THE STUDY OF TOXICOLOGICAL PROPERTIES OF “METROXAL” CREAM

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Demodicosis is an invasive dermatozoonosis caused by abnormal multiplication of mites of Demodex genus, which are opportunistic parasites because they can parasite on the human skin for a long time in a small amount, mainly on the face, and do not reveal any symptoms and pathological changes of the skin [10, 11]. However, under favourable conditions, in which the parasites propagate rapidly and increase their activity, there are clinical signs of demodicosis in the form of the skin inflammation [5, 10, 11]. The presence of Demodex folliculorum mites exacerbates the number of dermatological conditions, first of all, rosacea and perioral dermatitis [5]. Besides some usual manifestations, the presence of skin demodicosis can lead to micropapulae and follicular pustules that contain mites [5].

The treatment of demodicosis includes both systemic and topical therapy, in which the acaricidal therapy takes the main place [4]. The use of metronidazole, birch tar, benzyl benzoate is rather effective, besides the treatment regimen includes the drugs that contain salicylic acid and resorcinol [5, 6, 9]. The composition of a cream that contains metronidazole, salicylic acid and troxerutin under conditional name “Metroxal” has been developed. Metronidazole has long proven itself to be an effective remedy in treating rosacea and demodicosis as it exhibits the bacteriostatic effect, as well as the antiparasitic properties in relation to Demodex folliculorum [4, 6]. Metronidazole intensifies the protective and regenerative functions of the skin and mucous membranes and has a pronounced anti-edematous effect [6, 8]. Acting on the autonomic nervous system metronidazole also stimulates its adrenergic structures, reduces congestions, erythema and even telangiectasian changes [6, 8]. Salicylic acid exhibits antibacterial and anti-inflammatory, keratolytic or keratoplastic (5%) properties, troxerutin provides venotonic, capillary-restorative, angioprotective, anti-edematous, antioxidant and anti-inflammatorious effects [6].

According to the guidelines when studying a new medicine its toxicity must be researched to assess the degree of the drug safety. The more efficient and safer a medicine is, the greater is its potential use in medical practice. Taking it into consideration the purpose of our work was to study the acute toxicity and to evaluate the possible effect of the local irritant action of the cream developed.

Materials and Methods

Acute toxicity was studied by G.V. Pastushenko method on non-linear outbreak mature white rats of both sexes weighing 180-230 g with a single cutaneous application using two dose levels. Assessment of toxicity was performed by the standard classification of K.K. Sidorov.

The study of anti-alternative properties of “Metroxal” cream was performed on the model of non-allergic contact subchronic dermatitis caused by turpentine [2]. The study was conducted on white female rats weighing 180-230 g. The rats’ skin was previously depilated in accordance with the guidelines. Animals were divided into 2 groups of 5 rats in each. The groups were divided in the following way: 1 – untreated control, 2 – animals with the cream applied. After modelling the disease within 10 days once a day the rats were applied with a thin layer of the cream under research.

The condition of the skin covers of animals was evaluated in points: 0 points – no visible dama-
The study of acute toxicity of the cream

<table>
<thead>
<tr>
<th>The group of animals</th>
<th>Dose, mg/kg</th>
<th>Number of animals in groups</th>
<th>The visual effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cream</td>
<td>5000</td>
<td>0</td>
<td>dead</td>
</tr>
<tr>
<td>Cream</td>
<td>15000</td>
<td>0</td>
<td>surviving animals</td>
</tr>
</tbody>
</table>

The results of the study of the anti-alterative activity of the cream on the model of non-allergic contact subchronical dermatitis (n=5) on the tenth day

<table>
<thead>
<tr>
<th>Conditions of the study</th>
<th>The condition of the skin of animals, points</th>
<th>Change of the skin fold thickness, mm</th>
<th>Anti-alterative activity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial data</td>
<td>After application</td>
<td></td>
</tr>
<tr>
<td>Untreated control</td>
<td>2.40±0.25</td>
<td>0.80±0.20</td>
<td>0.460±0.070</td>
</tr>
<tr>
<td>&quot;Metroxal&quot; cream</td>
<td>2.40±0.25</td>
<td>0.40±0.25</td>
<td>0.242±0.080</td>
</tr>
</tbody>
</table>

Results and Discussion

The study of acute toxicity of the cream with cutaneous application to rats.

Taking into account the fact that the cream is used for external use we investigated the possible toxic effects after a single cutaneous application. Acute toxicity was studied in rats, the cream was applied on the clipped skin. To assess the severity of inflammation and the action of medicines in animals we studied the skinfold thickness. All parameters were determined before the beginning of the experiment, at the peak of the disease modelling and on the tenth-day of the topical treatment of dermatitis.

The anti-alterative activity was determined by the degree of inhibition of the skin expression state in animals with the cream applied to the animal of the control pathology, and it was expressed in percentage [2].

All results were processed using a special computer programme Statistica 5.0 for Windows. Statistical analysis of the results of the research was carried out by coefficients of Student’s (t) and Wilcoxon-Mann-Whitney (w) [1, 3, 7].

REFERENCES

ВИВЧЕННЯ ТОКСИКОЛОГІЧНИХ ВЛАСТІВОСТЕЙ КРЕМУ «МЕТРОКСАЛ»

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Наявність кліща Demodex folliculorum ускладнює перебіг низки дерматологічних захворювань, таких як розацеа і періоральний дерматит та утруднює їх терапію. Актуальним є розробка та впровадження у практичну медицину лікарських препаратів комплексної дії, які проявляють антипаразитарні властивості щодо Demodex folliculorum, володіють антибактеріальною, протизапальною, капілярозміцнюючою, протиинфільтративною, антиоксидантною та антиалергічною дією. Одним із етапів впровадження нових лікарських препаратів є дослідження токсичності, що дозволяє оцінити ступінь їх безпеки. Експериментально досліджені ознаки токсичності, шкірноподразнювальна дія крему при одноразовому нашкірному нанесенні у дозах 5000 і 150000 мг/кг, що дає змогу віднести його відповідно до VI класу практично нетоксичних речовин (ЛД > 15000 мг/кг). У результаті вивчення антиальтеративної активності, встановлено, що досліджуваний крем проявляє протизапальну (антиальтеративну) дію.

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