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EFFECT OF NIOSOMAL ANTIMICROBIAL PEPTIDE hBD-1 ON THE HEALING RATE OF INFECTED WOUNDS IN RATS

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ВЛИЯНИЕ НИОСОМАЛЬНОГО АНТИМИКРОБНОГО ПЕПТИДА hBD-1 НА СКОРОСТЬ ЗАЖИВЛЕНИЯ ИНФИЦИРОВАННЫХ РАН У КРЫС

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In this study we investigated the effect of an antimicrobial peptide hBD-1 capsulated in organosilicon nanocontainers (niosomes) on the healing rate of experimental wounds infected with the clinical strain of *Staphylococcus aureus*. It was shown that the niosomal gel containing recombinant hBD-1 (1 µg/ml) increases the linear healing rate of infected wounds in rats compared to the control group.

Keywords: antimicrobial peptide, defensin, niosome, antibiotic resistance, hBD-1

Определялось влияние антимикробного пептида из класса бета-дефензинов (hBD-1), инкапсулированного в кремнийорганические наноконтейнеры (ниосомы), на скорость заживления экспериментальных ран, инфицированных клиническим штаммом *Staphylococcus aureus*. Было показано, что ниосомальный гель, содержащий рекомбинантный hBD-1 (1 мкг/мл), увеличивал линейную скорость заживления инфицированных ран у крыс по сравнению с контрольной группой.

Ключевые слова: антимикробные пептиды, дефензины, ниосомы, антибиотикорезистентность, hBD-1

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The steady growth of antibiotic resistance is a global threat. To overcome this problem, it is necessary to study compounds having a pronounced antimicrobial activity [1]. Recently, the possibility of using antimicrobial peptides as promising antibiotics has been actively discussed. However, the practical application of these peptides is complicated because of their rapid degradation and therefore a short period of action [2]. To increase antimicrobial peptides' time of action it is possible to encapsulate them in silicone nanocontainers (niosomes) [3]. Niosomes could become a tool that protects antimicrobial peptides from destruction, increase the duration of their action, improve the penetration into tissues. The aim of this study is to investigate the ability of recombinant human beta-defensin-1 (hBD-1) capsulated in niosomes to heal infected wounds in rats.

Material and Methods. Methicillin-sensitive *Staphylococcus aureus* clinical strains were isolated from patient with diabetic foot syndrome. Strain identification and susceptibility testing were determined in accordance with the EUCAST protocol.

Niosomal topical gel with 1 µg/ml recombinant hBD-1 (Cloud-Clone Corp., USA) was prepared by using method described us earlier [4]. Animal studies were conducted according to Geneva Convention of «International Principles of biomedical research using animals» (1985). Male Wistar rats weighing 180–200 g was used for the study. The site of hair was removed with the help of a cosmetic cream for depilation. Sterile instruments for punch biopsy (Medax, Italy) were used for wound defects. All the wounds were inoculated with 1 ml of *S. aureus* suspension with a turbidity of 0.5 McFarland units (10^8 CFU/ml) on day 1 of the experiment. The animals were divided into two groups: 1 – without treatment (control, n=10) and 2 – treated on the wound area with the topical niosomal gel with 1 µg/ml hBD-1 once a day (n=10). Treatment started on day 2 of the experiment and ended on day 14 – the full course of treatment was 13 days.

Wound area (mm²) and perimeter (mm) was calculated by using Wound Pro Application on day 2, day 7 and day 14 of the experiment. Linear speed of wound healing (V, mm²/day) was used to compare the rate of wound regeneration between groups:

$$V = 2 \cdot (S_0 - S_t) / t \cdot (P_0 - P_t), \quad (1)$$

P_0 and S_0 – are the perimeter and area of the wound surface at the previous measurement, P_t and S_t –

perimeter and area of the wound surface after a time interval t .

For statistical analysis was used SPSS Statistics (IBM Corp.), the Mann – Whitney U test and Fisher's exact test.

Results and Discussion. All the animals studied tended to heal infected wounds. The linear speed of wound healing (V, mm²) from day 2 to day 7 of the experiment (the first 5 days from the start of treatment) was calculated. Mean of V in the control group was 0.0053 ± 0.0154 mm²/day. The rats treated with the niosomal 1 µg/ml hBD-1 gel showed a high rate of wound healing – mean $V = 0.0208 \pm 0.0130$ mm²/day ($p < 0.05$).

When calculating the rate of wound regeneration from day 7 to day 14, similar data were obtained. Mean of V in the control group was 0.0049 ± 0.0086 mm²/day. Mean of V in the niosomal hBD-1-treated group was 0.0241 ± 0.0175 mm²/day. Differences between the groups were statistically significant ($p < 0.05$).

Also, it must be noted that the average area of wounds in the control group on the last day of experiment was 4 ± 1.9 mm². In this case, the maximum wound area was 8 mm² (in one rat), one had 6 mm², two had 5 mm², four rats had 3 mm² and two animals had 2 mm². While animals treated with the topical niosomal 1 µg/ml hBD-1 gel demonstrated a better regeneration – the average wound area on day 14 was 1.3 ± 1.2 mm². Wherein, in three rats wounds were completely healed, in three the area of wounds was 1 mm², in three – 2 mm², and for one animal – 4 mm². For Fisher's exact test it was accepted that if the area of wound ≤ 1 mm², the wound healed completely. If more than 1 mm², the wound is not healed. According to this analysis, it was proved that the regeneration of infected wounds on day 14 was statistically significant in the group receiving the antimicrobial gel ($p < 0.05$). There was no wound healing in the control group.

Conclusions. In this work we have demonstrated for the first time that recombinant antimicrobial peptide – human beta-defensin-1 (1 µg/ml) – capsulated in organosilicon nanocontainers when used as the topical gel once a day could be an effective medicine for the healing wounds infected with *S. aureus*. The data obtained show that the antimicrobial gel we developed significantly increases the linear speed of healing of *S. aureus*-infected wounds compared to control. Human beta-defensin-1 capsulated in niosomes demonstrated a high activity in the healing of infected wounds. This may be due, firstly, high defensin antimicrobial activity, secondly with immunomodulating and regenerative properties of the compound.

Disclosures:

The authors declare no conflict of interest.

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MORPHOLOGIC EVALUATION OF THE DILATED SPERMATIC VEINS IN CHILDREN WITH VARICOCELE

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МОРФОЛОГИЧЕСКАЯ ОЦЕНКА РАСШИРЕННОЙ ЯИЧКОВОЙ ВЕНЫ ПРИ ВАРИКОЦЕЛЕ У ДЕТЕЙ

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Morphological method is one of the most objectives in assessing the condition of both varicose and convoluted veins in varicocele. In the present study fragments of varicose veins from children 12–18 years old with varicocele were investigated. The SEM studies showed numerous clusters on the clear surface of erythrocytes and other blood cells with strands of fibrin that may be precursors of the thrombi formation. Erythrocytes are the most numerous among the clusters of blood copuscles, echinocytes being their pathological forms. The data obtained should be considered in finding the method of surgical correction of this pathology.

Keywords: varicocele, children, morphology

Морфологический метод – один из самых объективных методов в оценке состояния варикозных вен и извитых вен при варикоцеле. Для изучения варикозного расширения вен были получены оперативно удаленные фрагменты у детей от 12 до 18 лет. Исследования SEM показали многочисленные скопления на прозрачной поверхности эритроцитов и других клеток крови с нитями фибрина, которые могут быть предвестниками образования тромбов. Среди кластеров образующихся элементов крови преобладают эритроциты и их патологические формы – эхиноциты. Выявленные особенности следует учитывать при выборе хирургической тактики коррекции этой патологии.

Ключевые слова: варикоцеле, дети, морфология

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