

CONTEMPORARY VIEWS ON THE MECHANISMS OF DEVELOPMENT OF INTESTINAL SUTURES INSUFFICIENCY

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The article is devoted to research the role of local changes of some biochemical processes in the tissues of intestinal wall in the conditions of development of sutures insufficiency. The changes of indices of fibrinolysis, proteolysis, and lipid peroxidation in the sutured tissues of bowel were researched in 60 experimental animals with the model of intestinal sutures insufficiency. It was detected that increased fibrinolytic and proteolytic activity may be one of the mechanisms of disturbance of the primary (biological) leak-resistance of the suture line in the early (12-24 h.) terms. At a later stage (24-72 h.) excessive activation of enzymatic fibrinolysis and collagen degradation was combined with disbalance of the pro- and antioxidant systems. Such combination of rising of destructive processes with the depletion of protective systems may contribute in a disturbance of regeneration of the connection area with the onset of sutures insufficiency.

Keywords: intestinal sutures insufficiency, fibrinolytic activity, proteolytic activity, lipid peroxidation, regeneration.

Problem statement. Despite the reduction of share of full-size operations in abdominal surgery, intestinal sutures insufficiency (ISI) continues to be quite serious complications after operations on the hollow digestive organs. The frequency of the onset of ISI is variable with range 2,3-32% and depends of type of surgery according urgency, region of digestive tract and technical conditions of intervention [3, 8]. The mortality rate in case of this one is up to 50% [11]. The unsatisfactory results of treatment of this poly-ethiological complication are largely associated with an insufficient study of all its pathogenetic aspects [4].

Analysis of last investigations and publications. Successful healing of anastomotic region provides of supporting of conditions to optimal regeneration of sutured tissues. It is known [5, 6] that primary biological leak-resistance of sutures on the hollow digestive organs is provided by the formation of fibrin on the serous membranes at the place of their connection. Furthermore, the tissue fibrin network is a matrix for fibroblasts that stimulates their growth and synthesis of the collagenous fibers, contributing to an optimal healing of the suture line. Blood supply, bacterial contamination and adequate load of suture line have a significant influence on regeneration of sutured tissues of intestine [7, 8, 10]. Speed of regeneration depends on the processes of formation and destruction of the connective tissue controlled by the activity of the proteolytic, fibrinolytic, pro- and antioxidant systems. Individual papers are partially devoted to a study of the some biochemical processes in the tissue of the hollow organs of digestion [3, 4]. These investigations contain scattered data mainly about changes of biochemical processes in the serum of venous blood in case of ISI. Based of these data it is impossible to make convincing conclusions about of the essence of the changes that occur in site of connected tissues.

Marking of the unsolved aspects of the problem. The state of the fibrinolytic and proteolytic activity and contents of products of lipid peroxidation in tissues of the intestine directly in the region of applied sutures in case of their incompetence remains obscure [9].

The purpose of the research: to study changes of fibrinolytic and proteolytic activities, content of products of lipid peroxidation and activity of antioxidant system of the tissues of intestine in the region of sutures under conditions of the development of their insufficiency.

Presentation of the base material. The experiments have been carried out on 56 albino nonlin-

ear male rats, weighting 180 ± 20 g. All the animals underwent a resection of the cupula of the cecum with suturing the intestinal foramen by means of interrupted stitches (polyamide 5-0). ISI was modelled by way of excessive mobilization of the area of junction and a rare application of stitches in the animals of the experimental group. In 12, 24, 48 and 72 hours following a surgical interference an euthanasia of the animals was performed under ether anesthesia and the samples of the intestinal tissue in the region of sutures were taken for an analysis. The indices of fibrinolytic activity: total (TFA), non-enzymatic (NFA), enzymatic (EFA) and proteolytic activity been researched according to Kukharchuk's procedure (1996). The indices of proteolytic activity by the lysis of: azoalbumin (AA), azocollagen (ACg), azocasein (ACs) and the indices of the lipid peroxidation: diene conjugates (DC), malonic aldehyde (MA) and activity of the antioxidant enzymes: superoxide scavenger (SOS), catalase (Ct) and glutathione peroxidase (GPO) were researched with the aid of an assay kit «Simko Ltd» (Ukraine). Statistical processing of the results of the investigation was performed on PC by means of the application «Primer of biostatistics, 4th ed.». Data from the groups were compared using Mann-Whitney's t-test. To reject the null hypothesis the significance level was used equal to $p < 0,05$. The experiments were carried out with the observance of the requirements of the European convention as to the protection of vertebrate animals that are used for experimental and other scientific purposes (Strasbourg, 1986).

Below in the text, we present the results of research on the tables 1, 2, 3.

According to the obtained data the parameters of the fibrinolytic and proteolytic activity under study were reliably higher in the animals of the experimental group as compared with the control one. The reliable rising of the level of DC was detected since 24 h. of the observation, while the more increased indices of MA have been observed in the ISI group in comparison with control one since 12 h. after operation. The indices of activity of all the antioxidant enzymes (SOS, Ct, GPO) were reliably lower in the animals with ISI as compared with the animals without this one throughout the entire period of observation.

When analysing the obtained findings it has been established that the steady activation of tissues proteolysis take place in the animals with ISI. So, in 12-24 h. following the operation a reliably higher activity of lysis of AA, ACs and ACg was detected in the animals of the experimental group ($p < 0,001$). It's

testify about increase of proteolytic modification of the low- and high-molecular proteins. In particular, the activity of ACg lysis in the animals of the trial series exceeded twice the control findings which indicates a deeper degradation of collagen molecules in investigated tissues. Increased proteolytic activity also contributes the intensified lysis of fibrin in the junction area at the expense of a direct enzymatic action [1]. At this period of observation in the animals with IIS there occurs a proved rise of TFA, both at the expense of NFA and EFA ($p < 0,001$).

As it is generally known, an activation of the non-enzymatic fibrinolysis is a counterbalance of a stress reaction [2]. The formation of the adrenaline-heparin-antithrombin III complex, activating plasminogen, contributing to its transformation into plasmin and splitting of fibrin, underlies it. However, such an impetuous and pronounced activation of fibrinolysis in the region of the connection may bring about a disturbance of the primary biological leak resistance of the suture line, infecting the thread canal and a penetration of microorganisms out of the intestinal lumen on their surface. The formation of loose adhesions with the participation of infiltrated hyperemic tissues of the omentum, the loops of the small intestine and the adjacent loops of the large intestine

constituted visual manifestations of primary biological leakage of a junction zone in all the animals of the experimental group during this period.

During a later period (48-72 h.) we observed a tendency to rise of the indices of tissue proteolysis, especially indices of ACg lysis, which were one and a half time higher than data of the control group. The long increased degradation of collagen molecules in tissues of the junction zone on the conditions of insufficient blood supply may be one of the mechanisms of disturbance of regeneration of sutured tissues [6]. An elevation of the tissue fibrinolytic activity was detected in the animals with IIS, largely at the expense of EFA which exceeded twice the control data. Such an excessive activation of the tissues fibrinolysis at the expense of lysis of the fibrin matrix may cause a disturbance of the fixation of fibroblasts in the tissues of the connection area and its regeneration [5, 9].

At this period we defined a great accumulation of final products of lipid peroxidation in the animals of the experimental group ($p < 0,001$). So, concentrations of DC and MA were higher in 3-6 times in latter as compared with the control ones. The indices of activity of majority from the investigated antioxidant enzymes were 10 times less in the animals with ISI. Such disbalance of the pro- and antioxidant systems

Table 1

Indices of fibrinolytic activity of the tissues of the rat cecum in the region of the suture line

Indices	Intact	12 hours		24 hours		48 hours		72 hours	
		C	E	C	E	C	E	C	E
Total fibrinolytic activity (E440/h × g)	40,48± 1,56	55,80± 1,48	82,60± 1,024***	43,04± 1,99	86,64± 1,12***	48,76± 1,97	80,32± 1,12***	45,52± 2,19	83,44± 1,34***
Nonenzymatic fibrinolytic activity (E440/h × g)	21,20± 1,079	28,80± 1,29	44,36± 0,995***	22,32± 1,64	45,04± 1,072***	24,40± 1,035	40,16± 0,54***	21,96± 1,19	40,40± 0,95***
Enzymatic fibrinolytic activity (E440/h × g)	19,28± 0,64	27,00± 0,43	38,24± 0,508***	20,72± 0,49	41,60± 0,32***	24,36± 0,94	40,16± 0,58***	23,56± 1,007	43,04± 0,57***

Notes: C – control; E – experiment

* – $P < 0,05$; ** – $P < 0,01$; *** – $P < 0,001$ – statistical reliable distinctions.

Table 2

Indices of proteolytic activity of the tissues of the rat cecum in the region of the suture line

Indices	Intact	12 hours		24 hours		48 hours		72 hours	
		C	E	C	E	C	E	C	E
Azoalbumin lysis (E440/h × g)	43,80± 1,27	56,80± 1,19	77,76± 1,33***	74,40± 1,73	101,80± 1,24***	83,52± 0,86	114,04± 1,47***	80,08± 0,98	124,96± 1,84***
Azocollagen lysis (E440/h × g)	14,68± 0,92	17,40± 1,296	31,52± 1,602***	18,04± 1,62	55,92± 1,602***	32,84± 1,48	48,24± 1,68**	23,36± 1,36	46,88± 0,91***
Azocasein lysis (E440/h × g)	56,78± 1,45	81,84± 1,54	106,64± 1,401***	67,00± 1,84	120,00± 1,77***	103,56± 1,39	116,64± 1,97**	90,20± 1,45	111,84± 1,19***

Notes: C – control; E – experiment

* – $P < 0,05$; ** – $P < 0,01$; *** – $P < 0,001$ – statistical reliable distinctions.

Table 3

Indices of products of lipid peroxidation and antioxidant activity of the tissues of the rat cecum in the region of the suture line

Indices	Intact	12 hours		24 hours		48 hours		72 hours	
		C	E	C	E	C	E	C	E
Diene conjugates (nmole/mg of protein)	-	0,333± 0,017	0,470± 0,021	0,385± 0,037	0,675± 0,018***	0,131± 0,015	0,793± 0,012***	0,223± 0,023	0,589± 0,007***
Malonic aldehyde (nmole/mg of protein)	-	0,154± 0,024	0,594± 0,057***	0,331± 0,046	0,461± 0,021	0,286± 0,006	1,211± 0,089***	0,545± 0,074	1,578± 0,110***
Superoxide scavenger (Units/mg of protein/min)	-	0,627± 0,041	0,237± 0,018***	0,962± 0,089	0,469± 0,025**	0,572± 0,070	0,476± 0,024	1,130± 0,118	0,270± 0,031***
Catalase (mmole H ₂ O ₂ /min/mg of protein)	-	20,734± 1,31	0,309± 0,041***	29,82± 2,091	0,316± 0,057***	23,941± 1,16	0,554± 0,034***	29,966± 2,030	0,429± 0,045***
Glutathione peroxidase (Gsh/mg of protein/min)	-	0,076± 0,018	0,013± 0,003*	0,186± 0,030	0,009± 0,0003**	0,230± 0,037	0,010± 0,0003***	0,207± 0,035	0,010± 0,0007***

Notes: C – control; E – experiment

* – $P < 0,05$; ** – $P < 0,01$; *** – $P < 0,001$ – statistical reliable distinctions.

may be one of the mechanisms of implementation of the damaging effect of active oxygen forms on the conditions of ischemia in the area of sutures with the ISI development. Thus, numerous hemorrhages and solitary films of fibrin in the region of the connection with separate defects and interintestinal abscesses were revealed within the specified period in the trial series against a background of a considerable amount of serous-fibrinous exudate in the abdominal cavity.

Conclusions.

1. On the model of intestinal sutures insufficiency an increase of fibrinolytic and proteolytic activity with accumulation of products of lipid peroxidation are observed in the tissues of the junction area.

2. In the early terms (12-24 h.) increased fibrinolytic and proteolytic activity may be one of the mechanisms of disturbance of the primary (biological) leak-resistance of the suture line.

3. At a later stage (24-72 h.) excessive activation of enzymatic fibrinolysis and collagen degradation in a combination with disbalance of the pro- and anti-oxidant systems may contribute in a disturbance of regeneration of the connection region with the onset of sutures insufficiency.

4. We consider it expedient to study correlations between the fibrinolytic and proteolytic activity and degree of microbial contamination of the region of the interintestinal connection in case of sutures insufficiency.

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НОВІ ПОГЛЯДИ НА МЕХАНІЗМИ РОЗВИТКУ НЕСПРОМОЖНОСТІ КИШКОВИХ ШВІВ

Анотація

Стаття присвячена розкриттю ролі місцевих змін деяких біохімічних процесів в тканинах кишкової стінки в умовах розвитку неспроможності швів. Досліджені зміни показників фібринолізу, протеолізу та перекисного окиснення ліпідів у зшитих тканинах кишок у 60 експериментальних тварин з моделлю неспроможності кишкових швів. Встановлено, що підвищена фібринолітична та протеолітична активність може бути одним із механізмів порушення первинної (біологічної) герметичності лінії швів у ранні терміни (12-24 год.). У пізніші терміни (24-72 год.) надмірна активація ферментативного фібринолізу та деградації колагену поєднується із дисбалансом про- і антиоксидантних систем. Така комбінація зростання деструктивних процесів з виснаженням систем захисту може бути в основі порушення регенерації зони з'єднання з виникненням неспроможності швів.

Ключові слова: неспроможність кишкових швів, фібринолітична активність, протеолітична активність, перекисне окиснення ліпідів, регенерація.

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Аннотация

Статья посвящена раскрытию роли местных изменений некоторых биохимических процессов в тканях кишечной стенки в условиях развития несостоятельности кишечных швов. Исследованы изменения показателей фибринолитической, протеолитической активностей и перекисного окисления липидов в сшитых тканях кишечника у 60 экспериментальных животных с моделью несостоятельности кишечных швов. Установлено, что повышенная фибринолитическая и протеолитическая активность может быть одним из механизмов нарушения первичной (биологической) герметичности линии швов в ранние сроки (12-24 ч.). В более поздние сроки (24-72 ч.) чрезмерная активация ферментативного фибринолиза и деградации коллагена сочетается с дисбалансом про- и антиоксидантных систем. Такая комбинация нарастания деструктивных процессов с истощением защитных систем может быть в основе нарушения регенерации зоны соединения с возникновением несостоятельности швов.

Ключевые слова: несостоятельность кишечных швов, фибринолитическая активность, протеолитическая активность, перекисное окисление липидов, регенерация.