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EVALUATION OF THE EFFECTIVENESS OF TREATMENT OF THE ORAL MUCOSA WITH PHYTO-OINTMENT BASED ON PHYTOECDYSTEROIDS

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ABSTRACT

An indicator of the health of the human body in the state of the oral mucosa. Mechanical and chemical factors constantly influence it. At the first stage of the study, a comparative analysis of the frequency of various forms of traumatic injuries of the oral mucosa was carried out. The distribution of patients into groups was also carried out, depending on the medicinal product used. Then clinical examinations were carried out. After that, the therapy of traumatic erosive and ulcerative lesions of the oral mucosa began. The developed method for treating traumatic lesions of the oral mucosa with medicine based on phytoecdysteroids provides for eliminating the traumatic factor, applying ointment based on phytoecdysteroids to the dried out focus twice a day. The use of phyto-ointment leads to complete repair of traumatic erosive and ulcerative lesions of the oral mucosa on average by the eighth day from the start of treatment; a similar effect with the use of "Solcoseryl dental adhesive paste" is achieved by the tenth day, and the gel "Cholisal Dental" - at a later date, which is confirmed in this study. The most significant positive effect on the level of quality of life associated with the effectiveness of treatment of traumatic erosive and ulcerative lesions of the oral mucosa in comparison with the dental "Solcoseryl dental adhesive paste" and the gel "Cholisal Dental" is exerted by phyto-ointment, where a decrease in the total points was recorded. When conducting routine examinations of patients, it is necessary to pay attention to the oral mucosa damage. Moreover, in treating traumatic injuries of the oral mucosa, it is recommended to use phytoointment, which contains phytoecdysteroids.

Keywords: oral mucosa, phytoecdysteroids, erosive and ulcerative lesions, trauma to the oral mucosa

1. INTRODUCTION

The condition of the oral mucosa is an indicator of the health of the human body. The mucous membrane of the mouth is often constantly exposed to various influences beyond physiological parameters (Utyuzh *et al.*, 2020).

The mucous membrane of the mouth is continuously exposed to various stimuli. Factors such as mechanical and chemical affect the mucous membrane even when eating. However, due to the enormous strength of immunity: local and general, these factors do not exert much harm since the mucous membrane has good regenerative and protective properties (Ajayi *et al.*, 2019, Bokov *et al.*, 2020). According to the mechanism of action and the nature of the course, acute and chronic mechanical trauma is distinguished. Acute trauma mostly occurs in the presence of a strong shortterm blow, once, for example, with trauma by foreign metal objects. In most cases, children have an acute mechanical injury, which can be caused by a blow, biting the tongue when falling, and damage to the mucous membrane by stabbing or cutting objects, such as toys. Acute trauma provokes a local tissue defect and is also accompanied by bleeding, swelling, and pain, which in turn can increase during conversation and eating (Zibareva *et al.*, 2017; Dikhit *et al.*, 2018).

In chronic mechanical injury, the stimulus is weak, but the effect is longer. The chronic effect can be manifested by biting the mucous membrane with teeth, trauma with lamellar prostheses, dental defects with caries, as well as poor-quality filling. At the site of injury, swelling and redness occur. Then this area is transformed into erosion and then into a decubital ulcer (Olennikov *et al.*, 2017).

Erosions are superficial defects of the epithelial layer without the inclusion of the underlying connective tissue base. Their size, shape, and localization often coincide with the shape and size of the source of injury (Jurenka *et al.*, 2017).

Secondary infection of wounds causes ulcers or cracks that do not heal for a long time. Limited inflammation and infiltration of the lamina propria of the mucous membrane occur around the wound. An uninfected wound epithelializes rather quickly. Ulcers can appear due to trauma of any kind and against the background of autoimmune infectious diseases (Kaçar *et al.*, 2013; Gafurovich *et al.*, 2020).

An ulcer is defined as a more profound defect in the mucous membrane that extends beyond the epithelial layer. The difference between erosion and an ulcer is that a scar remains after the ulcer heals. Moreover, a dehydrated exudate - crust may appear (Rahman *et al.*, 2017).

It is noted that the development of chronic mechanical trauma is accompanied by the development of local congestive hyperemia and edema. At this point, erosion may occur. In the future, a pressure ulcer is a single, painful pressure ulcer surrounded by an inflammatory infiltrate, with a fibrinous plaque at the bottom. The mucous membrane around is hyperemic and painful. Regional lymph nodes are enlarged, painful on palpation. With a prolonged course, the edges and base of the ulcer become denser (Reaper *et al.*, 2017).

The anatomical structure of the gum is divided into several parts, the marginal part or gingival margin; the alveolar gum or attached; the papillary part or gingival papilla. Furthermore, the papillary and marginal shell in the soy turn is transformed into the gingival margin or free gum (Tarkowská *et al.*, 2020).

The movable part of the gum is more susceptible to injury, as opposed to its fixed part. With the subsequent development of inflammation, violations of the integrity of the epithelium of the oral mucosa are infected. If the oral hygiene is unsatisfactory and the traumatic factor has a long-lasting character, then the mechanism of chronic inflammation begins

(Timoshin et al., 2019; Yumashev et al., 2020).

The question of how quickly and fully therapeutically eliminate the traumatic complications of the oral mucosa with the development of new, more effective therapeutic agents, which in particular have a combined analgesic and regenerative ability, is acquiring a rather high significance (Miclín *et al.*, 2014; Yusupova *et al.*, 2019).

Treatment of mechanical injury involves the mandatory elimination of the traumatic agent, anesthesia, treatment of the area of the injured mucous membrane with antiseptic solutions (Kim *et al.*, 2013, 2014; Kuznetsova *et al.*, 2018).

To correct pathological conditions in oral mucosa diseases, drugs of both synthetic and natural (including plant) origin are used. Herbal remedies, unlike synthetic ones, have several advantages: a mild effect, low toxicity, activation of the functions of not only the immune but also the nervous and endocrine systems due to the presence in their composition of a complex of biologically active substances that affect the body as a whole (Wang *et al.*, 2017; Dinan *et al.*, 2020).

Due to the urgency of finding new ways to treat traumatic injuries of the oral mucosa, we set out to develop a new treatment algorithm using a drug that would provide a powerful analgesic and epithelial effect without having negative effects.

As a promising basis for such a drug, in particular, ecdysteroids can be considered substances that are structurally identical or close true hormones molting to the of and metamorphosis of insects. In mammals and humans, these compounds have anabolic and wound-healing effects. A. Butenand and Carlson first obtained these hormones in 1954 from silkworm cocoons. In addition to insects, ecdysteroids have now been found in plants (phytoecdysteroids) belonging to more than 100 families from the divisions Polypodiophyta, Pinophyta, and Magnoliophyta. Screening studies have shown that these hormones are present in about 400 plant species. The largest detections of ecdysteroids were recorded in ferns and gymnosperms. Phytoecdysteroids are also found in some representatives of red algae and fungi.

Phytoecdysteroids are also responsible for the biological activity of some species of medicinal plants used in medicine of many peoples of the world: Achyranthes fauriei and Cyathula capitata (go-shitsu) — in ancient China, Ajuga iva (chenjoura) — in North Africa, Pfaffia iresinoides (suma) — in Latin America, Serratula coronata (serpia) — in Siberia, Silene tatarica and Oberna behen (shlachkan turun) — in the European North near the Komi-Zyryans. Ecdysteroids also enter the human body with fairly common food plants, such as spinach and rice quinoa. The literature notes the fact that ecdysteroids are found in plants in negligible amounts. And only in some species, the amount of these hormones reaches 2%-3%.

The main therapeutic effect of ecdysteroids is a significant stimulation of anabolic, mainly protein-synthetic processes, which is supplemented by the possibility of their long-term use in combination with the absence of any negative manifestations.

In the works of S. O. Volodina (2012), the universal hormone-like role of phytoecdysteroids is described. They have the ability to alter the body's homeostasis by affecting cell growth, differentiation, and programmed cell death. In this regard, a wound-healing effect is also assumed. It is also indicated on the processes of protein synthesis in the body. In experiments, it was proved that phytoecdysteroids do not cause any negative effects on the part of androgendependent organs. In contrast to true steroid hormones, they do not exhibit androgenic, thymolytic, or antigonadotropic effects (Kharazmi et al., 2014; Plakhova et al., 2020).

For many years, experimental and clinical studies of drugs based on phytoecdysteroids have been conducted at the basis of the Ryazan State Medical University. There are data on the use of this active substance in patients in dentistry, ophthalmology, gastroenterology. A positive therapeutic effect was also obtained in the treatment of burns of the skin and mucous membranes. The study of phytoecdysteroids in the course of these studies revealed a multi-sided positive effect on the body without showing toxic effects (Sevbitov et al., 2020).

Thus, based on the indicated list of necessary properties of a new drug, the most rational is to manufacture it based on a drug collection that has analgesic, antibacterial, antiinflammatory, and anabolic effects in combination with acceleration and optimization of regeneration processes.

Such a medicinal collection, which has the necessary properties, can be presented in the form of a combination:

- marigold flowers (*Calendula officilalis* L.) - anti-inflammatory, antimicrobial, decongestant, antitoxic, hyposensitizing, reparative, antiviral effect;

- herbs of the drooping gum (Silene nutans L.) - analgesic, anti-inflammatory, antitoxic and hemostatic effect;

- herbs of meadowsweet (Latin: Filipéndula ulmária) – antibacterial effect and promotes epithelization of trophic ulcers on the legs, wounds, and burns;

- rhizomes and roots of Leucea safflower (lat. Rhapónticum carthamoídes), rich in ecdysteroids that have an anabolic effect.

Among other things, a significant advantage of the proposed herbal collection is the availability and relative cheapness of its components. Its natural biologically active substances are widely used in the form of dietary supplements, some of them are included in the official pharmacopoeia.

The method of treatment developed by us on the basis of this phytomasy has significant prospects in the treatment of erosive and ulcerative lesions of the oral mucosa of traumatic etiology (Patent No. 2577240 of 09.12.2014)

In connection with the above, the search for a new modern method of treating traumatic erosive and ulcerative lesions of the mucous membrane is an important area of therapeutic dentistry and orthodontics.

This study aims to increase the effectiveness of treating erosive and ulcerative lesions of the oral mucosa.

2. MATERIALS AND METHODS

The study involved 110 patients with erosive and ulcerative lesions of the oral mucosa. The local ethics committee (protocol № 05-16) approved the study of Sechenov University. All patients signed voluntary informed consent for the study before the study. The distribution of patients into groups was carried out depending on the type of drug used (Table 1).

| No of group | Medicine name | Number of observations |
|----------------|-------------------|---------------------------|
| 1 | Phyto-ointment | 38 |
| 2 | "Cholisal Dental" | 35 |
| 3 | "Solcoseryl | 37 |
| | dental adhesive | |
| | paste" | |

Therapy of traumatic erosive and

ulcerative lesions of the oral mucosa was carried out after a clinical examination, photographing the lesion, and cytological examination.

For treatment, phyto-ointment with phytoecdysteroids (group 1), gel "Cholisal Dental" (Jelfa SA, Poland) with a predominant analgesic effect (group 2), and dental paste "Solcoseryl dental adhesive paste", (Legacy Pharmaceuticals Switzerland, GmbH), mainly with an effect that stimulates regeneration (group 3).

Phyto-ointment was developed jointly by the teams of the Department of Pharmacognosy with the course of botany at the Ryazan State Medical University and the Department of Propedeutics of Dental Diseases of the Sechenov University. The developed phytopreparation has the following composition: 40% alcohol (1: 5) tincture of resinous herbs and rhizomes with roots of leuzea, marigold flowers (calendula), meadowsweet herb taken in mass parts (3: 1: 1) respectively - 30 ml; petrolatum, anhydrous lanolin taken in parts by weight (3: 2) respectively - 68.0 g; essential clove oil - 1.0 g; eucalyptus essential oil - 1.0 g.

"Cholisal Dental" - a medicine for treating ulcerative necrotic and trophic lesions of the oral mucosa. It has a pronounced anti-inflammatory and analgesic effect at the site of application. Cholisal Dental composition: water, propylene glycol. hypromellose, methvl parahydroxybenzoate, peppermint oil, propyl parahydroxybenzoate, disodium edetate. aprotinin, sodium hydroxide. It is quickly absorbed from the surface of the application; the active substances of the drug penetrate to the nerve endings and are held there for a long time. According to the pharmacological action, it is active against Gram-positive bacteria, to a lesser extent Gram-negative, as well as fungi and viruses, i.e., it has an active antimicrobial effect.

"Solcoseryl dental adhesive paste" represents such drugs that stimulate regeneration and have a cytoprotective, membrane-stabilizing, wound-healing effect. Solcoseryl dental adhesive paste in the area of application may cause partial taste changes and swelling. Composition of "Solcoseryl dental adhesive paste": deproteinized dialysate from the blood of healthy dairy calves (Bos Taurus), chemically and biologically standardized (in terms of dry matter), polidocanol 600, preservatives, methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), auxiliary substances: sodium carboxymethyl cellulose - 22.875 mg; peppermint oil - 2.925 mg; menthol - 0.075 mg, paste base: (sodium

carboxymethyl cellulose, gelatin, pectin, polyethylene 350,000, liquid paraffin) - 960 mg.

After the elimination of the traumatic factor, local application of these medicines was carried out. The erosive and ulcerative areas were dried with a cotton swab, on which the medicinal preparation was applied 2 times a day until the complete epithelialization of the traumatic injury.

The distribution of acute and chronic traumatic injuries by observation groups is presented in Table 2.

| Table 2. Distribution of the frequency of acute | | | | | |
|---|--|--|--|--|--|
| and chronic erosive and ulcerative lesions of the | | | | | |
| oral mucosa by observation groups | | | | | |

| No of group | Medicine name | | nber of rvations |
|----------------|--|-------|---------------------|
| | | Acute | Chronic |
| 1 | Phyto-ointment | 34 | 4 |
| 2 | "Cholisal Dental" | 33 | 2 |
| 3 | "Solcoseryl dental adhesive paste" | 34 | 3 |
| TOTAL | | 101 | 9 |

Control examinations of patients were carried out at least once every 2-3 days. Cases with severe pain symptoms were observed daily. The treatment was discontinued when complete healing of traumatic erosive and ulcerative lesions of the oral mucosa was established, that is, on the 8-10th day.

All patients were surveyed using a special questionnaire, "Oral Health Impact Profile" (OHIP-14), before and after traumatic injury treatment. The questioning was used to determine the level of quality of life before and after treatment (Appendix 1) (Sevbitov *et al.*, 2020).

The obtained results were processed in the IBMSPSS program, version 21.0.

3. RESULTS AND DISCUSSION:

The degree of edema and hyperemia of the wound surface in patients decreased with time at different rates, depending on the applied therapeutic agent.

The disappearance of signs was evidenced by the indicator of the intensity of hyperemia. In group 1 - by the 6th day of observation, in group 2 - by the 10th day, and in group 3 - by the 8th day. The final disappearance of edema signs in group 1 was on the 8th day of observation and in 2 and 3 - on day 10.

Simultaneously, the statistical significance $(p \le 0.05)$ of the difference between similar average intensity indicators in groups 2 and 3 relatives to the corresponding values in group 1 was recorded starting from the 4th day of observation and further.

The highest rates of decrease in the average point indicators of the intensity of hyperemia and edema were noted in group 1, the lowest - in group 2. Intermediate values of the corresponding indicators were recorded in group 3.

Thus, of the three considered medications, signs of hyperemia and edema in the zone of erosive-ulcerative traumatic lesions of the oral mucosa are most effective and quickly eliminates ointment with phytoecdysteroids.

Compared to the initial data, the most pronounced changes in the indicators of the quality of life associated with dental health following the treatment results were stated in the scale "Problems in eating".

Similar but slightly less pronounced changes were recorded following treatment results in the scale "Problems of everyday life".

The sum of average points on this scale in group 1 before treatment was 18.0 points, in group 2 - 18.2, and in group 3 - 17.6. As a result of treatment, the corresponding indicators in group 1 were determined at the level of 10.4 points, in group 2 - 14.3, and group 3 - 12.8. Thus, as a result, the sum of the average points characterizing the scale "Problems of everyday life" at the end of treatment decreased.

Changes in the indicators of the quality of life associated with dental health determined by the treatment results in the scale "Communication problems" are recorded in the minimum range. The initial sum of mean points on this scale in group 1 before treatment was 4.7 points and in group 2 and 3 - 4.8. At the end of treatment, the corresponding indicators in group 1 were determined at the level of 4.3 points, in group 2 -4.7, and in group 3 - 4.4. Thus, the sum of the mean points characterizing the scale "Communication problems" at the end of treatment decreased compared to the initial indicator.

4. CONCLUSIONS:

It was concluded that the healing time of erosive and ulcerative lesions of the oral mucosa is faster when using phyto-ointment based on phytoecdysteroids than when using "Cholisal Dental" and "Solcoseryl dental adhesive paste" (p <0.05)

An insignificant dependence of changes in the quality of life indicators concerning the methods and outcome of treatment, traumatic erosive and ulcerative lesions of the oral mucosa was established.

Changes in the indicators of the quality of life associated with dental health, determined by the treatment results, compared to the initial values were found most pronounced in group 1, where a decrease in the total score from 35.6 to 20.2 (by 43, 3%).

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Appendix 1. Oral Health Impact Profile (OHIP-14) (Slade G.D., Spencer A.J., 1994)

| Question | Very often | Rarely | Usually | Almost never | Never |
|---|---------------|--------|---------|-----------------|-------|
| | 5 | 4 | 3 | 2 | 1 |
| 1. Have you had trouble pronouncing any words | | | | | |
| because of problems with your teeth, mouth or dentures? | | | | | |
| 2. Have you felt that your sense of taste has | | | | | |
| worsened because of problems with your teeth, mouth or dentures? | | | | | |
| 3. Have you had painful aching in your mouth? | | | | | |
| 4. Have you found it uncomfortable to eat any foods because of problems with your teeth, mouth or dentures? | | | | | |
| 5. Have you been self conscious because of your teeth, mouth or dentures? | | | | | |
| 6. Have you felt tense because of problems with | | | | | |
| your teeth, mouth or dentures? | | | | | - |
| 7. Has your diet been unsatisfactory because of problems with your teeth, mouth or dentures? | | | | | |
| 8. Have you had to interrupt meals because of | | | | | |
| problems with your teeth, mouth or dentures? | | | | | |
| 9. Have you found it difficult to relax because of | | | | | |
| problems with your teeth, mouth or dentures? | | | | | |
| 10. Have you been a bit embarrassed because | | | | | |
| of problems with your teeth, mouth or dentures? | | | | | |
| 11. Have you been a bit irritable with other | | | | | |
| people because of problems with your teeth, mouth or dentures? | | | | | |
| 12. Have you had difficulty doing your usual | | | | | |
| jobs because of problems with your teeth, | | | | | |
| mouth or dentures? | | | | | |
| 13. Have you felt that life in general was less | | | | | |
| satisfying because of problems with your teeth, | | | | | |
| mouth or dentures? | | | | | + |
| 14. Have you been totally unable to function because of problems with your teeth, mouth or | | | | | |
| dentures? | | | | | |