Short Paper

Clinical and biomechanical effects of morphine on skin wound healing

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Summary

Opioids analgesics are used as premedication and in maintenance of anesthesia and in post-operative pain control. 20 female rabbits were assigned to experimental and control groups and followed for healing process for 20 days. Each rabbit was anesthetized, and a full-thickness skin incision, 3 cm long, was made on its back. The wounds were closed with non-absorbable suture. Morphine and saline were administered to experimental and control groups, respectively. The rate of wound healing was similar in both groups. While tensile strength of normal intact skin was significantly (P<0.05) higher than that of both groups, it was not different between the study and control groups. Collagen content and its maturity may be responsible for the this observation.

Key words: Biomechanical, Morphine, Wound healing, Skin

Introduction

Wound healing represents a dynamic physiological process initiated and influenced by many factors. Collagen synthesis and its maturation play an important role in the healing process. Collagen synthesis represents an important phase in the healing process and cross linked mature collagen is essential for platelet adhesion and subsequent aggregation (Pierard, 1986; Graven et al., 1995).

Mechanical properties of skin have so long seek the attentions of dermatologists and bioengineers, as biomechanical skin parameters at various sites change by age and in different disease conditions. Therefore, an objective functional assessment of the skin mechanics was necessary to correlate the mechanical properties of skin with anatomical and biomechanical findings (Berardesca et al., 1995). For lack of data on the effect of morphine on biomechanical parameters of skin surgical wounds, we decided to determine the effect of this drug on the biomechanical parameters of healing surgical wounds.

Materials and Methods

Twenty female adult New Zealand white rabbits, weighing between 3.1–3.6 kg, were used in this study. The animals were obtained from the Laboratory Animal Center and kept under air conditioning (21 ± 2° C; 70%–80% humidity; 12 hrs light/darkness cycle) in the animal holding unit for at least 72 hrs before use. Food and water were supplied ad libitum. Rabbits were randomized into two groups, the experimental (morphine-treated) and control. General anesthesia was induced by intramuscular (IM) injection of 40 mg/kg ketamine (Ketamine HCl, Park Davis, USA) and 20 mg/kg IM injection of xylazine (Xylazine, Bayer, Germany). The animals were shaved and placed in prone position on the operating table. The dorsal aspect of the right lumbar region was prepared and draped under sterile conditions. A 3 cm full-thickness incision was made dorso-ventrally.
After homeostasis was achieved, the wound was closed with a 2/0 silk suture, in a cross mattress pattern. The animals were then taken to the recovery room and allowed to emerge from anesthesia under observation. When the animals were in a stable state, they were transferred to individual housing. One mg/kg/day of morphine sulphate (Darou Paksh Co., Iran) was administered IM to the animals in the experimental group for five consecutive days. The dose of morphine used in this study was adopted from its ED$_{50}$ value. Normal saline was administered IM to the animals in the control group for five successive days. The animals in each group, were sacrificed 20 days after the operation. The duration of 20 days was chosen because rabbit skin gets completely healed after three weeks. For test of the tensile strength, a rectangular segment of each wound was excised. Each specimen was two cm in width at each side. The middle of the specimen was the line of repair.

Tissue strips were held in grips on a tensiometer (Universal Instron testing Machine, England). A 450-N load cell transducer was used. The load was gradually increased to determine the tensile strength of the repaired tissue. In addition to testing the wounded skin, 20 normal intact skin samples were harvested from the other side of each rabbit.

Biomechanical testing parameters between morphine-treated and control groups were compared using two tailed Student’s t-test for independent samples. The significance level was set at $p<0.05$.

**Results**

All animals were noted to eat and behave normally after surgery. Animals from the morphine-treated group had a better condition in regard to eating and activity in the first three days after surgery. The data show that the values of MTS (1.25 ± 0.14 kg) and YTS (0.23 ± 0.9 kg) in the morphine-treated group, though not statistically significant, were higher than those in the control groups (1.17 ± 0.26 kg and 0.24 ± 0.05 kg, respectively). The tensile strength values of normal intact skin (MTS of 17.41 ± 2.11 kg and YTS of 3.11 ± 0.81 kg) were higher as compared to both the control and morphine-treated groups ($p<0.05$).

Clinically, the rate of wound healing was similar in both saline- and morphine-treated groups. No differences in wound appearance could be discerned when sections taken from the central portion of the wound were compared to those taken from the edge of the wounds.

**Discussion**

This study was designed to determine whether morphine is an effective means of promoting wound healing.

Three days after surgery, the general condition and eating in rabbits of morphine-treated group were better than the control rabbits. It was assumed that morphine had reduced the pain from surgery, hence a better appetite. The result of this study showed that morphine does not influence the collagen content and cross-linkage. We found equal tensile strength values in morphine and control groups.

In mammalian skin, the parameters that indicate strength or stiffness can be correlated with the amount and the orientation of collagen fibers (Graven et al., 1995). Total collagen content and its cross-linkage are the major contributing factors for the tensile strength of wounds and a decrease in these two factors can result in a lower tensile strength of wounds (Pierard, 1986; Berardesca et al., 1995).

Sanderson et al., (1998) have reported that hemorphin-7 had no effect on the inflammatory response in the recurrent injury or the chronic injury models. Hemorphins are non-classical opioid peptides found in the region of the -chain of hemoglobin. Also Zagon et al., (1998) have reported that an opioid peptide plays a direct role in the repair of injury to the corneal epithelium in the rabbit and that acts as a receptor-mediated and a constitutively expressed inhibitory molecule. However, Mather, (1992) showed that while administration of non-steroidal anti-inflammatory drugs (NSAIDs) may
compromise healing of gastrointestinal anastomoses, has no effect on corneal healing and bone remodeling. The main benefits of NSAIDs are their opioid sparing effect that results in reduced rates of preoperative nausea and vomiting and improvement in ventilation. Some studies, however, showed an enhanced quality of analgesia by using a combination of drugs rather than use of either NSAIDs or opioids alone.

Kramer et al., (1999) have reported that development of surgical site complication was associated with intra-operative receipt of morphine nerve paste and that this product delays wound healing and increases post-operative morbidity.

However, effects of opioid on mechanical properties of the skin are still not well understood. Collectively, these data indicate the morphine do have a desirable analgesic property without irritating or causing any adverse effects on cutaneous wound healing.

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References