necessity to use pharmaceuticals which influence on various links of DN pathogenesis is extremely topical [8]. Currently, there are two main groups of medications which are actively

used in pathogenic therapy for DAN: tioctic (alpha lipoic) acid medications [9–11] and group B vitamins [12–14].

Objective of the research. To study dynamics of DU in type 1 and type 2 DM patients with urogenital DAN against the background of pathogenesis-based treatment with alpha lipoic acid and group B vitamins.

MATERIAL AND METHODS

Type 1 and type 2 DM patients with DU degree II (identified on the base of the ranged questionnaire data which was developed to determine DU degree and form in DM patients) were included into the trial [6]. LQ was determined with the aid of SF-36 questionnaire which allowed to determine total values of physical (Physical Health — PH) and mental (Mental Health — MH) components of health. The patients with acute and chronic renal and urinary tract diseases, mental and neurological comorbidities, diseases of nervous-muscular transmission, acute cerebral flow disorder in past history were excluded from the trial.

45 patients with type 1 DM and 48 patients with type 2 DM were under our observation. Being questioned according to the DM ranged

questionnaire, all of them gained from 11 to 19 points (degree II DU). Besides the therapy, aimed at normalizing their glycemic level, the treatment pattern included: in the morning: alpha-lipoic acid, 600 mg intravenously in drops № 10 + group B vitamins — Milgamma, 2.0, intramuscular 10; in the evening: 1 tabl. Benfotiamin, 300 mg; after the infusion therapy course was completed: alpha-lipoic acid, 600 mg, 1 tabl/day, during 3 months + 1 tabl. Benfotiamin, 300 mg were given.

Description of the patients is presented in table 1.

The patients were examined while admitting the hospital, to the endocrine department, and in 3 months after the beginning of treatment.

RESULTS AND THEIR DISCUSSION

Questioning of the patients with degree II DU at type 1 DM by the ranged questionnaire revealed that 16 patients (35.56 %) were determined incontinence clinically, 7 patients (15.56 %) — were diagnosed retention, and 22 patients (48.88 %) had DU mixed form. HbA_{1c} mean level in this group was of $(9.6 \pm 1.8)\%$, duration of the disease was (15.7 ± 8.6) years. Mean score according to the ranged questionnaire was (13.40 ± 2.07) points (table 2).

In three months after the course of treatment with lipoic acid and group B vitamins against the basic blood sugar lowering therapy was provided, 7 patients (15.6 %) showed a reduced expression of DU clinical manifestations confirmed by significant decrease of the score by the ranged questionnaire at DM from 14.4 ± 1.9 points to 11.5 ± 1.3 points, $p < 0.05$ (table 2).

We registered various degree reduction of HbA_{1c} level from (9.7 ± 1.1) to $(8.0 \pm 1.4)\%$,

Table 1

Clinical description of DM patients

Parameter	Type 1 DM, n = 45				Type 2 DM, n = 48			
	age, years	DM duration, years	HbA_{1c} , %	BMI, kg/m^2	age, years	DM duration, years	HbA_{1c} , %	BMI, kg/m^2
M±m	39.8 ± 9.5	15.7 ± 8.6	9.6 ± 1.8	25.6 ± 4.2	53.6 ± 9.1	13.7 ± 5.8	9.1 ± 1.9	33.2 ± 3.6
Min	22	6	5.9	21.3	35	1	7.4	26.3
Max	55	28	12.6	31.9	65	22	11.9	45.6

Table 2

Dynamics of the parameter values in type 1 DM patients

Parameter	All patients (n = 45)	Patients with positive dynamics (n = 7)	
		pre-treatment	post-treatment
HbA _{1c} , %	9.6 ± 1.8	9.7 ± 1.1	8.0 ± 1.4*
BNI, kg/m ²	25.6 ± 4.2	24.6 ± 3.1	26.1 ± 4.3
Σ PH	39.1 ± 6.8	40.6 ± 7.2	40.3 ± 4.8
Σ MH	28.8 ± 7.3	28.6 ± 5.1	32.9 ± 3.9
Ranged questionnaire at DM (points)	13.4 ± 2.1	14.4 ± 1.9	11.5 ± 1.3*

Note.

* — significant in relation to pre-treatment data (p<0.05).

Table 3

Dynamics of the parameter values in type2 DM patients

Parameter	All patients (n = 48)	Patients with positive dynamics (n = 6)	
		pre-treatment	post-treatment
HbA _{1c} , %	9.1 ± 1.9	8.8 ± 1.7	7.9 ± 1.5
BMI, kg/m ²	33.2 ± 3.9	33.6 ± 3.1	31.8 ± 4.0
Σ PH	34.2 ± 5.5	34.8 ± 7.1	36.9 ± 3.9
Σ MH	30.7 ± 6.6	29.5 ± 4.2	35.3 ± 5.5*
Ranged questionnaire at DM (points)	13.5 ± 2.6	15.7 ± 1.4	11.6 ± 2.0*

Note.

* — significant in relation to pre-treatment data (p<0.05).

p < 0.05 in all patients with the above mentioned positive dynamics. Also this improvement was accompanied by raised mental component of life quality (Σ MH) from (28.6 ± 5.1) to (32.9 ± 3.9) points. BMI increased from (24.6 ± 3.1) to (26.1 ± 4.3) kg/m².

Questioning of the patients with degree II DU at type 2 DM by the ranged questionnaire revealed clinically determined incontinence in 18 patients (37.5 %), retention in 11 patients (22.92 %), and DU mixed form in 19 patients (39.58 %). HbA_{1c} mean level in this group was of (9.1 ± 1.9) %, duration of the disease was (13.7 ± 5.8) years. Mean score by the ranged questionnaire was (13.5 ± 2.6) points (table 3).

In three month after the completed course of treatment with alpha lipoic acid and group B vitamins against the background of continuing blood sugar lowering therapy, we registered reduced degree of DU clinical manifestations in 6 patients (12.5 %), that fact was reflected in significant reduction of score obtained from the

ranged questionnaire at DM with (15.7 ± 1.4) to (11.6 ± 2.0) points, p < 0.05 (table 3).

All patients with the mentioned positive dynamics demonstrated various degree reduction of HbA_{1c} level: from (8.8 ± 1.7) to (7.9 ± 1.5) %. A significant improvement of LQ mental component was registered: from (29.5 ± 4.2) to (35.3 ± 5.5) points, p < 0.05. As well, BMI reduced from (33.6 ± 3.1) to (31.8 ± 4.0) kg/m².

DU dynamics according to the DM ranged questionnaire in the patients with positive dynamics before and after treatment course is presented in Figure 1.

Conclusions. For DM patients with DU various degree, it is reasonable to use the ranged questionnaire aiming at assessment of the dynamics seen during the treatment. Pathogenic therapy with alpha lipoic acid and group B vitamins against the background of appropriate blood sugar lowering therapy in the patients with degree II DU (by the results of the ranged questionnaire) allows to improve

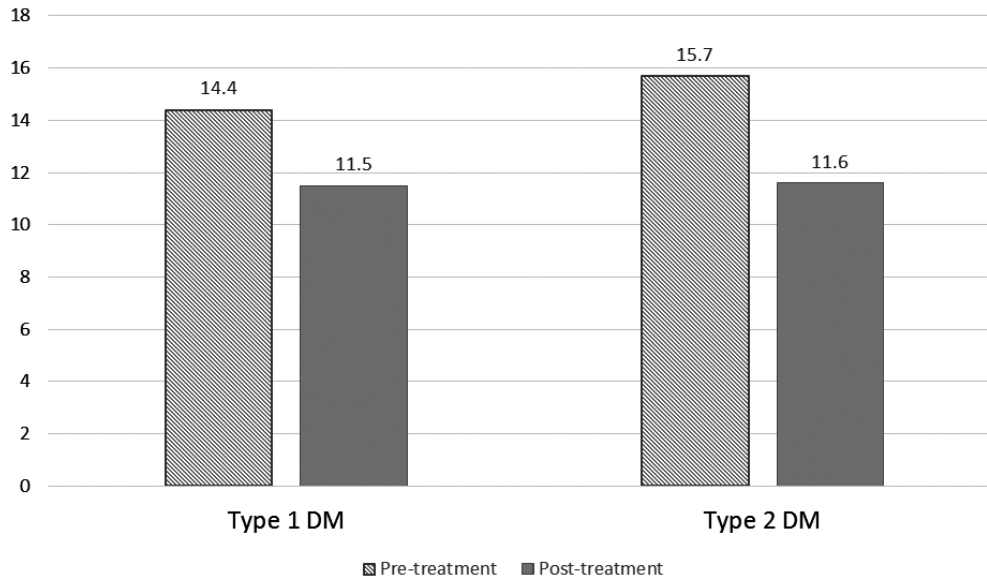


Figure 1. Dynamics of the disorders of urination

LQ and reduce clinical manifestations of diabetic cystopathy in 15.6 % patients with type 1 DM and 12.5 % patients with type 2 DM, that was manifested by significant reduction of the DU expression, decreased HbA_{1c} level

(significant in type 1 DM group), improvement of LQ by SF-36 (mental component, significant in type 2 DM group) and reduced body mass in type 2 DM, and increased body mass in type 1 DM.

REFERENCES

1. Stwhrer M, Blok B, Castro-Diaz D. *Eur Assoc Urol* 2010; 48 p.
2. Aljaev JuG, Grigorjan VA, Gadzhieva ZK. *Rasstrojstva mocheispuskanija, Moskva*, 2006: 208 p.
3. Dubenko EG. *Zdorov'ja Ukrainy* 2009, lystopad: 14-15.
4. Shvare PG. *RMZh* 2011;32: 2063-2067.
5. Gadzhieva ZG. *Narushenija mocheispuskanija: rukovodstvo, GJeOTAR-Media*, 2010: 180 p.
6. Tkachuk EJu, Kravchun NA. *Probl Endokryn Patologii'* 2016;2: 47-53.
7. Physical and Mental Health Summary Scales SF-36, available at: <http://www.sf-36.org>.
8. Galstjan GR. *Consilium Medicum* 2006;8(9): 5-9.
9. Bregovskij VB. *Bol'* 2008;1(18): 29-34.
10. Ametov A, et al. *Diabetes Care* 2003;26: 770-776.
11. Strokov IA, Strokov KI, Afonina ZhA. *Lechashhij Vrach* 2008;3: 46-47.
12. Zinov'eva OE. *Consilium Medicum* 2009;12: 43-47.
13. Strokov IA, Strokov KI, Solujanova TV. *Farmateka* 2006; 122: 7.
14. Babaci-Jadid R, Karachalias N, Ahmed N. *Diabetes* 2003; 3: 2110-2120.

**PATHOGENIC THERAPY OF DIABETIC CYSTOPATHY
WITH ALPHA LIPOIC ACID AND GROUP B VITAMINS
IN TYPES 1 AND 2 DIABETES MELLITUS PATIENTS**

Kravchun N. A.¹, Tkachuk E. Yu.²

¹ *SI «V. Danilevskiy Institute for Endocrine Pathology Problems of NAMS of Ukraine», Kharkiv;*

² *Regional Clinical Hospital – Center for Emergency Medical Aid and Medicine of Catastrophes, Kharkiv
allen-tkachuk@yandex.ua*

The work presents the results of treatment of 45 patients with type 1 and type 2 diabetes mellitus for diabetic bladder disorders. Pathogenesis-based therapy with alpha lipoic acid and group B vitamins allowed to improve life quality and reduce clinical manifestations of diabetic bladder disorders in 15.6 % patients with type 1 diabetes mellitus and 12.5 % women with type 2 diabetes mellitus, that was accompanied with a significant reduction of glycated hemoglobin in all patients.

Key words: type 1 and type 2 diabetes mellitus, urogenital form of diabetic autonomous neuropathy, lipoic acid, group B vitamins, disordered urination, ranged questionnaire at diabetes mellitus.

**ПАТОГЕНЕТИЧЕСКАЯ ТЕРАПИЯ ДИАБЕТИЧЕСКОЙ ЦИСТОПАТИИ
α-ЛИПОЕВОЙ КИСЛОТОЙ И ВИТАМИНАМИ ГРУППЫ В
У ПАЦИЕНТОК С САХАРНЫМ ДИАБЕТОМ 1 И 2 ТИПОВ**

Кравчун Н. А.¹, Ткачук Е. Ю.²

¹ *ГУ «Институт проблем эндокринной патологии им. В. Я. Данилевского НАМН Украины», г. Харьков*

² *Областная клиническая больница –
Центр экстренной медицинской помощи и медицины катастроф, г. Харьков
allen-tkachuk@yandex.ua*

В работе представлены результаты лечения диабетической цистопатии 45 пациенток с сахарным диабетом 1 и 2 типов. Патогенетическая терапия с использованием α-липоевой кислоты и витаминов группы В позволила улучшить качество жизни и уменьшить клинические проявления диабетической цистопатии у 15,6 пациентов с сахарным диабетом 1 типа и 12,5 % женщин с сахарным диабетом 2 типа, что сопровождалось достоверным снижением уровня гликозилированного гемоглобина у всех пациенток.

Ключевые слова: сахарный диабет 1 и 2 тип, урогенитальная форма диабетической автономной нейропатии, липоевая кислота, витамины группы В, нарушение мочеиспускания, шкала-опросник при сахарном диабете.

**ПАТОГЕНЕТИЧНА ТЕРАПІЯ ДІАБЕТИЧНОЇ ЦИСТОПАТІЇ
α-ЛІПОЄВОЮ КИСЛОТОЮ І ВІТАМІНАМИ ГРУПИ В
У ПАЦІЄНТОК ІЗ ЦУКРОВИМ ДІАБЕТОМ 1 І 2 ТИПІВ**

Кравчун Н. О.¹, Ткачук О. Ю.²

¹ *ДУ «Інститут проблем ендокринної патології ім. В. Я. Данилевського НАМН України», м. Харків*

² *Обласна клінічна лікарня – Центр екстреної медичної допомоги і медицини катастроф, м. Харків
allen-tkachuk@yandex.ua*

В роботі представлені результати лікування діабетичної цистопатії 45 пацієнток із цукровим діабетом 1 і 2 типів. Патогенетична терапія з використанням α-ліпоєвої кислоти і вітамінів групи В дозволила поліпшити якість життя і зменшити клінічні прояви діабетичної цистопатії у 15,6 % пацієнтів із цукровим діабетом 1 типу та 12,5 % жінок із цукровим діабетом 2 типу, що супроводжувалося достовірним зниженням рівня глікозильованого гемоглобіну у всіх пацієнток.

Ключові слова: цукровий діабет 1 і 2 типів, урогенітальна форма діабетичної автономної нейропатії, ліпоєва кислота, вітаміни групи В, порушення сечовипускання, шкала-опитувальник при цукровому діабеті.