

# SHORT- AND LONG-TERM EFFECTS OF REGIONAL APPLICATION OF MORPHINE AND BUPIVACAINE ON THE ILIAC CREST DONOR SITE

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**We investigated the analgesic effect of regional application of bupivacaine and a morphine-bupivacaine combination on iliac crest donor-site pain in a randomized, double-blind controlled study of 45 patients. Patients were divided into three groups: group I (control group), group II (bupivacaine) and group III (morphine-bupivacaine combination).**

**Pain in the acute stage was evaluated by visual analogue scale scoring and analgesic consumption. Chronic pain and dysesthesia were evaluated at 12 weeks after operation at a follow-up visit.**

**It was found that local bupivacaine administration with or without morphine provided satisfactory analgesia in the acute stage following iliac crest bone harvesting. The amount of analgesic consumption was found to be significantly less with the addition of morphine to bupivacaine, when compared to bupivacaine alone.**

**Effective pain control in the acute stage had a favorable effect on long-term pain and dysesthesia, which are the main complaints after iliac crest bone harvesting. This effect was augmented significantly by addition of morphine to the local anesthetic solution.**

**Keywords :** iliac crest ; bone graft ; morphine ; bupivacaine

**Mots-clés :** crête iliaque ; greffe osseuse ; morphine ; bupivacaine

Regional application of local anesthetics like bupivacaine to the iliac crest donor site has been shown to decrease early postoperative pain (1, 11, 14). Opioids like morphine have also been shown to decrease pain with local application through suggested peripheral opioid receptors (4, 6, 8, 10, 12, 13). It has been reported that effective pain control in the acute stage may reduce the likelihood of long-term pain (1,9).

The purpose of this study was to investigate the acute and long-term effects of regional application of bupivacaine and a morphine-bupivacaine combination on iliac crest donor-site pain in a prospective randomized study of 45 patients in whom harvesting of a bone graft had been performed.

## PATIENTS AND METHODS

After approval from the local committee for human studies was obtained, 45 ASA (American Society of Anesthesiology) physical status I or II patients, requiring iliac crest bone harvesting during a three-year period, were randomly allocated to three groups, each consisting of 15 patients. Informed consent was obtained from each patient before surgery. A standardized general anesthesia protocol was followed. Anesthesia was induced with thiopental (4mg/kg). Vecuronium (0.1mg/kg) was administered to facilitate tracheal intubation and muscle relaxation. Anesthesia was maintained

## INTRODUCTION

Harvesting of an iliac bone graft is one of the most frequent procedures performed in orthopedic surgery (3,7). Donor-site pain which is the most commonly cited complication after this procedure, may sometimes persist for more than 3 months (2,3,11).

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ned with 66% N<sub>2</sub>O in O<sub>2</sub> and isoflurane (0.8-2%). Surgical procedures included vertebral fusion, fracture grafting and grafting for tumor resection.

Regional application of infusions was done through a fine bore (17 gauge) epidural catheter with a bacterial filter. The tip of the catheter was located at the iliac crest donor site between muscle and bone at the lateral surface of the ilium. All regional drug infusions were started within 10 minutes after surgery. Patients in group I received 20 ml of 0.9% sodium chloride (control group). Patients in group II received 20 ml of 0.9% sodium chloride solution, which contained 50 mg of bupivacaine (bupivacaine only group). Patients in group III received 20 ml of 0.9% sodium chloride solution, which contained 5 mg of morphine and 50 mg of bupivacaine (morphine-bupivacaine group).

Preoperatively, patients were instructed on the use of the visual analogue scale (VAS) scoring for pain (0 : no pain, 10: worst pain imaginable). Supplemental analgesic medication for the current operative site pain was available from a patient-controlled analgesia (PCA) pump, for which patients received instruction before surgery. The PCA pump was set to infuse a 1-mg bolus dose with 5 minutes lockout time. The four-hour limit was 20 mg. Patients were also instructed to request reinjection of local anesthetic into the iliac crest when the donor site again became painful (5 ml 0.9% sodium chloride solution with 12.5 mg bupivacaine).

VAS scores were obtained 24 hours after the operation. Records were also noted for requests of reinjection of local anesthetic into the donor site and analgesic consumption through the PCA pump.

Table I. — Demographic data and types of surgery performed in each group.

	Group I	Group II	Group III
Vertebral fusion	6	5	6
Fracture grafting	6	7	7
Tumor grafting	3	3	2
Age (mean)	46	48	51
	(16-70)	(18-71)	(19-73)
Gender (male/female)	5/10	6/9	6/9

Patients were evaluated at the twelfth postoperative week by an anesthesiologist through a simple questionnaire asking whether or not they had dull pain, discomfort and dysesthesia at the donor site.

Data are expressed as mean values  $\pm$  SD and range. VAS scores and analgesic consumption were compared using a one-way ANOVA test and Tukey-Kramer multiple comparisons test among the three groups. Fisher's exact test was used for categorical data. A p-value of  $<0.05$  was considered statistically significant.

## RESULTS

Demographic data and the type of surgery were similar in all three groups (table I). The patients were between the ages of 16 and 73 years, and the mean age in each group was similar (46, 48, 51 years respectively). No clinical signs or symptoms of local anesthetic toxicity were noted in any patient.

Table II. — Comparison of three groups with respect to the VAS score, analgesic consumption and request for reinjection of local anesthetic into the donor site for the early postoperative period and dull pain and dysesthesia for long-term donor site pain.

	Group I	Group II	Group III	p-value between group I-II	p-value between group I-III	p-value between group II-III
Mean values for total amount of morphine received through PCA pump	90.8 mg. $\pm 36.4$	70 mg. $\pm 32.3$	43 mg $\pm 25$	0.05	0.001	0.01
Reinjection of local anesthetic into iliac crest when the donor site again became painful	4 times	2 times	-	0.001	0.001	0.05
Mean VAS Score, 1st postoperative day	3.6 $\pm 0.7$	2.0 $\pm 0.3$	1.8 $\pm 0.7$	0.001	0.001	ns
Number of patients who have long-term complaints (12 <sup>th</sup> week)	5/15	2/15	0/15	ns	0.05	ns

ns: not significant.

All patients were able to differentiate the pain at the donor site from pain at the major operative site. Acute and long-term donor-site pain and the response to medication in each group are summarized in table II.

The VAS score, analgesic consumption and request for reinjection of local anesthetic into the donor site in the early postoperative period (24<sup>th</sup> hour) were significantly higher in the control group than in the other two study groups ( $p < 0.001$ ). The mean VAS score was lower in group III than in group II, but the difference was not significant. However analgesic consumption through the PCA pump and requests for reinjection of local anesthetic into the donor site were significantly lower in group III compared to group II ( $p < 0.01$  and  $p < 0.05$ , respectively) for the same period.

Patients were evaluated 12 weeks after the surgery. Dull pain and dysesthesia were noted in five patients in group I and two patients in group II. The difference was not significant. However, none of the patients in group III had long-term complaints, and the difference between group I and group III was significant ( $p < 0.05$ ). Addition of morphine to bupivacaine solution (group III) makes a significant difference.

## DISCUSSION

Donor-site pain is the most frequently cited complication after iliac crest bone harvesting (2, 3, 11). Pain persisting for more than 3 months has been reported in up to 15% of patients (7). There is no difference in incidence between anterior and posterior wounds, and the amount of pain seems to be proportional to the amount of dissection (7). A greater number of patients who had spine surgery reported pain when compared to patients having other surgical procedures (3). This may be explained by the fact that a greater amount of dissection was necessary for procurement of more bone graft in spinal fusion (3,7). In our study each group included similar numbers of patients with vertebral fusion (table I).

The infusion of a peripherally-acting agent into an operation site to decrease early postoperative pain is a known procedure (1, 4, 5, 6, 8, 14).

Bupivacaine, a long-acting peripheral anesthetic, has been shown to decrease postoperative pain and discomfort when applied locally into the iliac crest donor site (1, 11, 14). In recent years it has been postulated that centrally-acting agents like morphine may have an analgesic effect when applied locally (4, 5, 6, 8, 9). This effect is supposed to be mediated by peripheral opioid receptors (10, 12, 13). Controlled clinical trials have shown that local administration of morphine significantly relieves acute postoperative pain (4,6,8). In fact Likar *et al.* have shown that an intraarticular injection of morphine has an analgesic effect that lasts more than a week (9).

The decrease in long-term complaints of patients who received a local anesthetic or morphine infusion for acute pain has been documented in some articles (1,9). Several mechanisms have been postulated to explain this effect, such as reducing the spinal cord hyperexcitability and receptor field changes (1).

We conclude that local bupivacaine administration with or without morphine provides satisfactory analgesia in the acute stage following iliac crest bone harvesting. However, the combination of morphine and bupivacaine results in significantly less analgesic consumption, compared to bupivacaine only. Effective pain control in the acute stage has a favorable effect on long-term pain and dysesthesia, which is the main complaint after iliac crest bone harvesting. This effect is augmented significantly by addition of morphine to the local anesthetic solution.

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### SAMENVATTING

*H. GÜNDEŞ, L. KILIÇKAN, Y. GÜRKAN, A. ŞARLAK, K. TOKER. Uitwerking, op korte en lange termijn van regionale toepassing van morphine en bupivacaine, in de donorzone van heupkam-enten.*

We bestudeerden het analgetisch effect van de regionale toepassing van bupivacaine, ofwel bupivacaine gecombineerd met morphine, versus nulbehandeling, voor wat betreft pijn in de donerzone van heupkam-enten, in een dubbel-blinde gerandomiseerde studie op 45 patiënten. De patiënten werden verdeeld in drie groepen : groep I (controlegroep), groep II (bupivacaine), en groep III (morphine-bupivacaine).

In het acute stadium werd de pijn gemeten aan de hand van "visual analogue scales" en analgeticaverbruik. Vastgesteld werd dat in het acute stadium bupivacaine met of zonder morphine een aanvaardbare pijnstilling verzekerde. Bupivacaine gecombineerd met morphine verminderde het analgeticaverbruik op significante wijze, in vergelijking met bupivacaine alleen. Ook de pijn en de dysesthesieën op lange termijn werd gunstig beïnvloed door afdoende pijncontrole in het acute stadium, een effect dat significant verhoogd werd door het toevoegen van morphine. Het is bekend dat pijn en dysesthesieën de klassieke hoofdklachten zijn na het afnemen van heupkam-enten.

### RÉSUMÉ

*H. GÜNDEŞ, L. KILIÇKAN, Y. GÜRKAN, A. ŞARLAK, K. TOKER. Les effets à court et long terme de l'application régionale de morphine et de bupivacaine au site de prélèvement de greffes iliaques.*

Nous avons recherché, dans une étude randomisée et contrôlée portant sur 45 patients, les effets analgésiques de l'application régionale de bupivacaine et d'une association de morphine-bupivacaine sur la douleur au site donneur après prélèvement osseux à la crête iliaque. Les patients ont été divisé en trois groupes: groupe 1 (contrôle), groupe 2 (bupivacaine) et groupe 3 (association morphine-bupivacaine).

La douleur au stade aigu a été évaluée par un score sur une échelle visuelle analogique et par la consommation d'analgésiques. La douleur chronique et la dysesthésie ont été évaluées lors d'une visite de contrôle à 12 semaines de l'intervention.

Nous avons observé que l'application de bupivacaine au site donneur de la crête iliaque a significativement diminué la douleur aiguë post-opératoire. La consommation d'analgésiques était moindre avec l'addition de la morphine à la bupivacaine que avec la bupivacaine seule au stade aigu de la douleur.

Le contrôle effectif de la douleur au stade aigu a un effet positif sur la dysesthésie et la douleur à long terme, qui sont les plaintes principales après une greffe d'os prélevée à l'aile iliaque. Cet effet a été augmenté significativement par addition de la morphine à la solution d'anesthésique local.