Cryoanalgesia: Effect on Postherniorrhaphy Pain

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Cryoanalgesia versus sham treatment was applied to the ilioinguinal and iliohypogastric nerves after mesh repair of an inguinal hernia under local anesthesia in 48 male patients in a prospective, randomized, and observer- and patient-blinded trial. Pain was scored daily during rest, while coughing, and during mobilization to the sitting position for 1 wk and weekly for 8 wk on a four-point verbal rank scale. Use of supplementary analgesics and sensory disturbances were recorded. Assessments were made for allodynia, hyperalgesia, and mechanical pain detection thresholds 8 wk postoperatively. Cumulative pain scores for the first postoperative week were equal in the two groups, as was the use of analgesics. Eight weeks postoperatively, three cases of hyperalgesia to pinprick were detected in the cryoanalgesia group, and 10 patients in the cryoanalgesia group versus 5 in the sham-treatment group reported disturbed sensibility. We conclude that cryoanalgesia of the iliohypogastrical and ilioinguinal nerve does not decrease postherniorrhaphy pain. **Implications:** Does freezing of sensory nerves in the groin reduce pain after hernia repair? Extreme cold (−60°C) was applied in a double-blind, randomized study. No difference in pain scores was found. Sensory disturbances were seen in treatment and control patients. Freezing cannot be recommended for pain relief after hernia repair.

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Postherniorrhaphy pain is a significant clinical problem that may have economic consequences because it can prolong convalescence (1). Cryoanalgesia provides functional neurolysis for 2–4 wk (2), and it may be a rational therapy for postherniorrhaphy pain because two large sensory nerves without motor branches (ilioinguinal and iliohypogastric nerves) traverse the surgical area. Previous studies of cryoanalgesia in patients undergoing herniorrhaphy have been inconclusive (3,4); therefore, we conducted a prospective, randomized study to assess the analgesic efficacy of cryoanalgesia after tension-free mesh repair of a primary direct inguinal hernia under local anesthesia.

Methods

The study was approved by the local ethical committee and The Danish Data Protection Agency. Before surgery, all male patients 40–75 yr of age scheduled for elective surgical correction of a primary inguinal hernia were asked to participate in the study, and patients were only included after they gave their written, informed consent. After intraoperative verification of a direct inguinal hernia, the patients were randomized to cryoanalgesia of the ilioinguinal and iliohypogastric nerves or sham treatment. Patients were randomized by using a precoded list of numbers and group allocation, and the allocation of each patient was kept in a closed numbered envelope. All patients underwent Lichtenstein's tension-free mesh repair (5).

Carbon dioxide cryoanalgesia equipment (SL 2000 Neurostat; Spembley Medical Ltd., Hampshire, UK) that generated temperatures to −60°C was used. After identification of the iliohypogastric and ilioinguinal nerves in the lateral part of the incision, two-phased cryolysis of each nerve was performed (2 × 60 s with a 30-s thawing interval) at the end of surgery. Alternatively, sham treatment without tissue contact was performed. The patients, the person responsible for collecting and processing the postoperative pain data, and the clinical control 8 wk postoperatively were blinded to the treatment.

All operations were performed under unmonitored local anesthesia (6) consisting of an inguinal field block and incisional infiltration with bupivacaine

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2.5 mg/mL combined with light sedation with midazolam. Perioperative analgesia consisted of a nonsteroidal antiinflammatory drug (tenoxicam orally 40 mg) in the evening and 2 h before surgery, as well as oral methadone 10 mg (5 mg in patients >60 yr) immediately before surgery. The patients received methadone 5 mg orally 8 h postoperatively and tenoxicam 20 mg daily for 4 days. Paracetamol 1 g up to four times a day was ordered for supplementary analgesia.

Data were obtained by detailed chart reviews, from two questionnaires, and by clinical examination. A questionnaire was given to the patient after surgery and provided information about pain and wound problems, supplementary use of analgesics, and possible visits to physicians during the first postoperative week. Pain was scored during rest, cough, and mobilization to sitting position on a four-point verbal rank scale (no, light, moderate, or severe pain) daily for the first postoperative week (to be returned in a prestamped return envelope), and weekly on a similar, separate questionnaire covering the first 8 wk postoperatively (to be returned at the control visit 8 wk postoperatively). The patients were seen in the hospital 8 wk postoperatively, and a sensory examination of the operated area was performed. Hyperalgesia to paint brush and any secondary hyperalgesia in the surrounding skin was noted. The mechanical pain detection threshold (MPDT) was determined 1 cm cephalad and caudad to the incision, as well as at the distal part of the scrotum, and was compared with the contralateral side by using von Frey hairs (Somedic A/B, Stockholm, Sweden) (7). Pinprick was performed with each hair, beginning with thinnest, and the MPDT was defined as the number of the hair that produced a definite painful or unpleasant sensation on repeated stimulation. The procedure was repeated twice thereafter, and the median value of these three estimations was used.

Descriptive statistics were used for demographics and pain course. For comparison between groups, cumulative pain scores during rest, cough, or mobilization over the first week were obtained for each patient using the following numbers from the daily scores: no = 0, light = 1, moderate = 2, and severe pain = 3. Thus, for a 7-day period, the cumulative pain score would range from 0 to 21. Cumulative pain scores were used to eliminate the risk of mass significance by multiple comparisons at different time points. Differences in MPDT were calculated between the operated and the contralateral sides. A numeric difference ≥2 von Frey numbers was considered the least detectable difference. The Mann-Whitney *U*-test for unpaired observations for each scoring condition (cryoanalgesia versus sham treatment) and χ^2 test with Yates correction for comparison of frequencies between groups were used, and 5% was chosen as the level of significance. To estimate the necessary number of patients, a normal distribution of cumulative pain scores, $2\alpha = 0.05$, $\beta = 0.2$, with a standard deviation of 4 cumulative pain score units were assumed, corresponding to standard deviations of 20 mm in a 100-mm visual analog scale found in other studies on postherniorrhaphy pain (1). To detect a minimal relevant difference (MIREDIF) of four cumulative pain score units, 16 patients in each group were required, using the equation $n = (C_{2\alpha} + C_{\beta})^2 \times 2(SD/MIREDIF)^2$. Considering the possibility of a nonnormal distribution, as well as possible dropouts, 2 × 24 patients was accepted as the necessary number in each group.

Table 1. Age and Surgery Data

	Cryoanalgesia (n = 24)	Sham treatment (n = 24)
Age (yr)	58 (49–69)	56 (53–64)
Duration of surgery (min)	60 (54–65)	55 (45–60)
Bupivacaine 0.25% (mL)	50 (40–50)	49 (40–50)
Midazolam (mg)	2.0 (1.4–2.5)	2.0 (2.0–2.0)

Data are median (interquartile range).

Results

The two groups did not differ significantly with respect to distribution of age, duration of surgery, or use of anesthetic drugs (Table 1). All patients were ASA physical status I or II except for one patient who was ASA physical status III in the cryoanalgesia group. One patient (cryoanalgesia group) did not complete the 1-wk questionnaire, and two patients in each group did not return for the 8-wk follow-up. One patient (cryoanalgesia group) did not complete the questionnaire for the sixth, seventh, and eighth weeks because of a new hernia operation on the contralateral side. One patient (cryoanalgesia group), who had an infected hemorrhage at the incision, did not fill in the 8-wk questionnaire. The hematoma required surgical intervention for hemostasis, and a subsequent infection required repeated surgical intervention. No other surgical complications occurred.

The distribution of pain scores during the first postoperative week and after four and eight weeks are shown in Figure 1, and the cumulative pain scores for the first week are shown in Figure 2. Neither the cumulative pain scores nor the pain scores at any time point during the first 8 wk differed significantly.

A *post hoc* calculation showed that the minimal detectable differences of statistical significance, expressed as cumulative pain score units, were 3.0 (rest), 4.3 (coughing), and 3.9 (mobilization to sitting position); the risk of overlooking a difference of 4.0

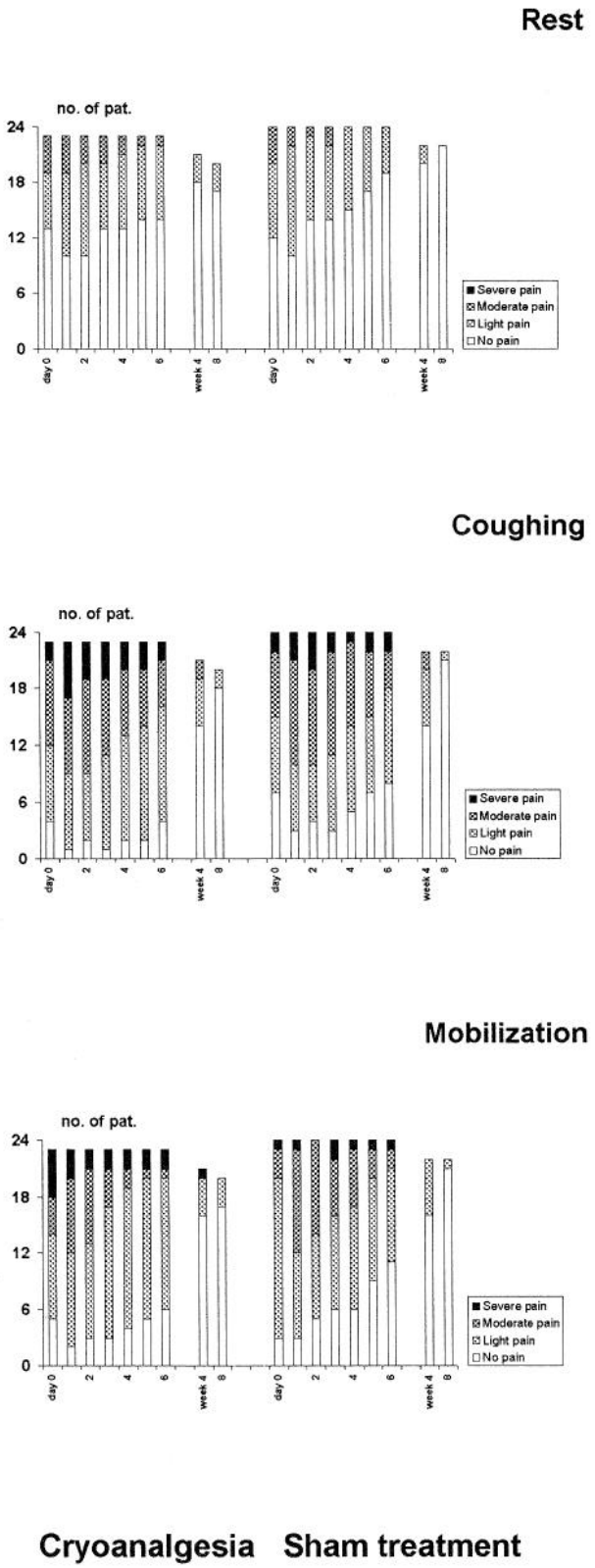

Figure 1. Pain scores at rest, while coughing, and during mobilization to sitting position on Days 0–6 and 4 and 8 wk postoperatively.

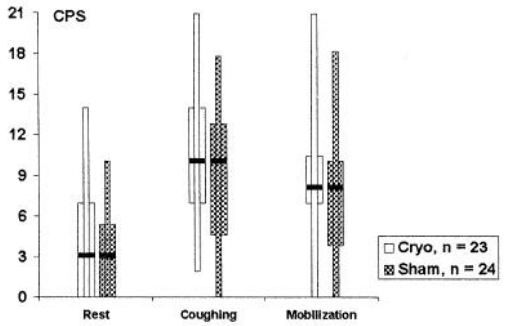

Figure 2. Cumulative pain scores (CPS) for the first postoperative week (sum of daily four-point rank scores). Median (black lines), interquartile range (broad boxes), and range (narrow boxes). There were no significant differences between groups (Mann-Whitney *U*-test).

cumulative pain score units was 11% (rest), 21% (coughing), and 19% (mobilization to sitting position), respectively.

The number of patients with clinically detectable differences in MPDT between the operated and the nonoperated side in the cryoanalgesia group were 9 (cephalad to incision), 14 (caudad to incision), and 3 (distal part of scrotum), whereas the corresponding figures were 3, 12, and 3 patients, respectively, in the sham treatment group (no significant difference).

The number of patients who required supplementary analgesics or who experienced disturbed sensation at the incision, scrotum, or inner thigh (as reported in the 8-wk questionnaire) is shown in Figure 3. There were no significant intergroup differences at any time point.

No patient experienced allodynia to touch cephalad or caudad to the incision or at the scrotum. Three patients in the cryoanalgesia group experienced some degree of hyperalgesia, whereas no patient in the sham group experienced hyperalgesia (no significant difference).

Discussion

The theoretical basis for the use of cryoanalgesia for postoperative pain relief is long-lasting neurolysis combined with axonal regeneration. Freezing of a nerve results in axonal disintegration, as well as degeneration of the myelin sheaths. The structure of the connective tissue is preserved, however, and regrowth of the axons takes place in the original peri- and epineurium at the rate of 1–3 mm per day (2). Cryoanalgesia has been used as a supplementary postoperative analgesic after thoracotomy (8,9), as well as in the treatment of late or chronic pain after hernia repair (10). With regard to postherniorrhaphy pain, only two controlled studies are available (3,4). Wood et al. (3) compared cryoanalgesia with paravertebral blockade and oral analgesia (12 patients in each group) and

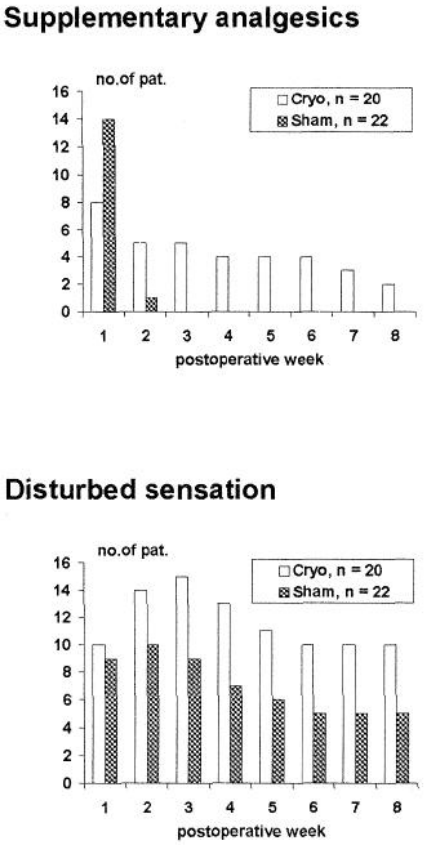

Figure 3. Number of patients who reported using supplementary analgesics or experiencing disturbed sensation during the first 8 wk postoperatively. There was no significant difference between groups at any time point (χ^2 test with Yates correction).

found decreased requirements for oral analgesics in the cryoanalgesia group. However, neither randomization nor blinding was appropriate, analgesic therapy was different between the cryoanalgesia and control groups, and no pain scoring was performed, all of which hinder interpretation of the results. Khiroya et al. (4) found no significant differences in pain scores, pulmonary function, or use of analgesics in a randomized study in 36 patients. In both studies, only the ilioinguinal nerve (not the iliohypogastric nerve) was frozen, and neither study describes the hernia pathology or surgical technique.

We conducted a randomized, blind study with well defined anesthesia and surgical approaches and cryoanalgesia of the ilioinguinal and iliohypogastric nerves. Our main finding was that pain scores, estimated as the cumulative pain score over the first postoperative week, did not differ between the cryoanalgesia and sham-treatment groups. In addition, no significant difference in the supplementary use of analgesics was seen. The explanation of our negative findings may be that postherniorrhaphy pain originates from the deep muscle layers, which are innervated from nerves other than the iliohypogastric or ilioinguinal nerves. This explanation is supported by the finding that subfascial administration of lidocaine results in better pain relief than subcutaneous administration (11). Another factor that may contribute to the negative findings is that cryoanalgesia of the iliohypogastric or ilioinguinal nerves would not influence nerve transmission by the genitofemoral branch of the femoral nerve or by contralateral overlapping innervation.

In the cryoanalgesia group, three patients experienced some degree of hyperalgesia of the surrounding skin area, and more patients in this group reported disturbed sensibility, although neither of the findings reached statistical significance. Skin incision itself may lead to disturbed sensation due to lesion of cutaneous nerve branches, but the frequency of this phenomenon in relation to hernia surgery has not been quantified in large consecutive series. It is reflected by the large number of patients in both groups who had detectable differences in mechanical pain detection thresholds caudad to the incision when the operated and the nonoperated were compared (14 in the cryoanalgesia group and 12 in the sham-treatment group). The effect of the temporary sensory nerve fiber damage by cryolysis might add to that of skin incision.

In conclusion, cryoanalgesia of the iliohypogastric and ilioinguinal nerves did not improve postoperative analgesia after mesh repair of a direct inguinal hernia. Cryoanalgesia cannot be recommended for postoperative pain relief after hernia surgery.

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