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Using New Technologies in the Complex Treatment for Chronic Parenchymatous Sialadenitis

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Abstract

The use of new technologies in complex treatment of chronic parenchymal sialadenitis. The use of vasaprostannucellary form in complex treatment of patients with chronic parenchymatoussialadenitis in a stage of an aggravation in the field of amazed salivary gland renders good therapeutic effect, which is proved by clinical data and results of reografic and biocнemical researches (lactoferrin concentration, middlemolecularpeptids and sum of primary and secondary products of hyperoxide acidification lipids, basis of Shiff).

Keywords: Chronic parenchymal sialadenitis, Nanotechnology, Vasaprostan, Products of lipid peroxidation.Treatment of chronic parotitis with the using of nanotechnologies.

Contents

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1. Introduction

The use of the mycelian form of vazaprostan in the complex treatment of patients with parenchymatoussialadenitis in the period of exacerbation in the affected area of a salivary gland provides good therapeutic effect that is proved by clinical data and results of rheographic and biochemical studies (lactoferrin level, MMP and total primary and secondary products of lipid peroxidation).

Keywords: chronic parenchymatous sialadenitis, nanotechnology, vazaprostan, lactoferrin, products of lipid peroxidation, midmolecular peptides.

Treatment for chronic parotitis with using nanotechnology.

Chronic parenhymatous sialadenitis accounts 41,5-67,9 % of cases among the diseases of salivary glands [1]. Chronic course of parenhymatous sialadenitis with frequent severe exacerbations reduces the quality of life of patients, results in steady dysfunction of the salivary glands, the principal of which is the participation in the maintenance of homeostasis of the mouth and digestive tract as well as the whole body [2]. In the pathogenesis of chronic parenchymatous sialadenitis microcirculation disturbance plays an important role, so the search for new methods of treatment continues, contributing to improve it Varshavskiy and Guberskaya [3]. With this purpose vazaprostan is widely used in various fields of medicine and it has multifunctional action: provides metabolic, antioxidant, immunomodulatory, anti-inflammatory and cytoprotective action by combining the effects of various cardiovascular drugs (vasodilators, disaggregantsand angioprotectors) [4].

In the Republic of Kazakhstan under the guidance of RK NAS academician Gilmanov M.K. there was created mycelian (liposomal) form of a drug delivery based on nanotechnology. Nanocapsules having no analogues, sized less than 1 μm and based on vegetable phosphotidylinositol were obtained [5]. Methods of treatment of patients with different pathologies with using mycellia, "loaded" by medicinal preparations have been developed and successfully used [6, 7]. The objective of the work was to study the efficacy of applying mycelian form of delivering vazaprostan in the complex treatment for chronic parenchymatous sialadenitis during the period of exacerbation.

2. Material and Methods of Studying

Mycelianform of vazaprostan was prepared in the laboratory of the structure and regulation of the enzymes of M.A. Aitkhozhin Institute of Molecular Biology and Biochemistry (the head is Doctor of Biology, Professor, RK NAS Academician Gilmanov M.K). To download medicinal preparations there was applied a mycelium property to be open in the hydrophobic phase (Figure 1), followed by "collapsing" when transferred into the aqueous phase, thus capturing the downloaded substance, in particular, vazaprostan (Figure 2).The transdermal form of mycelia with vazaprostan, prepared by this method, is quite inert, neutral and stable during the storage (up to 1 year).

Under the observation there were 91 patients (75 - females 16 – males, aged 20 to 63 years) with chronic parenchymatous parotitis in the period of exacerbation. All patients underwent conventional complex treatment such as the prescribed antibiotic, detoxification, restorative therapy and physiotherapy. Depending on the nature of the local treatment, the patients were divided into two groups: basic (47 patients) and comparison (44 persons). Mycelian form of vazaprostan in the form of an ointment was given to the patients of the main group for local use. It was applied to the skin in the affected parotid salivary gland (PSG) area and spread evenly on the skin surface by light rubbing motions one dose per day in the morning. The duration of the treatment was 10 days. In the comparison group there were used compresses with 30% dimethyl sulfoxide solution to the area of the salivary gland for 20-30 minutes during 10 days as local treatment.

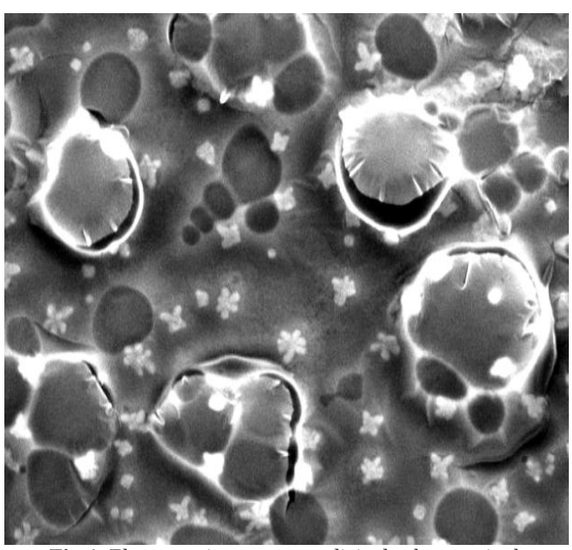

Fig-1. Electron microscopy. medicinal substance in the hydrophobic phase.

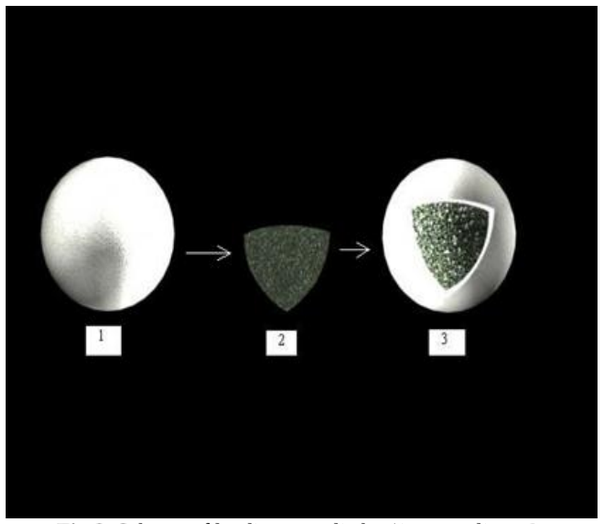

Fig-2. Scheme of loading mycelia by (1 – mycelium, 2-vazaprostan, 3 - loaded mycelium).

For using in the treatment of patients with chronic parenchymatous sialadenitis at clinics a mycelian form of vazaprostan was approved by Ethics Commission of S.D. Asfendiyarov Kazakh National Medical University (protocol № 4 of 11.03.2010 y.) and by decision of Pharmacological Centre of Almaty of 12.03.2010 (protocol № 05-10).

At admission to the hospital and in the dynamics of treatment the rheographic and biochemical studies were carried out to all patients. Biochemical studies were conducted in the practically healthy persons (23 males) and 57 patients in the dynamics: at admission, after 7, 10, and 14 days. The level of lactoferrin (LF), midmolecular peptides (MMP) and the state of lipid peroxidation (LPO) in the secretion, taken from the excretory duct of the parotid salivary glands with a help of a polyethylene catheter from 8 to 10 a.m. on an empty stomach were studied. Determining the concentration of LF was conducted by using enzyme multiplied immunoassay with a help of EJA (Germany) diagnostic kits on the"Antos 2010" (Austria) diagnostic system. LF concentration was expressed as ng / ml. MMP level was determined spectrophotometrically by ultraviolet light at a wave length of 254 nm and expressed in conventional units (c.u.) [8]. Lipid peroxidation (LPO) intensity was studied by determining the total primary (TPP) and secondary products (TSP) and Schiff bases (SB) [9]. Conventional units were the units of measurement. Rheograms were recorded according to tetrapolar technique on the rheograph 4RG-2M and electrocardiograph was used as a recording device.

3. Results of the Study

Complex treatment of patients with chronic parenchymal in acute sialadenitis with using mycelian form of vazaprostan showed that the dynamics of clinical improvement of clinical picture in patients of the main group was faster towards patients of comparison group, which resulted in a more rapid disappearance of pain, normalization of gland sizes. Thus, stopping purulent discharge from the duct of the parotid salivary gland in the main group patients occurred on average on the 4,2 ± 0,23 day, and in the comparison group- much later - on the 5,4 ± 0,17 day (P <0.01). The average number of bed-days of the main group patients was 7, 0 ± 0, 22, in the comparison group patients were discharged much later-on the 10,1 ± 0,21 day (P <0.001).

Table-1. Dynamics of changes in the level of lactoferrin (ng/ml) in the saliva of patients with chronic parenchymatous sialadenitis in the period of exacerbation, symptomatic, and advanced stages in the treatment by mycelian form of vazaprostan.

Groups of patients	**Terms of observation, days**			
	1st	**7th**	**10th**	**14th**
The 1st main group	2006,7±16,42 P<0,001 P_1>0,05	1348,6±12,51 P<0,001 P_1<0,001	1014,2±12,30 P_1<0,001	
The 1st comparison group	2006,7±17,12 P<0,001	1631,90±15,22 P<0,001	1287,1±13,71 P<0,001	1031,7±14,17
Practically healthy persons, n = 17	1010,2±21,1			

Note: P - reliability of difference in the indices at different terms of treatment (previous and next) of one group of patients; P1 - reliability of difference in the indices of the main and comparison groups at the same term of treatment.

Comparative analysis of biochemical test results of PSG secretion confirmed that on using mycelian form of vazaprostan the normalization of indices occurred faster in the group of patients being conducted the complex treatment with mycelian form of vazaprostan (Tables 1 and 2).

Thus, the level of lactoferrin in practically healthy persons was 1010,2 ± 21,1 ng / ml, but in chronic acute parenchymatous sialadenitis (in the main and as well as in the comparison group) on the first day of visiting clinic it was 2006,7 ± 16.42 ng / ml (Table 1), testifying the inflammatory process in the affected gland.

As a result of the treatment with using vazaprostan a normalization of lactoferrin concentration occurred much faster in the main group than in the comparison one. So, in the main group lactoferrin level (1348,6 ± 12,51 ng / ml)

decreased by 32.8% on the 7th day as compared with the baseline values of lactoferrin, although there was still high, and there was a normalization of level (1014,2 ± 12,3 ng / ml, P> 0,05) already on the 10th day . In the comparison group dynamics of lactoferrin values normalization occurred only on the 14th day (Table 1). Fast dynamics of reducing the level of lactoferrin in the main group of patients showed a significant decrease in the inflammatory activity under the effect of the mycelian form of vazaprostan.

At admission to the hospital LPO indicators of parotid salivary glands secretion in patients significantly exceeded the normal values (Table 2), indicating a high rate of oxidation-restoration processes during exacerbation of chronic parenchymatous sialadenitis. On the day of visiting a clinic the level of TPP was significantly higher than normal ones (0,92 ± 0,057 c.u.), (P <0,05) in patients of the main group. On the 7th day, the level of TPP decreased by 0.25 c.u., that accounted 27,2% (P <0,01), on the 10 th day there was a normalization of data. In the comparison group dynamics of TPP values normalization was slower and only on the 14th day there were registered the levels corresponding to the normal data (Table 2).

Table-2. Dynamics of changing indices of LPO and MMP level (c.u.) in the PSG secretion in patients with chronic parenchymatous sialadenitis in the period of exacerbation, symptomatic, and advanced stages in the treatment by mycelian form of vazaprostan.

Groups of patients	Terms of studying	Biochemical data			
		TPP	TSP	ShB	MMP
Main group Comparison group	1st day	0,92±0,057 P<0,001 P_1>0,05 0,91±0,058 P<0,001	0,87±0,029 P<0,001 P_1>0,05 0,87±0,027 P<0,001	0,79±0,033 P<0,001 P_1>0,05 0,79±0,031 P<0,001	0,089±0,0005 P<0,001 P_1>0,05 0,088±0,0004 P<0,001
Main group Comparison group	7 th day	0,67±0,039 P<0,05 P_1<0,05 0,79±0,034 P<0,01	0,65±0,014 P<0,05 P_1<0,05 0,71±0,015 P<0,01	0,58±0,027 P<0,05 P_1<0,05 0,69±0,025 P<0,001	0,063±0,0002 P<0,001 P_1<0,001 0,078±0,0002 P<0,001
Main group Comparison group	10 th day	0,52±0,033 P>0,05 P_1<0,05 0,66±0,037 P<0,05	0,55±0,022 P>0,05 P_1<0,01 0,65±0,017 P<0,05	0,47±0,036 P>0,05 P_1<0,01 0,62±0,022 P<0,01	0,040±0,0003 P>0,05 P_1<0,001 0,062±0,0002 P<0,001
Main group Comparison group	14th day	0,51±0,04 P>0,05 P_1>0,05 0,53±0,05 P>0,05	0,55±0,032 P>0,05 P_1>0,05 0,56±0,033 P>0,05	0,47±0,033 P>0,05 P_1>0,05 0,48±0,033 P>0,05	0,040±0,0002 P>0,05 P_1>0,05 0,042±0,0003 P>0,05
Practically healthy persons		0,51±0,05	0,55±0,041	0,47±0,037	0,040±0,0002

Note: P - reliability of difference in the indices relative to normal values; P1 – reliability of difference in the indices of patients of the 1st main group and the 1st comparison group at the same terms of treatment.

At admission to the hospital the values of total secondary products (TSP) in the main group of patients exceeded the indices by 0.32 c.u. (P <0,001). On the 7th day the level of TSP in the main group significantly decreased by 0.22 c.u. (26.4%), accounting 0,65 ± 0,014 c.u., and the normalization of the indices occurred on the 10th day of treatment. In the comparison group changes dynamics was less marked: TSP level decreased by 0.16 c.u. (18.4%) on the 7th day , by 0.22 c.u.(25.3%)-on the 10th day, and the normalization values of TSP occurred on the 14th day (0,56 ± 0,033 c.u.).

At the admission to the clinic the values of the final products of lipid peroxidation - Schiff bases in the main group of patients exceeded the standard ones by 0.32 c.u. (68.1%). As a result of the complex treatment the ShB level decreased, resulting in normalizing metabolic processes and restoring the structural integrity of a cell. On the 7th day in the main group while using mycelian form of vazaprostan it decreased by 0.21c.u. (26.6%) and on the 10th day Sh.B. values were normalized. In patients of comparison group Sh.B values became normal only on the 14th day. At visits to the clinic MMP level in the saliva of patients accounted 0,089 ± 0, 0005c.u. (P <0,001) (Table 2). It indicated an accumulation of secondary metabolites in the saliva of patients due to the formation of tissue breakdown products resulting from changing metabolism towards catabolism, as well as the accumulation of toxins and waste products of infectious agents. On the 7th day MMP values in the main group were reduced by 29.2%, on the 10th day - by 55.1%, corresponding to normal ones, whereas in the control group they were 12.4% and 29.6% respectively and only on the 14th day normalization of the level occurred.

Analysis of the rheographic studies results showed that on the first day of treatment of patients in the clinic there were signs of microcirculation disturbance of the affected salivary glands: the ascending part of the rheogram was shallow; its peak was as a flattened plateau, rheogram amplitude lowered. The median rheographic index (RI) in the practically healthy individuals was 0, 07 ± 0,003 Om, but in patients - 0, 02 ± 0,001 Om. As a result of the treatment there was a positive dynamics of rheographic indicators, which occurred more rapidly in the main group of patients than in the comparison one. By the end of the therapy there was observed the improvement of quality of rheographic curve and its amplitude increased. On the 7th day of treatment RI of rheogram was 0, 05 ± 0.003 Om in patients of

the main group, whereas those of the comparison group - 0, 04 ± 0.002 Om(P <0.05). On the 14th day of the study, the quantitative and qualitative rheogram indicators of the main group of patients already reflect the data typical for the stage of remission (RI was equal to 0,07 ± 0,003 Ohm, P> 0,05), and in patients of the comparison group RI normalized only on the 18th day of observation (RI was 0,066 ± 0,003 Om (P> 0,05). Our data of the rheographic studies showed the improvement of blood flow in the vessels of the parotid salivary gland during the treatment process, besides on using the mycelian form of vazaprostan it occurred much faster than in the groups of comparison.

4. Discussion

The carried out studies have shown that the use of mycelian form of vazaprostan in the complex treatment of patients with chronic parenchymatous sialadenitis in the period of exacerbation (in comparison with the results of the treatment in the control group, where Dolobene gel or a 30% solution of dimethyl sulfoxide were used) significantly faster improves the clinical state of patients, reduces the number of bed-days on average by 3,0 ± 0,16 days, increases the duration of remission (in the main group - 13,8 ± 0,3 months, in the comparison groups - 7,1 ± 0,1 months, P <0,001).

During the exacerbation period of chronic parenchymatous sialadenitis (P <0.001) the level of lactoferrin (up to 2006,7 ± 17,12 ng / ml), the total primary products of lipid peroxidation (up to 0,91 ± 0,058c.u.), the total secondary products (up to 0,87 ± 0,027c. u.), Schiff bases (up to 0,79 ± 0,031 c.u.), midmolecular peptides (up to 0,088 ± 0,0004 c.u.) significantly increased. Transdermal use of mycelian form of vazaprostan in the complex treatment of patients with chronic parenchymatous sialadenitis in the stage of exacerbation resulted in a more rapid normalization of lactoferrin level in the saliva, LP indices (total primary products, total secondary products and Schiff bases) and midmolecular peptides (characterizing toxins discharge with salivary gland secretion) than when using a compress with 30% solution of Dimexidum or Dolobene gel. It showed a more marked (relative to the comparable drugs) anti-inflammatory, antioxidant properties of the drug, its ability to reduce the level of toxins and secondary metabolites in the saliva.

During exacerbation of chronic parenchymatous sialadenitis there were observed the microcirculatory disorders of salivary glands, which resulted in reducing the rheographic index of a rheogram to 0,02 ± 0,003 Om (P <0.001). The results of the rheographic studies on using vazaprostan showed the improvement of blood flow in the vessels of the parotid salivary gland, the increase of their elasticity, the reduction of their tonic tension in the treatment process, which was explained by lowering the inflammatory process, and it happened faster than in the comparison groups.

5. Conclusions

Mycelian form of vazaprostan has multifaceted effects: antioxidant and anti-inflammatory actions, reducing the level of toxins and secondary metabolites in the saliva of patients and improving microcirculation of the affected salivary glands tissues.

Micelian form of vazaprostan may be recommended for using in the complex treatment of patients with chronic parenchymatous sialadenitis in the period of exacerbation.

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