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# *The Effect of Local Infiltration of NSAIDs on Surgical Wound Healing in Rats*

**Chanon Somprasong, MD**
**Narong Lertakyarnanee, MD**
*Department of Surgery, Siriraj Hospital and Faculty of Medicine, Bangkok, Thailand*

***Abstract***

***Objective:*** **This study was designed to determine the effect of local infiltration of NSAIDs on the tensile strength of surgical wounds.**

***Materials and Methods:*** **In the experimental study, twelve male Sprague Dawley rats were divided into two groups. Under sterile technique, they were anesthetized with pentobarbital intraperitoneally (30 mg/kg bw). A linear wound was made on the midline of the abdomen. Bupivacaine (1 mg/kg bw) and normal saline was locally infiltrated to rats in group 1 and bupivacaine (1 mg/kg bw) with parecoxib was locally infiltrated to those in group 2. On the 7th postoperative day, the wounds were totally stitched off and tensile strength was measured by computerized tensinometer.**

***Results:*** **This study revealed no differences in the measurement of tensile strength between parecoxib and control group (P value = 0.394).**

***Conclusion:*** **Local infiltration of NSAIDs (parecoxib) did not impair wound healing.**

Wound healing is a vague term that often diverts the clinician from focusing on the specific mechanism involved in a particular healing process. Connective tissue matrix deposition is the process whereby fibroblasts are recruited to the site of injury and produce a new connective tissue matrix. This process is of major importance in primary wound closure. Primary closure approximates the acutely disrupted tissue with sutures, staples, or tape. With time, the synthesis, deposition, and cross-linking of collagen and other matrix proteins, which are of primary importance in this type of repair, provide the tissue with strength and integrity. The healing of acute wound that was created by any mechanism usually follows a predictable pattern under normal circumstances. Under normal conditions, the phases of healing are divided into four specific events: coagulation, inflammation, fibroplasias, and remodeling. The inflammatory phase is characterized by the sequential migration of leukocytes into the wound. Within 24 hours the wound is predominated by polymorphonuclear leukocytes, and then by macrophages. Inflammatory cells regulate the connective tissue matrix repair. In summary, the inflammatory phase is responsible for providing the initial tensile strength to a wound, the initiation of the removal of damaged tissue and the beginning of angiogenesis.

Since 1899, aspirin was the first non-steroidal anti-inflammatory drugs (NSAIDs) used for anti-inflammation and pain relief. It was used widely for pain relief more than a century. Reduction of

***Correspondence address:*** *Chanon Somprasong, MD, Department of Surgery, Siriraj Hospital and Faculty of Medicine, Bangkok 10700, Thailand. E-mail: chanon815@yahoo.com*

inflammation with anti-inflammatory drugs often results in relief of pain for significant periods. Later, new NSAIDs such as ibuprofen, diclofenac are synthesized. The effectiveness of NSAIDs is largely due to its capacity to inhibit prostaglandin biosynthesis. It blocks enzyme cyclooxygenase, which catalyzes the conversion of arachidonic acid to endoperoxide compounds. Cyclooxygenase (C0X) exists as two isoforms: COX-I, which is constitutively expressed in most body tissues and plays a role in homeostasis, particularly in the platelets, GI tract and kidney; and COX-2, which is predominantly a cytokine inducible enzyme expressed in high levels at sites of inflammation. In general surgery, NSAIDs have been shown to be effective analgesics when administered after surgery. The important adverse effect of NSAIDs is gastric irritation that occurs when large doses are employed. Upper gastrointestinal bleeding associated with NSAIDs may occur due to inhibition of protective prostaglandins. NSAIDs affect hemostasis by inhibition of platelet aggregation secondary to inhibition of thromboxane synthesis. Because its action is irreversible, NSAIDs will inhibit platelets aggregation until new platelets are formed. Adverse effects of NSAIDs including gastrointestinal distress, occult gastrointestinal bleeding, and gastric ulceration occur in approximately 20% of patients. Parecoxib sodium is an injectable product formulation of the COX-2-specific inhibitor valdecoxib that has demonstrated significant analgesic activity in post-operative pain. It is hypothesized that COX-2-specific inhibitors may be associated with lower incidences of hematologic and GI adverse effects than nonspecific COX inhibitors.

Local infiltration of NSAIDs may reduce its adverse effect and relief of pain effectively. NSAIDs may impair wound healing by inhibiting the inflammatory phase of wound healing but fibroplasia is a major factor in wound strength. Then, wound strength should not be affected by NSAIDs. We designed this experimental study in rats by local infiltration of NSAIDs into surgical wounds and measured the tensile strength on the 7th postoperative day.

## Materials and Methods

Twelve male Sprague Dawley rats were purchased from the National Laboratory Animal Center, Salaya, Mahidol University, Bangkok. They stayed in the hanging stainless steel cage in the air-conditioned animal room. They were fed with commercial pellet diet CP mice feed, produced by Pokphand Animal Feed Co, Ltd. Bangkok, Thailand. The rats were divided into two groups. Under sterile technique, they were anesthetized with pentobarbital administered intraperitoneally (30 mg/kg bw). A linear midline incision was made in the abdomen using surgical blade No. 15. The wound was a full thickness deep through the peritoneal cavity, 3 cm in length. Bupivacaine (Bu) (1 mg/kg bw) and normal saline solution (NSS) were locally infiltrated into rats in group 1 and bupivacaine (1 mg/kg bw) with parecoxib (Pa) (1.5mg/kg bw) were locally infiltrated into those in group 2. The wounds were closed with 2 stitches of 3-0 surgical silk simple suture. On the 7th postoperative day, the rats were euthanatized by overdosage of pentobarbital administered intraperitoneally and the wounds were totally stitched off and the tensile strength was measured by computerized tensinometer. Tensile strength = Breaking load (force)/area. Area = Thickness x Width. Results were represented as means + S.D. Data were evaluated statistically using Student's t-test. P value less than 0.05 was considered to be significant.

## Results

Breaking force applied to the healing wounds is shown in Figure 1. The measurement of the effect of parecoxib and control group on the tensile strength of the incision wound is shown in Table 1.

The tensile strength was almost the same. The tensile strength in the parecoxib group and the control group were comparable to each other. (Table 2)

Tensile strength in the two groups was not significantly different (P Value = 0.394). In the control group, complications occurred in sample No 6. Wound dehiscense occurred on the 2nd postoperative day. This complication occurred as a result of surgical technique.

## Discussion

Our experimental model showed no difference between parecoxib and the control group in tensile strength. Wound healing, a fundamental response to tissue injury, is a complex process involving a series of biological events and occurs by a process of connective

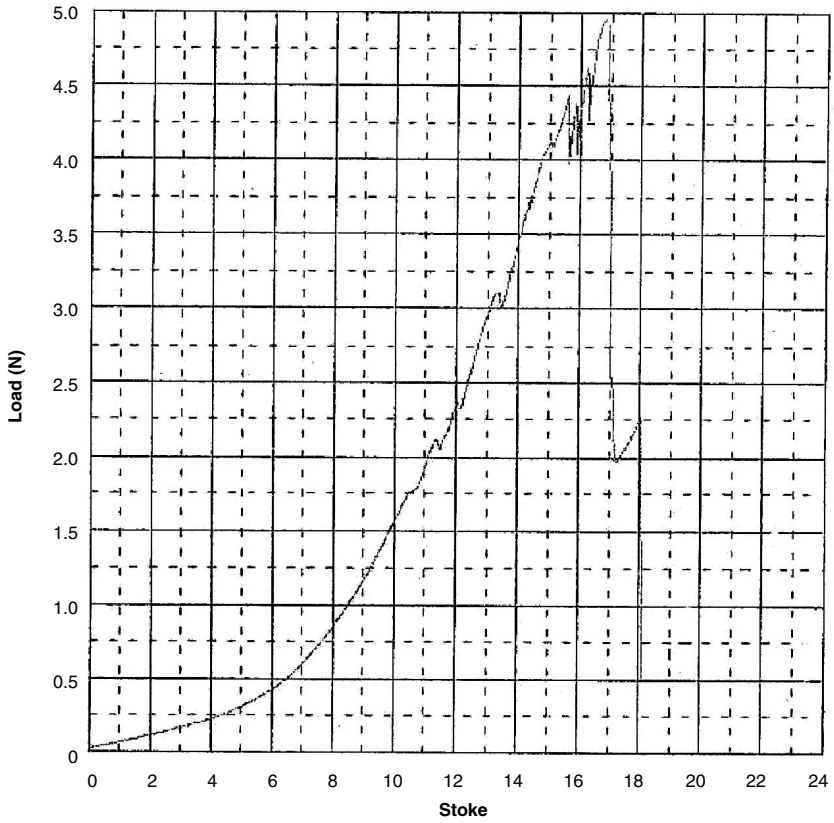


**Fig. 1** The breaking load (force) of rat skin.

**Table 1** Tensile strength of healing wounds in each rat.

| No | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Bu + Pa | 5.090025 | 4.86725 | 4.64125 | 4.82775 | 4.98050 | 5.40575 |
| Bu + NSS | 4.97475 | 4.96650 | 2.43575 | 5.30825 | 4.96250 | - |

*Bu = bupivacaine, Pa = parecoxib, NSS = normal saline solution*

**Table 2** Tensile strength in both groups, P Value = 0.394 NS

| | No | Mean | SD |
|---|---|---|---|
| Bu + Pa | 6 | 4.9687917 | 0.26203389 |
| Bu + NSS | 5 | 4.5295500 | 1.17971884 |

tissue repairs. A fibrous scar is the end product of this process, the predominant constituent of which is collagen. NSAIDs inhibit the inflammatory process of wound healing. But this study showed no difference in tensile strength of wound healing. The tensile strength of a wound represents the effectiveness of wound healing. The present study has shown that NSAIDs did not impair the healing of a wound and may be used safely by local infiltration. This may decrease adverse effects such as hematologic and GI adverse effects. In the future, we need to study whether local infiltration of NSAIDs can relieve pain effectively.

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