STATE OF COLLAGEN SYNTHESIS IN GASTRIC MUCOSA AND RENAL TISSUE IN INDOMETACIN GASTROPATHY IN ANIMALS WITH EXPERIMENTAL RHEUMATOID ARTHRITIS

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It was established that reparation of ulcer defect heals by cicatrization. Main element of cicatricial tissue is collagen having amino acid oxyproline in its structure. Results of studying the latter in biologic fluids adequately reflect process of collagen formation [1,2]. Therefore studying content of this amino acid in tissues it may be predetermined a state of collagen formation and regeneration processes of ulcerous-erosive disorders in mucosa of gastrointestinal tract (GIT). As regards renal tissue a content of oxyproline specifies a state of inflammation process accompanying by sclerosis of renal tissue [3, 4, 5, 6, 7].

Aim of research: was to study a state of collagen synthesis in gastric mucosa and renal tissue in indometacin gastropathy in animals with experimental rheumatoid arthritis.

Materials and methods of research: Experimental studies were carried out on 21 male rats of mixed population with mass 160-200 g that were on common ration of vivarium. Animals were divided into 3 groups of 7 animals each. The 1st group was intact, the 2nd group with experimental rheumatoid arthritis (ERA), the 3rd group – animals with ERA and indometacin gastropathy (GERA).

Experimental model of rheumatoid arthritis was reproduced by a single administration of 0,2 ml Freund's adjuvant into posterior right leg of animal [8]. Indometacin induced gastro- and nephropathies were produced by administration of indometacin per os as water suspension at a dose 2,5 mg/kg during 5 days [9]. All painful procedures were performed in accordance with the WMA Declaration of Helsinki. To perform biochemical studies all the animals were single-stage decapitated under etherization. Stomach was extracted, then purified, washed with a cold physiological solution, proventriculus was removed. Mucous layer then was scarified, weighed and slurried in distilled water at a rate 30 mg/ml.

Kidneys were crushed and homogenized in a glass homogenizer with Teflon pestle in 3-4-fold volume of excretion medium consisting of 0,25M saccharose, 0,05M KCl in 0,05M solution tris HCl buffer (pH 7,4). To precipitate nuclei, mitochondria and disordered cells homogenates were centrifuged in 9000 g during 20 minutes. Content of oxyproline in supernatant fraction of homogenate was determined by a method of A. Steven and coauthors [10].

Results obtained were treated with using of Student's t-criterion by a statistically standard package of Microsoft Excel. Differences considered valuable in $p < 0,05$.

Results and their discussion: Results of studying a content of oxyproline in gastric and renal tissue are given in the table.

How it is seen from the presented data a content of oxyproline in gastric mucosa in ERA is practically not differed from control group, whereas it is reliably increased 35,6% from index of control group. Reduction in content of oxyproline noted to be in gastric mucosa 79,3% from control group in using of indometacin (GERA). Content of oxyproline in renal tissue was increasing 174,8% in this group. Probably, suppression of regeneration processes by indometacin in gastric mucosa was caused by abnormalities in functioning of numerous intercaused cytoprotective factors that leads to lowering of post-epithelial factors of protection, which principal element are "cytoprotective" prostaglandins. It is established that prostaglandin E_2 implements its protective potential on suppression of formation of gastric acid, increase of mucus and bicarbonate secretion, stimulation of regeneration.

Unlike to stomach a considerable increase of oxyproline in application of indometacin observed to be in kidneys. It is likely to be caused by some

Content of oxyproline in gastric mucosa and renal tissue in indometacin gastropathy in animals with experimental rheumatoid arthritis.

№	Group of animals	Oxyproline, nmol/mg			
		Stomach	p	kidneys	p
1	Control	2,12 ± 0,077		5,28 ± 0,180	
2	ERA	1,95 ± 0,062		7,16 ± 0,315	
3	GERA	0,44 ± 0,019	0,001	14,51 ± 0,384	0,001

N o t e : p – reliability from indices of control group.

inter-related mechanisms. Block of synthesis of renal prostaglandins by indometacin increases and prolongs vasoconstrictive action of angiotensin II playing a key role in progressive lowering of renal function by means of hemodynamic and "non hemodynamic" mechanisms [11, 12]. Renin-angiotensin-aldosteron system actuates when release of renin by juxtaglomerular cells of kidneys occurs. The latter catalyzes transformation of angiotensin in angiotensin I in the liver. Then locally in tissues occurs transformation of angiotensin I in angiotensin II (active form) – under participation of angiotensin I converting enzyme. Production and release of aldosteron, proximal canalicular re-absorption of sodium, shortening of afferent and efferent arterioles, heightened saline appetite, inhibition of parasympathetic nervous system, stimulation of β-adrenoreceptors, intensification of proteinuria – it is not complete list of effects provoked by angiotensin II. Mechanisms considered prove involvement of both glomerular and tubular-interstitial apparatus in damage of kidneys by indometacin.

Conclusions

1. Indometacin considerably reduces a content of oxyproline in gastric mucosa that confirmed suppression of regeneration processes.

2. Preparation increases a content of oxyproline in renal tissues in indometacin gastropathy that exhibited appearance of inflammation process leading to renal tissue sclerosis.

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