



EXPERIMENTAL ARTICLE

SHIFTS IN THE CONTENT OF SOMATOSTATIN IN BLOOD SERUM OF INTACT RATS UNDER EXPERIMENTALLY INDUCED WOUND PROCESS WITH THE APPLICATION OF “ARMENICUM” DRUG AND PASTE

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ABSTRACT

The shifts in somatostatin content in blood serum of intact rats and experimental animals with a model of purulent wound were observed under the application of two compositions – “Armenicum” drug and paste,

Due to the immune-enzyme analysis it was established that the triple intramuscular administration of “Armenicum” drug during the first 9 days was accompanied with noticeable reduction in somatostatin levels in blood serum of intact animals. Low levels of somatostatin were detected in blood serum of the experimental animals in conditions of experimentally induced wound process under topical application of “Armenicum” paste on the wound surface.

The biological effect of “Armenicum” drug, set on the intact animals in respect of selective inhibition of somatostatin secretion processes in hypothalamus (and in the secretory cells of digestive system, which is not excluded) allows to recommend the tested drug for pathological conditions in the basis of which somatostatin and somatostatin-dependent hormonal disorders dominate.

On the other hand, “Armenicum” paste, which has shown quite favorable effect on the course of regional reparative-proliferative processes, can be considered as an effective symptomatic and pathogenic means for the treatment of purulent wounds of different geneses.

In the mechanism of induction of reparative-proliferative processes in connective tissue besides the important role of in situ produced fibronectin, great importance should be given to hypothalamic (as well as possibly to extra hypothalamic) somatostatin, because there are reciprocal interactions between the two endogenously active factors, in terms of their certain application point – effects on collagens of I and III types.

KEYWORDS: purulent wound, somatostatin, “Armenicum” drug and paste, therapeutic effectiveness.

INTRODUCTION

The approbation of new effective means of pathogenic and systematic therapies of wound process under experiment is firstly directed to the detection of possible regional mechanisms which eventually lead to wound healing by restitution or substitution.

For this purpose, the effects of “Armenicum”

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paste on the course and progress of regional inflammatory process have been observed on experimentally induced model of purulent wound over the last five years. Particularly, it was established, that “Armenicum” paste under its topical application has an expressed effect on the course of regional reparative-proliferative processes [Ghazaryan A, 2014; 2015]. It was also established, that early activation of collagenesis under drug approbation is attributed to the processes of intensification of fibronectin synthesis by phagocytic and fibroblastic lineage cells in the affected area [Ghazaryan A, 2015].

Currently, fibronectin plays an important role in the processes of fiber formation, as this cytokine activates the synthesis of I and III types of collagen in connective tissue [Vahehi A, Mosher D, 1978; Hedman K et al., 1979; Furcht L et al., 1980; Mosher D, 1980; Kleinman H et al., 1981].

Meanwhile, it is established, that somatostatin also has a modulatory effect on the synthesis of I and III types of collagen [Reynaert H et al., 2005].

In present research, it was attempted to determine new, previously unknown mechanisms underlying the favorable effects of the tested drug on the formation of reparative-proliferative processes in experimentally induced purulent wound. In this respect, the task was to detect how much the processes of remodeling of connective tissue in the aerobic wound were somatostatin-dependent under the topical application of "Armenicum" paste.

MATERIAL AND METHODS

Experiments were carried out on 90 white male rats weighing 150-180 g. The animals were divided into two series: first and second. In the first series of experiment, animals were divided into two groups: control and experimental. "Armenicum" drug was intramuscularly administered in the experimental group animals for three times, every 8 hours (the single dose was 0.5 mg per 100 g of animal body weight). Control group was consisted of animals that were intramuscularly administered only saline solution at the same volume that "Armenicum" drug was diluted. Animals of the first group were removed from the experiment on the 3rd, 5th, 9th and 15th days after the last injection of "Armenicum" drug.

In the second series of experiment, the animals were subdivided into two groups – the first and the second experimental groups. A model of purulent wound proposed by Hovhannisyan S.S. and co-authors (1987) was reproduced on laboratory animals of both groups. In 4 hours after the wound reproduction, "Armenicum" drug was applied on the wound surface of the second experimental group animals for three times every 4 hours (the single dose was 150 mg per 100 g of animal body weight). Animals of both groups of the second series were removed from the experiment on the 3rd and 5th days after the reproduction of purulent wound. In each subgroup 18 rats were used.

Blood serums of experimental animals of both series were subjected to immune-enzyme analysis (ELISA) for somatostatin determination with the help of anti-rat sets of "Cusabio Biotech Co., LDD" (China). The concentration of somatostatin was expressed in pg/ml.

The measurements were carried out with the help of automatic analyzer "Stat Fax-2002" (USA) using light filter with wavelength of 450-500 nm.

Statistical analysis was carried out with Student t-test using SPSS program, ANOVA, version 13.

RESULTS

Obtained results of the immune-enzyme analysis are represented in table 1.

As the table shows, somatostatin level was significantly increased in blood serum and was lower from the level, observed in blood serum of control group animals respectively for 2.4; 1.5 and 1.4 times in conditions of intramuscular administration of "Armenicum" drug in intact animals on the 3rd, 5th, 9th days of the experiment. Therefore, as shown in table, the lowest level of hormone was already observed on the 3rd day of the experiment. It is noteworthy, that a tendency was observed towards the increase of somatostatin level in blood serum on the 5th and 9th days; however, their levels were lower than those observed in blood serum of control group rats. On the 15th day of the experi-

TABLE 1.

Shifts in somatostatin content in blood serum of intact rats under intramuscular administration of "Armenicum" drug

Groups	Somatostatin level, pg/ml
Control	86.7±1.8
On the 3 rd day	35.55±1.7 p<0.0005
On the 5 th day	51.3±3.7 p<0.0005
On the 9 th day	63.4±3.1 p<0.0005
On the 15 th day	83.5±2.5 0.25>p>0.1

NOTE: p – in relation of somatostatin indices observed in experimental group to the indices of control group.

ment, i.e. under intramuscular administration of “Armenicum” drug, somatostatin indices normalized in blood serum, i.e. were almost like those observed in control group rats’ blood serum.

In this regard, the obtained results of somatostatin content detection in blood serum of subtest animals during induced purulent wound inflammatory process under topical application of “Armenicum” paste on the wound surface are of special interest.

It is noteworthy that the experiments were carried out at certain stages of the regional inflammatory process (on the 3rd day of experiment), i.e. noticeable fibronectin increase was observed both in interterritorial matrix and phagocyte (macrophage and leukocyte) and fibroblast lineage cells during the period when in wound soft tissue. This approved science-methodological approach will allow to answer to the question – how much the processes of fibronectin local synthesis activation are somatostatin-dependent, as it is established that there are evolutionary fixed reciprocal interactions between fibronectin and somatostatin in mammalian organisms.

Results of the immune-enzyme analysis are presented in table 2.

TABLE 2.
Shifts of somatostatin content in blood serum of experimental group animals on the 3rd day of the wound process course under the application of “Armenicum” paste on wound surface

Groups	Somatostatin level, <i>pg/ml</i>
I experimental	69.5±2.3
II experimental	49.3±3.5
	p<0.005

NOTE: p – in relation of II experimental group indices to I experimental group indices.

As table 1 and 2 show, somatostatin level in blood serum of I experimental group animals was noticeably reduced in relation to hormone level in blood serum of intact rats under the conditions of experimentally induced wound on the 3rd day of the

observation. The application of “Armenicum” paste on the wound surface on the 3rd day of the observation also led to noticeable reduction of somatostatin content in blood serum of experimental group animals (in comparison with I experimental group), i.e. in animals with induced purulent wound that had not been treated with “Armenicum” paste.

DISCUSSION

Summarizing the results of the immune-enzyme analyses it can be concluded, that the triple intramuscular administration of “Armenicum” drug during the first 9 days was accompanied with noticeable reduction of somatostatin level in blood serum of experimental animals.

The observed shifts in somatostatin content under the administration of “Armenicum” drug open up board perspectives for further research on biological effects of the tested drug – in terms of new somatostatin-dependent processes detection, which underlie on the basis of activity of mammalian organisms’ integrate system and firstly of endocrine and immune systems.

On the other hand, it is not excluded, that the tested drug has very favorable effect on the course and progress of the wound process. On the basis of the observations it can be concluded, that the activation of regional processes in soft tissues selectively aimed at the synthesis of fibronectin in phagocytic and fibroblastic cells *in situ* under topical application of the drug was in many ways due to the temporary reduction of somatostatin level. This conclusion is confirmed based on the well-known fact, according to which somatostatin has inhibiting effect on the processes of fibronectin synthesis in connective tissue in mammalian organism, i.e. existence of reciprocal interaction between both endogenously active compounds.

On the basis of conducted immune-enzyme analyses a new, previously unknown somatostatin-dependent mechanism underlying on the basis of earlier activation of reparative-proliferative processes is established, an important role in which should be given to *in situ* produced fibronectin.

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