THE EFFECT OF CORTISONE ON WOUND HEALING

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The widespread therapeutic use of hormones, not only in diseases of the endocrine system, but also in various diseases of an inflammatory nature and allergic states, necessitates a comprehensive study of their influence on certain physiological and pathological processes. The "anti-inflammatory" hormones, the physiological effect of which was established by Selye [9], are not particularly widely used in medical practice. It is necessary to determine the effect of the hormones of this group on the adaptive reactions of the organism and on processes directed towards the eradication of the results of injury. In this context their effect on processes of regeneration requires study.

The information given in the literature on this subject is very sparse [2-5, 7, 8]. A. I. Bukhanova [1] considers that under the influence of cortisone the inflammatory phase of regeneration is retarded, the differentiation of granulation tissue and its conversion into scar tissue are accelerated, and the proliferation of epithelium is inhibited.

Our object was to study the effect of cortisone, as a hormone in particularly wide use, on reparative regeneration after deep wounds of the skin and subjacent muscles.

EXPERIMENTAL METHOD

Experiments were conducted on sexually mature rabbits weighing 1.5-2.5 kg. Wounds 1 cm^2 in area, involving the skin, subcutaneous areolar tissue, fascia, and subjacent muscles, were inflicted on all the experimental animals in the lumbar region under morphine-novocain anesthesia. The day before the operation the rabbits received an injection of cortisone in a dose of 0.4 ml (10 μg cortisone)/kg body weight. Subsequently, intramuscular injections of cortisone in the same dose were given daily until the end of the experiments. An analogous operation was performed on the control animals, but without the injections of cortisone. On the 2nd, 4th, 6th, 8th, and 10th days after operation the wound edges were excised, treated histologically, and examined under the microscope. Throughout the time from the operation until the excision of the wound edges, general clinical observations were made. The excised wound edges were fixed in 10% formalin solution and embedded in celloidin. Sections, 6-8 μ in thickness, were stained with hematoxylin-eosin and picro-fuchsin.

EXPERIMENTAL RESULTS

General clinical observations revealed a difference between the behavior of the experimental and control animals. The experimental animals were less active and they reacted more weakly to the external environment. As a rule, their appetite was impaired, especially during the first days after the operation. The healing of the wounds in the experimental and control rabbits was also different, and the course of regeneration was noticeably sluggish in the experimental rabbits. In these animals the color of the wound in the days immediately after the operation was pale pink with a greyish hue, and there was a scanty discharge. The formation of granulations was retarded, and they were indolent, dry, and predominately grey in color. Epithelization was late in starting and its progress was slow.

An appreciable difference was seen in the course of the wound healing when the wounds in the experimental and control animals were studied histologically. This difference could be observed soon after infliction of the wounds. For instance, on the second day after the operation, when marked circulatory disturbances were observed at the edges and in the base of the wound in the control animals, mainly dystrophic processes were found in the experimental animals, especially prominent in the muscle fibers. The circulatory disturbances were slight in degree in the experimental animals, and much less marked than the dystrophic changes.

On the fourth day, when young granulation tissue elements were beginning to appear in the subcutaneous areolar tissue and, in particular, in the intermuscular connective tissue of the control rabbits, the dystrophic changes in the muscle fibers continued to develop in the experimental animals. On the sixth day the control rabbits showed considerable hypertrophy of the intermuscular connective tissue and marked proliferation of the connective tissue cells and vessels in the region of the defect in the skin, subcutaneous areolar tissue, and muscles. At the same time the experimental animals began to show the first signs of proliferation of the connective tissue cells. On the eighth day mature granulation tissue was seen in the control rabbits, replacing the defect in the skin, subcutaneous areolar tissue, and muscles, with a decrease in the number of its cells and blood vessels. Most of the cells were not round, but elongated or fusiform, interspersed with the occasional myoblast. Only one myoblast was seen in 3-4 fields of vision. "Sliding" of the epithelium from the wound margins for a considerable distance over the granulation tissue was observed. In the experimental rabbits on the eighth day the wounds were filled with young granulation tissue containing many round cells and thin-walled vessels. Another conspicuous feature was the presence of many myoblasts and muscle buds. From 2 to 4 myoblasts were found in nearly every field of vision. Although there was fairly intensive proliferation of the muscle elements, epithelization was only feebly developed.

Ten days after the operation the wounds in the control rabbits were drawn together by mature granulation tissue in which connective tissue fibers were seen. The surface of the granulations was covered by stratified squamous epithelium, invading the subjacent granulation tissue in the form of spikes. The myoblasts were more numerous than at the previous times. In the experimental rabbits at this period much of the defect near the base of the wounds and its edges was replaced by myoblasts and muscle buds, while the central part of the wounds was filled with mature granulation tissue. Epithelization of the wounds was still slow at this period in the experimental rabbits, and over a wide area only a single layer of epithelium was present.

Our findings show that in the animals receiving cortisone the processes of regeneration in the region of wounds involving the skin, the subcutaneous areolar tissue, and the subjacent muscles differ from those observed in control animals. So far as the diminished exudation and the depression of proliferation of the connective tissue elements in the initial stage of regeneration are concerned, our results agree with those obtained by other workers. So far as the muscle fibers are concerned, however, our results conflict with the findings described by other workers. At the beginning of regeneration we observed well marked dystrophic changes in the muscle fibers. Alongside and immediately after these regressive processes, progressive processes were observed in the shape of active proliferation and regeneration of muscle fibers, and the appearance of myoblasts and muscle buds at the edges and base of the wound. During certain phases of wound healing, cortisone may activate the adaptive reactions of the body, as manifested by increased proliferation of muscle fibers. Although epithelization of the wounds takes place slowly, nevertheless, it always develops.

The administration of cortisone is therefore especially recommended during the treatment of wounds of muscles.

SUMMARY

Healing of skin and muscular wounds of rabbits was studied under the effect of intramuscular cortisone administration. At the beginning of the regenerative process there were marked dystrophic changes in the muscle fibers. These regressive changes were soon replaced by progressive processes in the form of active multiplication, regeneration of muscle fibers, the appearance of myoblasts and muscular buds in the area of the floor and edges of the wounds. It is considered that cortisone therapy is justified in the treatment of muscular wounds.

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