

# The Effect of Single-Dose Bupivacaine on Postoperative Iliac Crest Graft Donor Site Pain

Olalere Omoyosola Gbolahan<sup>1</sup>, Babatunde Babasola Osinaike<sup>2</sup>, Adeola Olanike Olusanya<sup>1</sup>, Michael Oluyinka Okunola<sup>3</sup>

<sup>1</sup>Department of Oral and Maxillofacial Surgery, University College Hospital, Ibadan, Nigeria, <sup>2</sup>Department of Anaesthesia, College of Medicine, University of Ibadan/UCH, Ibadan, Nigeria, <sup>3</sup>Department of Orthopaedics and Trauma, University College Hospital, Ibadan, Nigeria

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## INTRODUCTION

Several procedures in maxillofacial surgery, orthopedic surgery, and neurosurgery require the use of bone grafts in the treatment of a number of conditions, and autologous bone remains the preferred choice in several of these procedures. Although there are several donor site options, the iliac crest is a common site of choice because of its relative advantages compared to other sites.<sup>[1-4]</sup> Despite these advantages, iliac crest bone graft harvesting (ICBGH) has a number of drawbacks including donor site morbidity and potential complications.<sup>[5-8]</sup>

The most common complication of ICBGH is pain (acute and chronic) at the donor site which almost all patients are reported to have and is often more

**ABSTRACT** **Background:** Postoperative donor site pain remains a major source of morbidity following iliac crest bone graft harvesting (ICBGH). **Aim:** The aim of this study was to investigate the effect of single-dose infiltration of bupivacaine on donor site pain following ICBGH. **Subjects and Methods:** This study was a double-blind randomized controlled trial of 30 adult individuals that required an ICBG as part of the treatment for mandibular reconstruction. Individuals were divided into two groups, to receive a single-dose subcutaneous infiltration of either 0.25% bupivacaine or 0.9% normal saline at the iliac crest graft incision site following ICBGH. Length of incision at the ICBGH site, dimensions of harvested graft, time taken for the iliac crest harvest surgery, total daily dose of postoperative analgesics, pain from the ICBGH site as well as gait disturbance were recorded. Data were analyzed using SPSS version 17.0, and  $P < 0.05$  was considered statistically significant. **Results:** There was a progressive decrease in pain score from the 1<sup>st</sup> to the 4<sup>th</sup> postoperative day, with no significant difference between the two groups. There was no statistical difference between the two groups in terms of dynamic median pain score at the early postoperative period as well as at the 4<sup>th</sup> and 12<sup>th</sup> week postoperative period. The analgesic consumption between the two groups also did not show any significant difference. **Conclusion:** Local injection of single dose of 0.25% bupivacaine did not offer additional benefit in the management of postoperative iliac crest donor site pain following ICBGH.

**KEYWORDS:** Analgesic, bupivacaine, iliac crest bone graft harvesting, normal saline, pain

severe than the pain at the primary surgical site.<sup>[9-12]</sup> The inevitable postoperative donor site pain following ICBGH can delay early ambulation of patients, increase risk of deep vein thrombosis, increase hospital stay, increase lost man-hours, affect patient satisfaction, and increase cost.<sup>[11,13,14]</sup>

The role of bupivacaine in reducing donor site pain has been investigated by several researchers either as a repeated bolus or continuous infusion via an indwelling catheter or as a single dose.<sup>[10,11]</sup> A well-designed randomized controlled trial on infiltration of single

**Address for correspondence:** Dr. Olalere Omoyosola Gbolahan, Department of Oral and Maxillofacial Surgery, University College Hospital, Ibadan, Nigeria.  
E-mail: gbolahanlere@yahoo.com

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dose of bupivacaine will add additional evidence to the literature to further clarify the role of infiltration of single dose of 0.25% bupivacaine in managing acute and chronic postoperative pain following ICBGH. If effective, infiltration of single dose of bupivacaine will be a very convenient and cost-effective way of managing pain, which is the most common complication of ICBGH.

## SUBJECTS AND METHODS

The study participants included thirty adult patients that required an ICBG as part of the treatment for mandibular reconstruction. The study was approved as a randomized, double-blind, prospective, placebo-controlled study by the institutional ethics committee. The study location was the main theatre of the hospital, and eligible individuals were consecutive consenting adult patients (18 years and above) who presented to the department of oral and maxillofacial surgery and required an ICBG as part of the treatment for mandibular reconstruction under general anesthesia at the main theatre. The inclusion criteria were willingness to participate in the study, weight not <50 kg, no previous iliac crest bone harvest, normal renal and hepatic function, no history of adverse reaction to local anesthetic agent, and no opioid addiction. Excluded from the study were those with a history of severe pelvic and medical conditions that can interfere with the outcome assessment of the study such as pregnancy, mental retardation, uncontrolled major depression, and any other psychiatric disorders as well as inability to understand the demands of the study and the instrument that will be used for measurement of the pain.

The details of the study including how and when the pain measurements would be done were explained to the patients who met the inclusion criteria preoperatively. Patients were randomly assigned to receive a single-dose subcutaneous infiltration of either 0.25% bupivacaine (treatment group) or 0.9% normal saline (control group) at the ICBGH site immediately after the iliac crest graft was taken. Computer-generated randomization method was utilized by a member of the research team not involved in patient recruitment and intervention to generate the treatment assignment (Group 1: 0.9% normal saline and Group 2: 0.25% bupivacaine). The assigned intervention was revealed to the anesthetist in charge (who is not a member of the research team) at the commencement of the surgical procedure. Both the patient and the surgeon were blinded to the contents of the syringe.

At surgery, all patients were treated in accordance with the standard operating protocol for the intended surgery

regardless of the randomization. The same standardized technique was used in harvesting the ICBG. Anterior iliac crest was used in all the patients. The iliac crest was exposed via an incision made along the region of the iliac crest 1.5 cm posterior to the anterior superior iliac spine to reduce the risk of injury to the lateral cutaneous femoral nerve. Full thickness of the ICBG incorporating both medial and lateral cortices was harvested with the use of an osteotome, hemostasis was achieved, and the wound is closed in layers. The followings were noted: length of incision at the ICBGH site, dimensions of harvested graft (length and breadth) in cm, and time taken for the iliac crest harvest surgery.

Immediately after the ICBG incision wound closure, 20 ml of normal saline solution or 20 ml of 0.25% bupivacaine solution was infiltrated into the soft tissue at the harvest site by means of a 20 ml disposable needle and syringe for the control group and the treatment group, respectively. Patients were provided with standard postoperative care irrespective of treatment groups; this included postoperative analgesics. The unit protocol utilized for postoperative analgesic includes the use of intramuscular (IM) pentazocine 1 mg/kg 6 hourly and IM paracetamol 15 mg/kg 8 hourly for 3 days, followed by oral paracetamol for 3 days (which could be altered depending on the need of individual patient).

The total daily dose of pain medication was recorded for 4 days postoperatively. Pain from the ICBGH site was assessed by a trained assistant blinded to the study objectives using the Numeric Rating Scale (NRS). The NRS measures subjective pain by the respondent selecting a number (0–10 integers) that best reflects the intensity of his or her pain, 0 representing no pain and 10 representing the worst imaginable pain. The first reading for the NRS was taken 4 h postoperatively in the recovery room. Subsequent NRS readings were taken daily on the ward at the following hours in the first 4 days postoperatively: 8:00, 14:00, and 20:00 h. Additional pain evaluations were done when the patient first sat up in bed and stood up to begin ambulation. On the day of discharge, pain was assessed while the patient laid supine in bed, sat up in bed, and ambulated. At 4-week postoperative review, pain evaluation from the ICBGH site on routine (like walking) and strenuous activities (like climbing stairs) as well as gait disturbance were assessed.

A power analysis, performed with the use of PASS software (NCSS, Kaysville, Utah), indicated that a total of thirty individuals, with 15 patients in each group, would be needed to achieve power equal to 0.80 with an alpha of 0.05 (standard deviation [SD] and attrition rate from previous similar study were utilized).<sup>[15]</sup> Data of all the enrolled 30 individuals were available with adequate

information for analysis. Data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 17.0, and results were presented in tables and figures and expressed as mean and SD. Statistical association was determined using Chi-square test for categorical variables. Student's *t*-test and analysis of variance were used for the continuous variables. *P* < 0.05 was considered to be statistically significant.

### RESULTS

A total of 30 individuals participated in the study. There were no significant differences between the two groups with respect to type of surgery, age, gender, weight, height, educational status (Oyedeji.<sup>[16]</sup>), and duration of hospital stay [patient sociodemographic characteristics are summarized in Table 1]. No untoward effect such as local anesthetic toxicity or wound complication at the iliac crest site was noted in any of the patients. Table 1 also shows the intraoperative characteristics in terms of iliac crest site incision length, length and breadth of graft, and the duration of ICBGH with no statistical difference between the two groups (with *P* = 0.46, 0.96, 0.14, and 0.68, respectively). There was also no significant difference between the two groups in terms of interval between surgery and first sitting in bed and time of ambulation (with *P* = 0.36 and 0.66). The pattern of pain score recorded in the two groups showed a progressive decrease between the 1<sup>st</sup> and 4<sup>th</sup> days with

a lower median pain score recorded in the bupivacaine group in the first postoperative day though the difference was not statistically significant [Figure 1].

There was no significant difference between the two groups in terms of dynamic median pain score in the early postoperative period [Table 2]. The consumption of pentazocine was noted to be higher for the control group on days 2–4, though this was not statistically significant [Table 3].

Table 4 shows the median pain score at the donor site at 4<sup>th</sup> and 12<sup>th</sup> week postoperative period. There was no statistically significant difference in the median pain scores at rest, during walk, and during exertion as the pain scores were mostly 0 in both the groups though the range values in the control group were higher.

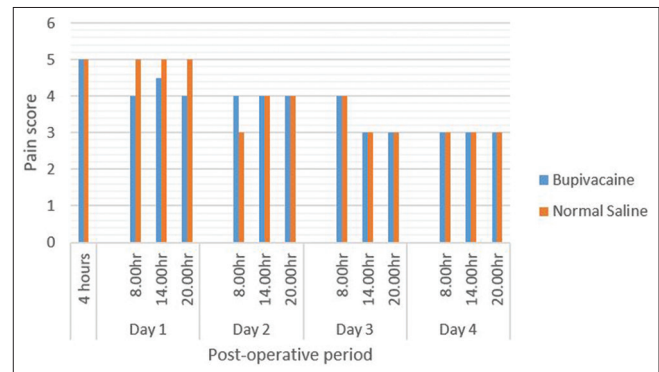


Figure 1: Postoperative median pain score (Numeric Rating Scale) in the first 4 days

Table 1: Patient characteristics and intraoperative iliac crest harvest details

	Bupivacaine group (n=15)	Saline group (n=15)	<i>P</i> *
Patient characteristics			
Age (year)±SD	32.07±10.50	34.73±10.22	0.50 <sup>f</sup>
Gender, n (%)			
Male	10 (66.7)	6 (40.0)	0.27 <sup>l</sup>
Female	5 (33.3)	9 (60.0)	
Weight (±SD) kg	75.61±16.04	69.41±17.40	0.32 <sup>f</sup>
Height (±SD) m	1.71±0.14	1.69±0.09	0.90 <sup>f</sup>
Educational status (%)±			
Tertiary	4 (26.7)	4 (26.7)	0.08 <sup>l</sup>
Postsecondary	5 (33.3)	0 (0)	
Secondary	5 (33.3)	7 (46.6)	
Postprimary	1 (6.7)	1 (6.7)	
Primary	0 (0)	3 (20.0)	
Duration of stay (±SD) min	411.60±110.55	381.60±170.03	0.57 <sup>f</sup>
Intraoperative iliac crest harvest details			
Length of incision (cm)	14.66±3.34	13.69±3.73	0.46 <sup>2</sup>
Length of graft (cm)	12.52±2.86	12.68±3.68	0.96 <sup>2</sup>
Breadth of graft (cm)	2.59±1.30	1.98±0.78	0.14 <sup>2</sup>
Duration from incision to Closure of graft site (min)	70.93±21.61	67.71±19.98	0.68 <sup>2</sup>

<sup>f</sup>Classification according to Oyedeji. <sup>l</sup>*t*-test, <sup>l</sup>Chi-square, <sup>2</sup>One-way ANOVA, \*Significant at *P*<0.05. ANOVA: Analysis of variance, SD: Standard deviation

**Table 2: Effect of pain on ambulation and dynamic median pain score in the early postoperative period in the two groups**

	Bupivacaine group (n=15)	Saline group (n=15)	P*
Effect of pain on ambulation in the early postoperative period			
Interval between surgery and first sitting up in bed (days)	1.87±0.52	2.13±0.99	0.36 <sup>f</sup>
Interval between surgery and ambulation (days)	3.33±1.23	3.13±1.25	0.66 <sup>f</sup>
Dynamic median pain scores in the early postoperative period (n [range])			
First day of sitting up in bed	4.0 (9)	5.0 (7)	0.62 <sup>e</sup>
First day of walking around	4.0 (10)	4.0 (5)	0.61 <sup>e</sup>
Day of discharge-supine in bed	0.0 (4)	1.0 (6)	0.55 <sup>e</sup>
Day of discharge-sitting in bed	0.0 (5)	1.0 (6)	0.75 <sup>e</sup>
Day of discharge-walking around	1.0 (5)	1.0 (6)	0.78 <sup>e</sup>

<sup>f</sup>t-test, <sup>e</sup>Chi-square, <sup>e</sup>One-way ANOVA. \*Significant at P<0.05. ANOVA: Analysis of variance

**Table 3: Postoperative analgesic consumption**

	Bupivacaine group (n=15)	Saline group (n=15)	P* (One-way ANOVA)
Postoperative analgesic consumption (mg) (mean±SD)			
Day 1			
Pentazocine	90.71±82.41	90.00±66.11	0.98
Paracetamol	1185.86±707.78	1266.67±533.77	0.72
Day 2			
Pentazocine	102.86±77.80	246.00±435.07	0.24
Paracetamol	1585.86±835.32	1666.67±308.61	0.73
Day 3			
Pentazocine	92.14±75.77	126.00±71.89	0.23
Paracetamol	1585.79±835.47	1520.00±308.84	0.78
Day 4			
Pentazocine	53.57±66.75	78.00±72.43	0.35
Paracetamol	1300.07±1039.87	1180.00±924.43	0.75
Diclofenac	5.00±19.37	0 (0)	0.32

\*Significant at P<0.05. ANOVA: Analysis of variance

By the 4<sup>th</sup> and 12<sup>th</sup> week postoperative period, slightly more participants in the normal saline group had some degree of gait disturbance more than the patients in the bupivacaine group, although the difference was not statistically significant (with  $P = 0.62$  and  $0.68$ , respectively) [Table 4].

## DISCUSSION

We set out to determine the effect of single dose of 0.25% bupivacaine on postoperative pain experience following ICBGH. We did not find any significant difference in donor site pain experience between patients that were administered 0.25% bupivacaine and normal saline (control). Bupivacaine hydrochloride, a potent local anesthetic agent with prolonged analgesic effect, continues to be used in many surgical procedures for the management of intra- and postoperative pain, but reports on its efficacy for postoperative analgesia remain controversial. The role of bupivacaine hydrochloride in the management of the inevitable pain that normally accompanies ICBGH has also been investigated by several authors, and results so far are inconclusive.<sup>[10,14,17,18]</sup>

Bupivacaine hydrochloride is commonly used in three concentrations: 0.25%, 0.5%, and 0.75%. However, for infiltration and peripheral nerve blockade, 0.25% and 0.50% concentrations are recommended and are both effective.<sup>[19-21]</sup> Similar to some previous studies,<sup>[10,22]</sup> 0.25% concentration was utilized in this study since it is equally effective as the 0.5% concentration but present with less risk of toxicity with more volume.<sup>[10,23]</sup> In the present study, bupivacaine hydrochloride did not appear to have any superior analgesic effect on donor site pain perception compared with normal saline in agreement with previous findings.<sup>[17]</sup> As reported by Puri *et al.*, both the groups of patients that had bupivacaine hydrochloride and normal saline injected to the ICBGH operation site had less perceived pain than the control (no injection), and this was attributed to the dilutional effect of pain mediators rather than analgesic effect of these agents.<sup>[17]</sup> Contrary finding to the report of Puri *et al.* was, however, reported in the study of Brull *et al.* that looked at acute and long-term benefits of iliac crest donor site perfusion with local anesthetics.<sup>[10]</sup> In their study, an indwelling catheter was placed at the ICBG donor site through



**Table 4: Pain score and effect of pain on gait at the 4<sup>th</sup>- and 12<sup>th</sup>-week postoperative period in the two groups**

	Bupivacaine group (n=15)	Saline group (n=15)	P*
Pain score at 4 <sup>th</sup> and 12 <sup>th</sup> week postoperative period (median [range])			
4 <sup>th</sup> week			
At rest	0 (2)	0 (0)	0.04 <sup>2</sup>
Walking	0 (1)	0 (5)	0.39 <sup>2</sup>
During exertion	0 (4)	1 (5)	0.80 <sup>2</sup>
12 <sup>th</sup> week			
At rest	0 (0)	0 (0)	-
Walking	0 (0)	0 (4)	0.48 <sup>2</sup>
During exertion	0 (1)	0 (6)	0.27 <sup>2</sup>
Effect of pain on gait at 4 <sup>th</sup> and 12 <sup>th</sup> weeks			
4 <sup>th</sup> week			
Gait disturbance, n (%)			
Yes	6 (40.0)	9 (60.0)	0.43 <sup>1</sup>
No	6 (40.0)	5 (33.3)	
No response	3 (20.0)	1 (6.7)	
Severity of gait disturbance, n (%)			
Mild	5 (33.3)	8 (53.3)	0.62 <sup>1</sup>
Moderate	1 (6.7)	1 (6.7)	
12 <sup>th</sup> week			
Gait disturbance, n (%)			
Yes	1 (6.7)	3 (20.0)	0.52 <sup>1</sup>
No	7 (46.7)	6 (40.0)	
No response	7 (46.7)	6 (40.0)	
Severity of gait disturbance, n (%)			
Mild	1 (6.7)	2 (13.3)	0.68 <sup>1</sup>
Moderate	0 (0)	1 (6.7)	

\*Significant at  $P < 0.05$ , <sup>1</sup>Chi-square, <sup>2</sup>One-way ANOVA. ANOVA: Analysis of variance

which 0.25% bupivacaine was administered whenever a patient complained of pain from the ICBG donor site. Their study showed bupivacaine hydrochloride to be an effective means of reducing immediate and residual postoperative pain. This is similar to the findings of Singh *et al.* that also reported continuous infusion of 0.5% bupivacaine to be capable of reducing both the immediate and long-term pain that may be associated with ICBGH site.<sup>[18]</sup>

The present study showed a gradual reduction in donor site pain score between the 1<sup>st</sup> and 4<sup>th</sup> postoperative days, and the reduction in pain was slightly better in the bupivacaine group only on the 1<sup>st</sup> postoperative day. Wilkes and Thomas, in a comparative study comprising two groups of continuous and single infiltration of bupivacaine hydrochloride at ICBGH site, reported an average pain score of 2.2 and 5.5 on a scale of 10, respectively, for the groups at 24 h postoperation and concluded that continuous infusion is a more effective way of managing postoperative pain following ICBGH.<sup>[24]</sup> The average pain scores in the present study were 4.2 and 5.0 (for the bupivacaine and normal saline groups, respectively) similar to the 5.4 reported for the bupivacaine single infiltration group in

the study of Wilkes *et al.*<sup>[24]</sup> The slightly lower score in the bupivacaine group could be due to the residual analgesic effect (period of analgesia after sensation has returned) normally exhibited by bupivacaine.<sup>[25]</sup> Bupivacaine is a long-acting local anesthetic agent and has an analgesic effect with clinical activity ranging between 3 and 12 h; however, it has a residual analgesic effect that may far outlast the clinical effect period.<sup>[16]</sup> This residual analgesic effect may be responsible for the reduced postoperative analgesic consumption in the bupivacaine group, though not statistically different from the consumption in the saline group. These findings are in agreement with the findings of some previous studies that used either single-dose infiltration or continuous infusion of bupivacaine in which no significant postoperative analgesic action of bupivacaine was found. Puri *et al.* reported no difference in pain on active hip motion and pain medication administered between the bupivacaine and normal saline groups in the first 48 h postoperation in a study of bupivacaine for postoperative pain relief at the ICBGH site. Similarly, Morgan *et al.* concluded that bupivacaine infusion does not offer any significant advantage in terms of hip pain relief and amount of narcotic analgesic consumption among their

study groups. In contrary, there are studies that are at variance with these observations. Sbitany *et al.* found a significant decrease in length of hospitalization, trend toward decreased opioid use, and a lower average subjective pain score in those with continuous infusion of bupivacaine similar to the findings in the study of Brull *et al.* We also found no significant difference between the bupivacaine and saline groups on median pain score and gait disturbance at 12<sup>th</sup> week contrary to the findings in the study of Brull *et al.* that found a significantly lower incidence of pain and dysesthesia 6 months postoperation and concluded that bupivacaine is effective in decreasing the immediate and residual postoperative pain.

Most studies that have looked at the effectiveness of bupivacaine in controlling postoperative pain following ICBGH utilized different methodologies, and these include intermittent or continuous infusion using an indwelling catheter with or without patient-controlled devices and bolus injection at intervals or as a single injection. This may explain the varied results and lack of consensus so far witnessed in the literature concerning this topic.

#### Study limitation

This study was conducted in a teaching hospital in a region of Nigeria; this together with the small sample size may limit the generalizability of the results obtained.

#### CONCLUSION

Local injection of single dose of 0.25% bupivacaine did not offer additional benefit in the management of postoperative donor site pain following ICBGH when compared to 0.9% saline. To clarify the present controversies on the efficacy of bupivacaine in the management of postoperative pain, there is a need for more randomized controlled trials. Currently, the option for the management of the inevitable postoperative pain that accompanies ICBGH will be at the discretion of the managing team.

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#### Conflicts of interest

There are no conflicts of interest.

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