

THE ROLE OF CYTOKINES IN THE KIDNEY DYSFUNCTION UNDER CONDITIONS OF IRRITABLE BOWELS SYNDROME DEVELOPMENT

Yu. Ye. Rogovy, Yu. V. Bilooka, V. V. Bilooky

Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsi

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cytokines, kidney bowels syndrome, pathogenesis.

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E-mail: rohovyy2012@gmail.com

The research is dedicated to the elucidation of the cytokines' role in the renal dysfunction under conditions of irritable bowels syndrome.

Objective - to carry out pathological analysis of cytokines' role of the blood plasma in the kidney dysfunction at irritable bowels syndrome with constipation and diarrhea.

Material and methods. 60 patients (18 - men, 42 - women aged 28 to 62 years) with irritable bowels syndrome were examined. Among them there were 28 patients with irritable bowels syndrome with constipation, 32 patients had irritable bowels syndrome with diarrhea. Control group consisted of 25 practically healthy patients. The level of cytokines was determined in the blood plasma: necrosis factor of tumor-alpha, interleukin-1-beta, interleukin-4 and interleukin-6. Statistical data processing was conducted by means of computer programs "Statgrafics" and "Exel 7.0".

Results. Contents increase of necrosis factor of tumor-alpha, interleukin-1-beta, interleukin-4 and interleukin-6 is accompanied by inhibition of the total, enzymatic, non-enzymatic fibrinolytic activity of the urine and proximal reabsorption of sodium ions in patients with irritable bowel syndrome.

Conclusions. More significant imbalance manifestations of cytokines and functional state of kidneys revealed in patients with the syndrome of irritable bowels with diarrhea in comparison with the previously mentioned syndrome with constipation are explained by the development of dehydration, hemoconcentration, hypoxia, lipid peroxidation activation and more essential damageable manifestations of inflammation process due to diarrhea.

Ключові слова:

цитокини, нирки, синдром подразненого кишечника, патогенез.

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РОЛЬ ЦИТОКИНІВ У РОЗЛАДАХ ФУНКЦІЇ НИРОК ЗА УМОВ РОЗВИТКУ СИНДРОМУ ПОДРАЗНЕНОГО КИШЕЧНИКУ

Ю.Є. Роговий, Ю.В. Білоока, В.В. Білоокій

Дослідження присвячене з'ясуванню ролі цитокинів в розладах функції нирок за синдрому подразненого кишечника.

Мета роботи - проведення патофізіологічного аналізу ролі цитокинів плазми крові в порушенні функції нирок за синдрому подразненого кишечника з закрепом та діареєю.

Матеріал і методи. Обстежено 60 хворих з синдромом подразненого кишечника. Чоловіків - 18, жінок - 42 віком від 28 до 62 років. Із яких: з синдромом подразненого кишечника з закрепом склали - 28 хворих, синдромом подразненого кишечника з діареєю - 32. Контрольну групу склали 25 практично здорових пацієнтів. Визначали в плазмі крові рівень цитокинів: фактору некрозу пухлин-альфа, інтерлейкіну-1-бета, інтерлейкіну-4 та інтерлейкіну-6. Статистичну обробку даних проводили за допомогою комп'ютерних програм "Statgrafics" та "Exel 7.0".

Результати. У хворих на синдром подразненого кишечника наростання вмісту фактору некрозу пухлин-альфа, інтерлейкіну-1-бета, інтерлейкіну-4 та інтерлейкіну-6 супроводжується гальмуванням сумарної, ферментативної, неферментативної фібринолітичної активності сечі та проксимальної реабсорбції іонів натрію.

Висновки. Виявлені більш істотні прояви дисбалансу цитокинів та функціонального стану нирок у хворих на синдром подразненого кишечника з діареєю порівняно до вищезазначеного синдрому із закрепом пояснюється розвитком зневоднення, гемоконцентрації, гіпоксії, активації перекисного окиснення ліпідів та більш істотних ушкоджувальних проявів процесу запалення за умов діареї.

Ключевые слова:

цитокины, почки, синдром раздраженного кишечника, патогенез.

РОЛЬ ЦИТОКИНОВ В РАССТРОЙСТВАХ ФУНКЦИИ ПОЧЕК В УСЛОВИЯХ РАЗВИТИЯ СИНДРОМА РАЗДРАЖЕННОГО КИШЕЧНИКА

Ю.Е. Роговий, Ю.В. Белоокая, В.В. Белоокій

Исследование посвящено выяснению роли цитокинов в расстройствах функции почек при синдроме раздраженного кишечника.

Цель работы - проведение патофизиологического анализа роли цитокинов плазмы

крови в нарушении функции почек при синдроме раздраженного кишечника с запором и диареей.

Материал и методы. Обследовано 60 больных с синдромом раздраженного кишечника. Мужчин - 18, женщин - 42 в возрасте от 28 до 62 лет. Из которых: с синдромом раздраженного кишечника с запором составили 28 больных синдромом раздраженного кишечника с диареей - 32. Контрольную группу составили 25 практически здоровых пациентов. Определяли в плазме крови уровень цитокинов: фактора некроза опухолей-альфа, интерлейкина-1-бета, интерлейкина-4 и интерлейкина-6. Статистическую обработку данных проводили с помощью компьютерных программ "Statgrafics" и "Exel 7.0".

Результаты. У больных с синдромом раздраженного кишечника нарастание содержания фактора некроза опухолей-альфа, интерлейкина-1-бета, интерлейкина-4 и интерлейкина-6 сопровождается торможением суммарной, ферментативной, неферментативной фибринолитической активности мочи и проксимальной реабсорбции ионов натрия.

Выводы. Выявлены более существенные проявления дисбаланса цитокинов и функционального состояния почек у больных с синдромом раздраженного кишечника с диареей по сравнению с вышеупомянутым синдромом с запором объясняется развитием обезвоживания, гемоконцентрацией, гипоксией, активацией перекисного окисления липидов и более существенным повреждающим проявлением процесса воспаления в условиях диареи.

Клиническая и экспериментальная патология Т.17, №3 (65), С.80-84.

Introduction

Irritable bowels syndrome is known to be one of the leading positions among chronic gastroenterological diseases [1].

The previously mentioned syndrome according to IV Roman consensus represents itself the functional disease of the bowels with the recurrent pain in the abdomen, associated with emptying or feces changes (diarrhea, constipation), meteorism. It should be noted that these symptoms are detected not less than 6 months before making a diagnosis and periodically arise during the last three months, in addition to that, frequency of the pain origin in the abdomen must be not rarely than once a week [1, 2].

Pro- and anti-inflammatory cytokines [3], changes of which may lead to strengthening of the inflammatory process and probably kidney function disorder, since proximal portion of nephron is very sensitive to the injured influence of various factors [4], may play a significant part in the pathogenesis of irritable bowels syndrome with constipation or diarrhea. Simultaneously the analysis of cytokines' role due to the development of irritable bowels syndrome with constipation or diarrhea in the dysfunction of the renal state is not sufficiently studied.

Objective

To carry out pathophysiological analysis of the role of necrosis factor of tumor-alpha, interleukine-1-beta, interleukine-6 in the blood plasma at irritable bowels syndrome with constipation and diarrhea in the kidney dysfunction.

Material and methods

60 patients with irritable bowels syndrome have been examined (18 men and 42 women) aged 28 to 62 years: 28 patients with irritable bowels syndrome with constipation, 32 patients with irritable bowels syndrome with diarrhea. The control group consisted of 25 practically healthy

patients.

The functional state of the kidneys was studied under conditions of water loading. The patients used water from the water pipe, warmed up to 37° C in the quantity of 2% from the body weight. Diuresis value (V) was estimated in 1/2 hours, the body surface area 1.72m². Blood from the vein was drawn with heparin into the tube following the water loading with object of getting plasma. Creatine concentration was determined by photometry flame method according to the reaction with picric acid, sodium ions on PhFL-1 in the blood and urine plasma. Proximal reabsorption of sodium ions (TNa) was calculated by formula: TNa = (C - V) PNa, where C - glomerular filtration rate, V - diuresis, PNa - sodium ions concentration in the blood plasma [5, 6]. Urine fibrinolytic activity under conditions of water loading 2% of the body weight and urine sampling during 2 hours was carried out according to azofibrin lysis determination with the total (TEA) estimation, non-enzymatic (NEA - incubation test at the presence of enzymatic fibrinolysis blocker of aminocaproic acid) with calculation of enzymatic fibrinolytic activity by the formular: FEA = TEA - NEA [7]. Investigation of cytokines concentration in the blood plasma: tumor - α necrosis factor, interleukine -1 β , interleukine-4 and interleukine-6 was conducted by the immunoenzymatic analysis method by means of "Diaclone" firm sets (France).

All investigations were conducted following "The rules of ethical principles of carrying out scientific medical investigations with the participation of a man", confirmed by Helsinki declaration (1964-2013), ICH GCP (1996), Instructions of EEC №609 (dated from 24.11.1986), MPH orders of Ukraine № 690 dated from 23.09.2009, № 944 of 14.12.2009, № 616 dated from 03.08.2012.

Data statistical processing was carried out by means of "Statgrafics" and "Exel 7.0" computer programs.

Results and their discussion

The results of the research have shown that cytokines level in the blood plasma increased in patients with the

irritable bowels syndrome: necrosis tumor- α factor, interleukine-1 β , interleukine-4 and interleukine-6 (fig.1), besides that, more significant growing of the previously mentioned cytokines was peculiar for the irritable bowels syndrome with diarrhea concerning the previously mentioned syndrome with constipation.

It should be noted that irritable bowels syndrome with diarrhea was characterized with more severe clinical

course than the previously mentioned syndrome with constipation. Total, enzymatic, non-enzymatic fibrinolytic activity of the urine and proximal reabsorption of sodium ions decreased at irritable bowels syndrome, besides that, more essential derangement of the previously mentioned indices of the renal function was peculiar for irritable bowels syndrome with diarrhea as regards the previously mentioned syndrome with constipation(fig. 2).

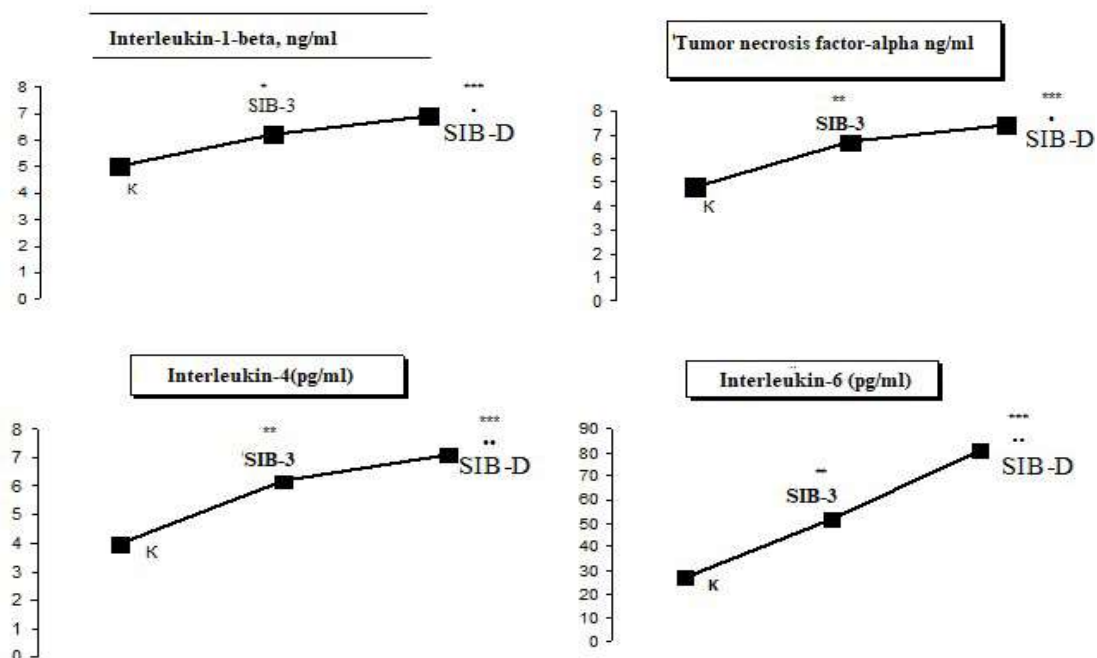


Fig. 1. Cytokines' level of the blood plasma in patients at irritable bowel syndrome development with constipation (SIB-3) and diarrhea (SIB-D).

Notes: difference authenticity in comparison with the control* - $p < 0.05$; ** - $p < 0.02$; *** - $p < 0.01$ comparatively irritable bowels syndrome with constipation ° - $p < 0.05$; °° - $p < 0.02$

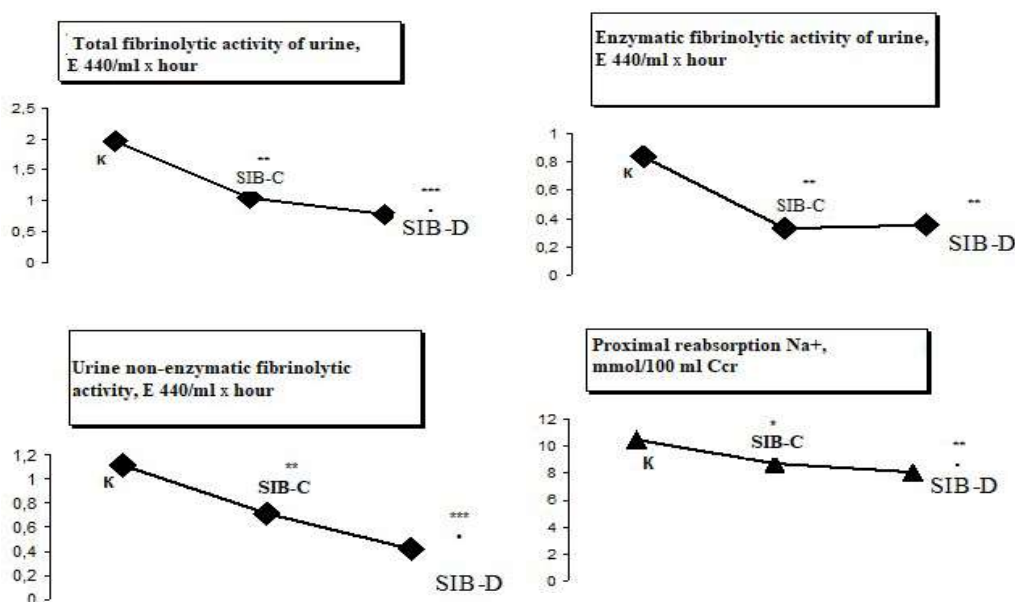


Fig.2. Total, enzymatic, non-enzymatic fibrinolytic activity of the urine and standardized proximal sodium ions reabsorption according to the glomerular filtration rate in patients at the development of irritable bowels syndrome with constipation (SIB-3) and diarrhea (SIB-D).

Notes: authenticity of differences in comparison with the control* - $p < 0.05$; ** - $p < 0.02$; *** - $p < 0.01$; compared to the irritable bowels syndrome with constipation · - $p < 0.05$

Pathogenesis of the irritable bowels syndrome is explained by chronic stress influence, substantial psychogenic disadaptations with manifestation in the form of anxiety that stipulated hyperplasia of APUD system cells (EC - enterochromaffinic, Mo-cells and others), which produce biologically active substances of serotonin, motilin type, P substance. Under the influence of the latter ones hyperfunctioning and development of the local inflammatory process with the intestinal barrier function disorders arise. The present local inflammatory process leads to an increase of anti-inflammatory cytokines of tumor- α necrosis factor, interleukine -1 β , interleukine -6 and increase of anti-inflammatory interleukine - 4 production, which may be estimated as the defence reaction to the development of anti-inflammatory process. It is impossible to exclude completely the defence properties of interleukine-6, which, besides pro -inflammatory properties, also shows anti-inflammatory properties. Large intestine hyperfunction under such conditions probably results in energy deficit, intensified use of *B. Bifidum*, *B. Lactis* to supply regeneration processes of intestinal epithelium. Decrease of *B. Bifidum*, *B. Lactis* level leads to the development of dysbacteriosis, intoxication, products' increase with the average molecular weight, intensification of the lipid peroxidation processes. The latter ones cause the nephron proximal portion damage with impede of standardized proximal reabsorption of sodium ions, urine total, enzymatic, non-enzymatic fibrinolytic activity, since urokinase-activator enzyme of the urine fibrinolysis is produced in standard by the nephron proximal portion. Extreme hyperfunction of the structures of the central nervous system and APUD-system cells of the bowels in future is accompanied by exhaustion of their reserve possibilities by disregulative pathological process type [8, 9] with transformation of anxiety reaction to depression, and hyperkinetic intestine state into its hypokinesis with constipation development. More essential disorders of cytokines' concentrations in the blood plasma and kidney function at irritable bowels syndrome with diarrhea in comparison with the indicated syndrome with constipation is caused by dehydration due to diarrhea, hemoconcentration, microcirculation derangements with more significant lipoperoxidation activation and essential disorders of the functional state of the proximal ducts.

Conclusions

1. Content growing of pro -inflammatory cytokines of the tumor- α necrosis factor, interleukine -1 β and interleukine -6 is accompanied with fibrinolytic activity impede of urine and sodium ions proximal reabsorption in patients with irritable bowels syndrome. Concentration increase of anti-inflammatory interleukine -4 should be considered as the protective reaction on inflammatory process development.

2. More significant manifestations of the functional kidney state and pro -inflammatory cytokines worsening, revealed in patients with irritable bowels syndrome with diarrhea compared to the previously mentioned syndrome with constipation, are explained by the dehydration development, hemoconcentration and activation of lipid

peroxidation due to diarrhea.

Perspectives of future investigations

Perspective of the following elaborations concerning the role of the pathogenic correction factors of the functional state of kidneys in patients with irritable bowels syndrome is substantiated.

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Відомості про авторів:

Роговий Юрій Євгенович - д.мед.н., проф., завідувач кафедри патологічної фізіології Вищого державного навчального закладу України "Буковинський державний медичний університет", м. Чернівці, Україна.

Білоока Юлія Вячеславівна - аспірант кафедри внутрішньої медицини та інфекційних хвороб Вищого державного навчального закладу України "Буковинський державний медичний університет", м. Чернівці, Україна.

Білоокий Вячеслав Васильович - д.мед.н., професор кафедри хірургії Вищого державного навчального закладу України "Буковинський державний медичний університет", м. Чернівці, Україна.

Сведения об авторах:

Роговой Юрий Евгеньевич - д.мед.н., проф., заведующий кафедрой патологической физиологии Высшего государственного учебного заведения Украины "Буковинский государственный медицинский университет", г.Черновцы, Украина.

Белоокая Юлия Вячеславовна - аспирант кафедры внутренней медицины и инфекционных болезней Высшего государственного учебного заведения Украины "Буковинский государственный медицинский университет", г.Черновцы, Украина.

Белоокий Вячеслав Васильевич - д.мед.н., профессор кафедры хирургии Высшего государственного учебного заведения Украины "Буковинский государственный медицинский университет", г.Черновцы, Украина.

Information about the authors:

Rohovyi Yurii Yegenievich - MD, professor, Head of the Department of pathological physiology of Higher state educational

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Рецензент – проф. В.П. Польовий

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