Scientific Research Publishing

Open Journal of Anesthesiology, 2023, 13, 58-74
https://www.scirp.org/journal/ojanes
ISSN Online: 2164-5558
ISSN Print: 2164-5531

Analgesic Efficacy of Intrathecal Bupivacaine with or without Morphine in Lower Limb Orthopedic Surgery. A Comparative Study

Alexis Dun Bo-ib Buunaaim[1], Comfort Adubia[2], Fidelis Bayor[3], Sylvanus Kampo[4*]

[1]Department of Surgery, School of Medicine and Health Science, University for Development Studies, Tamale, Ghana
[2]Department of Anaesthesia and Intensive Care, School of Medicine and Health Science, University for Development Studies, Tamale, Ghana
[3]Department of Physiology, School of Medicine and Dentistry, University of Ghana, Accra, Ghana
[4]Department of Anaesthesia and Intensive Care, School of Medical Sciences, C. K. Tedam University of Technology and Applied Sciences, Navrongo, Ghana
Email: abuunaaim@uds.edu.gh, adubiacomfort@gmail.com, bayorfidelis@gmail.com, *sylvanuskampo@yahoo.com

How to cite this paper: Buunaaim, A.D.B., Adubia, C., Bayor, F. and Kampo, S. (2023) Analgesic Efficacy of Intrathecal Bupivacaine with or without Morphine in Lower Limb Orthopedic Surgery. A Comparative Study. *Open Journal of Anesthesiology*, **13**, 58-74.
https://doi.org/10.4236/ojanes.2023.133006

Received: February 10, 2023
Accepted: March 27, 2023
Published: March 30, 2023

Abstract

Background: Lower limb orthopaedic surgeries are commonly associated with moderate to severe postoperative pain. Adequate pain relief is essential for patients undergoing such procedures, as uncontrolled pain can lead to delayed recovery, prolonged hospitalization, and increased morbidity. Intrathecal administration of bupivacaine, a long-acting local anesthetic, has been shown to provide effective analgesia after lower limb orthopaedic surgery. However, the duration of analgesia with bupivacaine alone is limited, and the addition of an opioid, such as morphine, can prolong the duration of analgesia. **Objective:** The objective of this study was to document the comparative effect of adding morphine to intrathecal bupivacaine or only intrathecal bupivacaine for lower limb trauma orthopedic surgeries in terms of onset of action, duration of analgesia, pain severity, and side effects. **Methods:** This was a comparative longitudinal study design conducted at the Orthopaedic Unit of the Tamale Teaching Hospital. A simple random sampling technique was used to recruit 60 patients. A standard structured questionnaire was also used to collect data on the socio-demographics, and clinical features of patients, drug used,side effects and severity of pain at 24,48 and 72 hrs after surgery. **Results:** Co-administration of intrathecal bupivacaine with morphine produced good and long-lasting postoperative analgesia with a mean time of 1004.25 ± 310.43 minutes, whiles using only bupivacaine produced shorter postoperative analgesia with a mean time of 294.75 ± 195.53 minutes. The p-value <

0.001 suggested that there was a statistically significant difference between the two groups. The onset of Anaesthesia (sensory and motor block) in those who received only bupivacaine was 68.65 ± 9.201 and 237.25 ± 57.617 secs whiles for those who received bupivacaine with morphine, was 70.50 ± 14.692 and 228.50 ± 77.95 secs with p values of $p = 0.635$ and $p = 0.689$ respectively. **Conclusion:** The study revealed that co-administration of intrathecal bupivacaine with morphine emerged as a better option for postoperative pain management after lower limb orthopedic surgeries as compared to administering only bupivacaine regarding the duration of analgesia. Milder side effects like pruritus, nausea, and vomiting were seen in group B than in group A and were promptly well managed to the patient's satisfaction.

Keywords

Bupivacaine, Morphine, Pain, Analgesia, Orthopedic Surgery

1. Introduction

Inadequate pain control may lead to haunting pain after surgery and has undesirable psychological and physiological impacts and limits one's functional capabilities leading to reduced patient satisfaction [1]. Studies have revealed a potential link between the cause of pain immediately after injury and subsequent depression and post-traumatic stress disorder (PTSD) [2]. As a result, the treatment of immediate postoperative pain is highly important. Also, the exposure of fractures and osteotomy or the reaming of long bones is associated with the release of a large amount of histamine, bradykinin, serotonin, prostaglandins, and substance P during Trauma orthopaedic surgeries. This leads to enhanced sensitivity and activation of peripheral receptors such that the threshold for signal conduction of pain decreases (allodynia) [3]. In the United States, for example, a study revealed that about 80% of patients had acute pain after surgery. Among these patients, 86% experienced moderate, severe, or extreme pain, with more patients complaining of pain post-discharge than before discharge [4]. Therefore giving suitable analgesia in the postoperative period reassures patient's trust in our health systems, proven by fewer hospital stays as well as a positive outcome of the interventions

Globally, orthopedic trauma injuries represent more than 25% of the over 500 million people injured annually [5] and most of these injuries require surgical intervention. Lower limb orthopaedic surgeries are commonly associated with moderate to severe acute postoperative pain even when an opioid protocol is used [6] [7].

Postoperative pain is frequent and should be treated as quickly and effectively as possible to minimize suffering, accelerate recovery and rehabilitation, and avoid complications [8]. Perioperative pain associated with orthopedic surgeries may persist and become chronic requiring aggressive and meticulous pain man-

agement [9] [10]. Despite far more scientific evidence in this area, clinical postoperative pain management is still far from successful [8].

Management of acute pain after orthopaedic surgery has evolved significantly during the last decade, thus, pain management which was earlier assigned to nurses and residents is now the duty of Anesthesiologists and members of the surgical team [11]. Also, the goal of every contemporary anesthetist or orthopedic surgeon is that, with the least pain and discomfort, there should be a faster onset of postoperative activity, mobility, and rehabilitation [12]. It is important to know that pain can be prevented before it is perceived, thus, as part of the role of the anesthetist, the cognitive or emotional response can be prevented with the use of anesthetics. These agents interrupt the pain pathway so that pain does not occur but can only be perceived soon after recovery [13] [14] [15]. As a result, it is necessary to add adjuvants to prolong analgesia as long as the drug remains in the system.

Modern pain management methods combine preemptive and multimodal analgesia to reduce the risk of side effects while maximizing the effectiveness of the procedure [16]. The timing and delivery of these medications, which include both modern and conventional painkillers, cause significant postoperative pain relief and, ultimately, accelerate the patient's recovery. Pharmacological treatments should not be the only postoperative pain management strategy. When compared to pain management techniques used within an enhanced recovery after surgery (ERAS) pathway, traditional approaches for major abdominal and traumatic surgery, such as opioid-based intravenous patient-controlled analgesia (IVPCA) or epidural analgesia, were associated with superior pain control [17]. Other pain management techniques that can be used in lower limb orthopedic surgery include the use of non-steroidal anti-inflammatory drugs (NSAIDs) [18] such as ibuprofen or naproxen, acetaminophen (paracetamol), regional anesthetic techniques [18] [19], such as a femoral nerve block or lumbar plexus block which can provide targeted pain relief to the lower limb, transcutaneous electrical nerve stimulation (TENS) which is a non-pharmacological method that uses electrical impulses to stimulate nerve fibers and relieve pain, physiotherapy, which can help improve range of motion, strengthen the muscles and decrease pain in the postoperative period.

In recent years, intrathecal analgesia has gained popularity as a safe and effective technique for postoperative pain management [20] [21]. Almost all lower limb orthopedic surgeries are ideally suited to use regional anesthesia which can help achieve the goal of adding adjuvants to subarachnoid block (SAB), epidural anesthesia, and conduction blocks. Intrathecal administration of bupivacaine, a long-acting local anesthetic, has been shown to provide effective analgesia after lower limb orthopedic surgery [22]. However, the duration of analgesia with bupivacaine alone is limited, and the addition of an opioid, such as morphine, can prolong the duration of analgesia. Also compared to other opioids, morphine stays longer in CSF and consequently produces long-lasting and adequate analgesia [15]. Karaman *et al.* affirmed that the addition of morphine to bupivacaine pro-

duced excellent intraoperative pain relief and also increased the duration of analgesia postoperatively [23].

Moreover, despite the increased awareness of the negative consequences of poorly controlled pain, analgesic therapy or pain control methods use among hospitalized patients after orthopedic trauma remains inadequate [2]. Studies have evaluated the analgesic efficacy of intrathecal bupivacaine with morphine in lower limb orthopedic surgery [24], but the results have been inconsistent. Some studies have reported improved pain relief and reduced opioid requirements with the combination of bupivacaine and morphine [24] [25] [26], while others have reported no significant differences in analgesic efficacy compared to bupivacaine alone. Poor monitoring, delayed response to patient's pain, and inaccurate pain score contributes to the challenge that is still faced in postoperative pain treatment [27]. There is however a paucity of studies regarding postoperative pain management despite the increasing number of surgical cases over the years in Ghana and Africa [28]. As a result, this study was designed to ascertain the effectiveness of morphine addition to intrathecal bupivacaine in reducing pain and improving postoperative recovery in comparison to other methods of pain management in patients undergoing lower limb surgeries at the Tamale Teaching Hospital. It will identify any potential side effects or complications associated with the use of intrathecal bupivacaine with morphine among this patient population. Further, the findings of this study will provide additional data on pain management strategies following traumatic orthopedic surgery.

2. Materials and Methods

2.1. Study Subjects and Ethical Statement

This was a randomized comparative study, conducted at the Orthopaedic unit of the Tamale Teaching Hospital from April to November 2021. The Ethical Review Board of the Kwame Nkrumah University of Science and Technology (CHRPE/AP/416/21) approved the study protocol. All methods were carried out following the applicable rules and regulations, and the study protocol followed the CONSORT recommendations.

This study recruited 60 patients who were undergoing lower limb trauma orthopedic surgeries, using Cochran's sample size formula. The inclusion criteria were made up of all patients who were undergoing elective lower limb orthopedic surgery and have consented to take part in the study, those without any comorbidity and should be 18 years and above. The exclusion criteria were as follows; patients who consented to the study but developed complications intraoperatively and those with respiratory disorders, uncontrolled hypertension, and diabetes

2.2. Sampling Procedure

Random sampling was used to select respondents who provided consent to take part in the study. The sample size for this study was determined using the Coch-

ran formula due to the unknown population size and the need to estimate the proportion of successes in a dichotomous outcome variable (yellow/blue) in a single population as follows:

$$n = \frac{Z^2 P(1-P)}{e^2}$$

where: N = sample size to be determined, Z = Z score (reliability coefficient) of 1.96 at 95% confidence level, e = margin of error of 5% = 0.05, P = the percentage of picking a choice (yes/no) and therefore the range of $p(1 - p)$ is 0 to 1. Therefore, our sample size estimated was 60 patients.

2.3. Randomization

A computer-generated random number table was used to assign each recruited patient at random to one of two groups. Those in Group A (n = 30) received bupivacaine alone, while those in Group B (n = 30) received bupivacaine along with morphine (Figure 1). The group allocation was concealed in a sealed opaque envelope which was opened just before anesthesia was given.

2.4. Recruitment and Follow-Up

Patients were recruited from 10th September 2021 to 29th November 2021. A standard structured questionnaire was used to collect data on the drug used, side

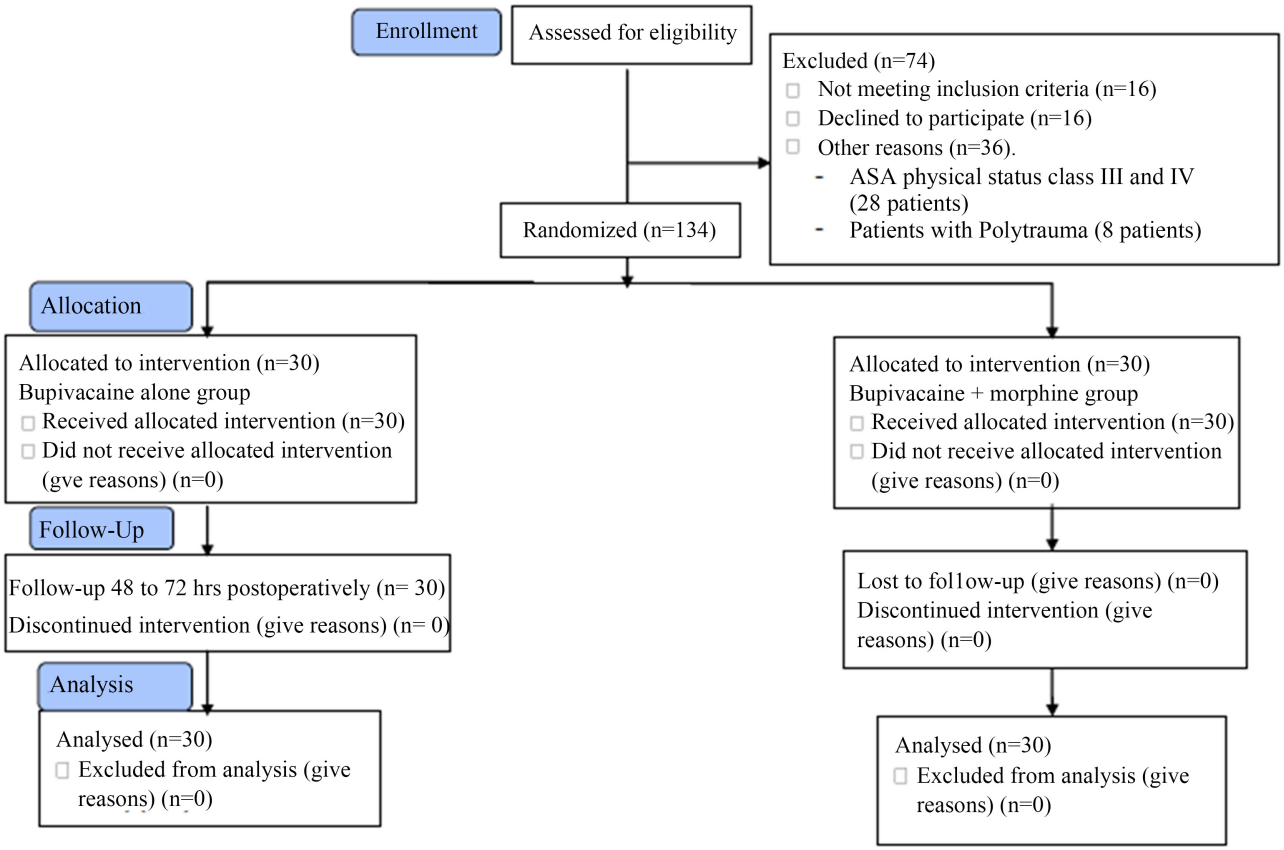

Figure 1. CONSORT flow diagram and checklist.

effects, and follow-up information on patient satisfaction with pain control in the postoperative period.

2.5. Trial Registration

The authors of this study confirm that all ongoing and related trials for this drug/intervention were registered with the ISRCTN registry (ISRCTN31685121)

2.6. Anaesthetic Technique and Drug Application

According to the physical status classification used by the American Society of Anaesthesiologists, all patients were prospectively evaluated and categorized. The baseline vital signs were examined and recorded, and basic intraoperative monitoring techniques (ECG, SpO_2, temperature, and non-invasive blood pressure) were used. On the operating table, the patients were positioned in a sitting position. Using a 21G hypodermic needle, 2 ml of 2% preservative-free lidocaine was infiltrated into the skin and interspinous ligaments in an aseptic environment. A 26G sterile disposable pencil-point spinal needle was inserted at the L3 - 4 intervertebral space using a midline approach. The free flow of cerebrospinal fluid was evidence that the spinal needle had successfully entered the subarachnoid space. The subarachnoid block was then established using 0.2 mg of morphine and 15 mg of preservative-free hyperbaric bupivacaine or 15 mg hyperbaric bupivacaine alone. To prevent the spinal agent from spreading further toward the head, the patients were then instructed to lie back down on their backs with their heads propped up on pillows. For the first 30 minutes, the patient's vital signs (pulse rate, blood pressure, oxygen saturation, and respiratory rate) were monitored and recorded every 5 minutes. After that, they were recorded every 15 minutes. To verify adequate sensory block up to T6 level, an ice cube was used. Through nasal prongs, additional oxygen was administered at a rate of 3L/min. 5 - 10 mg of IV ephedrine was used to treat intraoperative hypotension. 0.3 - 0.6 mg of IV atropine was used to treat heart rates (HR) under 50 beats per minute. Any estimated blood loss or fluid deficit was compensated for appropriately.

2.7. Parameters Assessed

The duration of analgesia, the degree of pain, the side effects, and the onset of analgesia was the dependent or outcome variables in this study. Following surgery, the pain was assessed for 72 hours on a 0-100 scale using the Visual Analog Scale (VAS), with 0 mm denoting no pain and 100 mm denoting intolerable pain [29] [30] [31]. The patient was given intravenous morphine, intramuscular pethidine, or intravenous acetaminophen if rescue analgesia was necessary.

Direct scheduled assessments or spontaneous complaints by the patients following surgery were used to identify the episodes of PONV. Using a three-point ordinal scale (0 = none, 1 = nausea, and 2 = vomiting), the incidence of PONV was tracked hourly for the first four hours and then four hours per hour for the

following 24 hours. The PONV incidence was calculated and classified as either early (0 - 4 hours) or delayed (5 - 24 hours). If nausea or vomiting occurs, intravenous Kytril 1 - 2 mg (anti-emetic) was given upon request.

Every four hours for 48 hours following surgery, the incidence of pruritus was noted using a four-point categorical scale: 0 = no pruritus, 1 = mild, 2 = moderate, and 3 = severe pruritus. To treat opioid depression, naloxone hydrochloride 2 μg/kg was injected, and cetirizine 10 mg was given upon request or if pruritus appeared.

On the day of discharge, during an interview, the level of overall perioperative satisfaction was assessed as follows: 4 = excellent, 3 = good, 2 = satisfactory, and 1 = poor.

2.8. Measurement of Variables

Outcome Variables

The main primary outcome variables include the duration of pain relief, the severity of pain, and the number of times they required rescue analgesic. The secondary outcome variable includes measurement of postoperative complications (such as POVN, respiratory depression, pruritus, etc.) and level of satisfaction.

2.9. Data Analysis

Version 22.0 of the Statistical Package for Social Science (SPSS) (IBM Corporation, Armonk, NY, USA) was used for the statistical analysis. Initial analysis was carried out using descriptive statistics. The metrics used to describe the results were mean, SD, and range. Frequencies were presented as percentages and numbers. Multiple group comparisons were made using one-way analysis of variance (ANOVA), and intergroup data was examined using the unpaired student's t-test (numerical) and chi-square test (categorical). Statistics was defined as statistically significant at P-value < 0.05.

3. Results

A total of 60 patients were recruited for this study. They were randomized into two groups of equal numbers of 30 each. The data showed that those from the bupivacaine alone group were 24 (80%) males and 6 (20%) females and those from the bupivacaine with morphine group were 25 (83.3%) males and 5 (16.7%) females. The mean age of patients from the bupivacaine alone group (37.47 ± 13.98 years) was similar to those from the bupivacaine and morphine combined group (37.90 ± 10.13 years). The results showed no significant difference between the groups regarding age, religion, and educational level (P < 0.891; P < 0.770; P < 0.485 respectively) (Table 1).

Duration of anesthesia (pain sensation) was significantly prolonged (1004.25 ± 310.425 minutes; p < 0.001) among patients from the bupivacaine + morphine group compared with 294.75 ± 195.532 minutes among those from the bupivacaine alone group. The data showed a significant difference between groups

Table 1. Demographic characteristics of respondents.

Variables		Intervention		*P*-value
		Bupivacaine Alone (n = 30) N (%)	Bupivacaine + Morphine (n = 30) N (%)	
Age	Years	37.47 ± 13.98	37.90 ± 10.13	0.891
Gender	Female Male	6 (20.0) 24 (80.0)	5 (16.7) 25 (83.3)	0.744
Employment Status	Employed Unemployed	22 (73.3) 8 (26.7)	27 (90.0) 3 (10.0)	0.098
Religion	Christian Muslim	8 (26.7) 22 (73.3)	7 (23.3) 23 (76.7)	0.770
Marital Status	Married Single	21 (70.0) 9 (30.0)	20 (66.7) 10 (33.3)	0.786
Education Level	Primary Secondary Tertiary	6 (20.0) 14 (46.7) 10 (33.3)	5 (16.7) 12 (40.0) 13 (43.3)	0.485

Independent student T-test: p-value < 0.05 considered statistically significant.

regarding sensitivity to pain at 24 hrs, 48 hrs, and 72 hrs after surgery ($p < 0.001$, $p < 0.001$, $p < 0.022$ respectively) with the lowest pain severity recorded in the Bupivacaine + Morphine group compared to the Bupivacaine group (Table 2).

Student's T-Test was used to generate the p-values

The data showed that for the first 24 hours, 6 (20.0%), 21 (70.0%), and 3 (10.0%) patients experienced mild, moderate, and severe pain respectively among those who received bupivacaine alone, while 10 (33.3%) and 20 (66.7%) patients experienced no pain and mild pain among those from the bupivacaine with morphine group. The result showed that after 48 hours, 10 (33.3%) and 20 (66.7%) patients from the bupivacaine alone group experienced mild and moderate pain respectively, whereas 24 (80.0%) and 6 (20.0%) patients from the bupivacaine with morphine group experienced mild and no pain respectively. At 72 hours after surgery, patients experienced mild to moderate pain with no significant difference observed among the groups (Table 3).

The results revealed that side effects seen among patients who received bupivacaine and morphine combined were more than that seen among those who received only bupivacaine for spinal anesthesia. The most occurred side effect observed among patients was pruritus, 11 (57.8%). Followed by the individual patient experiencing pruritus, nausea, and vomiting at the same time, 6 (31.60%). Urine retention observed was 1 (5.26%) (Table 4).

When patients were asked to indicate how satisfied they were with their pain management, a general impression depicted that, patients who received bupivacaine and morphine combined were more satisfied than those who received only bupivacaine. The data showed significant differences between the groups regarding patient satisfaction ($p < 0.001$) (Figure 2).

Table 2. Effect of Bupivacaine with or without morphine for spinal anesthesia.

Effects of intervention	Bupivacaine Mean ± SD	Bupivacaine + Morphine Mean ± SD	*P*-value
Duration of spinal anaesthesia (in minutes)	294.75 ± 195.532	1004.25 ± 310.425	<0.001
Pain severity in 24 hrs after surgery	4.80 ± 1.105	1.90 ± 0.641	<0.001
Pain severity in 48 hrs after surgery	3.00 ± 0.725	1.70 ± 0.657	<0.001
Pain Severity in 72 hrs after surgery	2.75 ± 1.020	2.00 ± 0.973	0.022

Table 3. Comparison of post-op pain severity between the two groups.

Duration	Pain severity using NRS	Bupivacaine N (%)	Bupivacaine + Morphine N (%)	*P*-value
24 hrs	No pain	0	10 (33.3)	[b]<0.001
	Mild	6 (20.0)	20 (66.7)	
	Moderate	21 (70.0)	0	
	Severe	3 (10.0)	0	
48 hrs	No pain	0	6 (20.0)	[b]0.017
	Mild	10 (33.3)	24 (80.0)	
	Moderate	20 (66.7)	0	
	Severe	0	0	
72 hrs	No pain	0	0	[b]0.376
	Mild	22 (73.3)	25 (83.3.0)	
	Moderate	8 (26.7)	5 (16.7)	
	Severe	0	0	

[b]Pearson Chi-Square used.

Table 4. Comparison of the type of adverse effects experienced between the two groups.

Adverse effects	Bupivacaine N (%)	Bupivacaine + Morphine N (%)	*p*-value
Nausea and vomiting	2 (25.0)	0	[b]<0.001
Headache	2 (25.0)	0	
Pruritus only	2 (25.0)	11 (57.8)	
Pruritus and Respiratory distress	0	1	
Chills	2 (25.0)	0	
Pruritus, Nausea, and Vomiting	0	6 (31.60)	
Urine retention	0	1 (5.26)	
Total	8	19	

4. Discussion

One of the most common complaints in the post-operative time is pain. The primary objective of anesthesia is to effectively relieve pain during and after surgical procedures [32]. Postoperative pain management in lower limb orthopedic

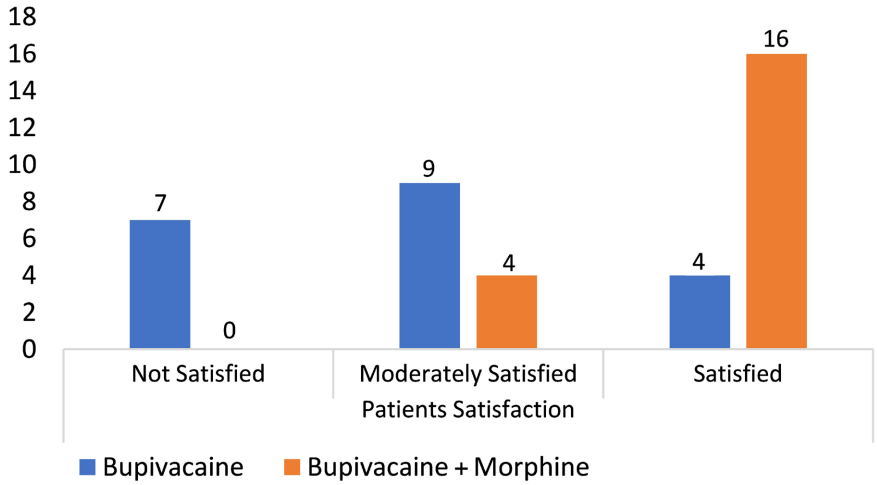

Figure 2. Comparing satisfaction between the two groups.

surgery can be challenging, therefore effective pain control is essential for optimal recovery and rehabilitation. Although intrathecal analgesia with bupivacaine has been found to provide effective postoperative pain relief, the addition of morphine to the mixture may enhance its analgesic efficacy [32]. The study aimed to explore the analgesic efficacy of the combination of intrathecal bupivacaine with morphine in reducing pain and improving postoperative recovery among patients undergoing lower limb orthopedic surgeries.

Age can be an important determining factor when contemplating intrathecal morphine for the management of postoperative pain. Even though the pain threshold increases with age, after years of research on age-related effects on pain perception, the only firm evidence found is that aging reduces pain sensitivity for lower pain intensities [33]. The dose of intrathecal morphine required for pain relief may vary depending on the patient's age. Older patients may require lower doses due to changes in their metabolism and decreased clearance of the drug. In contrast, younger patients may require higher doses due to their increased metabolic rate and greater sensitivity to the drug [34]. Intrathecal morphine can also cause side effects such as nausea, vomiting, pruritus, and respiratory depression [35] [36]. These side effects can be more common and severe in older patients due to their decreased renal and hepatic function, as well as a decreased respiratory reserve. Intrathecal morphine may also increase the risk of certain complications such as urinary retention, delayed respiratory depression, and neurotoxicity [35]. These complications may be more common in older patients due to the age-related changes in their physiology. Per the given data in this study, the distribution of cases was comparatively age-wise, without any significant difference. Age did not have a significant effect on the outcome of this study.

From the data analysis, there was a significant difference in the duration of postoperative pain sensation block between the two groups (p-value < 0.001). Patients from the bupivacaine with morphine group had a longer duration of

postoperative pain relief compared with those from the bupivacaine alone group. Similarly, Basnet and his colleagues revealed that the duration of postoperative analgesia among patients who received intrathecal bupivacaine with morphine was longer than patients who received only bupivacaine [37]. The result again confirms Gehling *et al.* who stated that intrathecal morphine provides effective analgesia for up to 48 hrs without the need for systemic opioids [38]. The current result also agrees with other studies that concluded that adding adjuvants to local anesthetics improves analgesia duration and better outcomes [39] [40]. This is probably because morphine being hydrophilic doesn't rapidly diffuse into non-neuronal tissues such as myelin and epidural fat hence maintaining its concentration in the CSF for a longer period giving a longer duration of action with more analgesic spread beyond the injection point [41].

Post-operative pain severity assessment revealed that almost all respondents had some level of pain. Our results indicated a significant difference in terms of sensitivity to pain between the groups. Patients who received bupivacaine alone after 72 hours still experienced moderate pain while those who received bupivacaine and morphine as adjuvant experienced mild to no pain. This evidence, therefore, suggests that bupivacaine alone is not a better choice for postoperative pain management. This confirms a similar finding by Shim *et al.*, (2021) [42]. Ashok *et al.*, 2016 also concluded that postoperative pain is not limited to the immediate postoperative phase but seems to remain a significant concern in the later postoperative period [43]. Philip Wagner concluded that 80% of respondents experienced some level of pain after surgery [44]. Barbosa MH *et al.* (2014) had a similar result [45]. Meanwhile, a study by Ekin Akmaz *et al.* (2018) revealed that pain was inadequately perceived by nurses and relatives and could mislead in the treatment of postoperative pain management [46]. The findings of our study revealed that the first 48 hrs after surgery is very important for adequate pain management since it is within this period that most patients experience severe pain. The side effects experienced by patients in this study were statistically significant (p-value < 0.001). There were more patients among the bupivacaine and morphine combined group who experienced side effects like pruritus, nausea, and vomiting compared to the bupivacaine alone group. This could be a result of the addition of morphine which commonly results in the mentioned common side effects. These effects are however mild and could easily be managed with promethazine without patients being unsatisfied. Those who received bupivacaine alone experienced headaches and chills. This confirms the finding by Ezzat *et al.*, 1988, who observed similar side effects [47]. The findings were again similar to the results gotten from Meco, (2016) [48] where 23% of patients who received 0.4mg intrathecal morphine with bupivacaine had an episode of vomiting with 26.9% having pruritus during the first 24 hrs postoperative period. Basnet, (2018) confirmed that 6 out of 100 (6%) respondents had respiratory depression, pruritus, nausea, and vomiting. Also, in the Shim *et al.* study, similar side effects were noticed but nausea and vomiting were marginally

higher than pruritus. The current result again agrees with Koning *et al.* (2019), who also revealed an increased incidence of pruritus [49].

The major strength was that the study had a relatively long follow-up duration, which could help to assess the long-term efficacy of the treatment. The analgesic effect of intrathecal bupivacaine with morphine may wear off after a few hours or days, so a longer follow-up is essential to determine the duration of the effect. This study is limited in the sample size in that probably a larger sample size could have been more explicit with the findings. A small sample size could also increase the risk of type II errors and reduce the power of the study. The study may have encountered selection bias in the patients who were enrolled in the study. Because the study excluded patients who experienced intraoperative problems, as well as those with respiratory diseases, uncontrolled hypertension, and diabetes, the results may be affected. The study included patients undergoing different types of orthopedic surgeries, which could introduce variability in the results. The analgesic efficacy of the treatment may vary depending on the type of surgery, so a more homogeneous sample would be ideal.

Further studies should be done on the effect of adding different dosages of morphine to bupivacaine for spinal anesthesia.

5. Conclusions

The distribution of cases was comparatively age-wise, without any significant difference. Age did not have a significant effect on the outcome of this study. Also, findings of the study showed that patients from the bupivacaine with morphine group had a longer duration of postoperative pain relief compared with those from the bupivacaine alone group. Our results indicated a significant difference in terms of sensitivity to pain between the groups. Patients who received bupivacaine alone after 72 hours still experienced moderate pain while those who received bupivacaine and morphine as adjuvant experienced mild to no pain. Again, there were more patients among the bupivacaine and morphine combined group who experienced side effects like pruritus, nausea, and vomiting compared to the bupivacaine alone group. Those who received bupivacaine alone experienced headaches and chills.

The findings of this study suggested the use of bupivacaine and morphine combination therapy in anesthesia practice for adequate postoperative pain management. Accurate perioperative pain assessment should be incorporated into pain monitoring.

Declarations

Ethics Approval and Consent to Participate

The Ethical Review Board of the Kwame Nkrumah University of Science and Technology (CHRPE/AP/416/21) approved the study protocol. Written informed consent was obtained from patients after providing them with adequate explanations regarding the aims of the study. Also, we have read and complied with the

instructions to the authors and in particular the policy of the journal on ethical consent and standards of animal care.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to patient confidentiality but are available from the corresponding author at a reasonable request.

Authors' Contributions

ADBB, and AC conceived and designed the study. SK and ADBB were responsible for the supervision and coordination of this study. ADBB, AC, and SK conducted the data collection. FB and SK led the data analysis with inputs from ADBB, and AC. The first draft of the manuscript was written by ADBB, SK, FB, and AC contributed to revising and reviewing the manuscript. All authors read and approved the final manuscript before submission.

Acknowledgements

We thank the staff of the department of anesthesia and intensive care of the Tamale Teaching hospital for providing all the necessary material we needed for this study. We also thank the management and staff of the department of surgery of the Tamale Teaching hospital for approving this study protocol and making available all the necessary materials needed for the study.

Conflicts of Interest

Authors declare that they have no competing interests.

References

[1] Joshi, G.P. and Ogunnaike, B.O. (2005) Consequences of Inadequate Postoperative Pain Relief and Chronic Persistent Postoperative Pain. *Anesthesiology Clinics of North America*, **23**, 21-36. https://doi.org/10.1016/j.atc.2004.11.013

[2] Castillo, R.C. *et al.* (2017) Improving Pain Management and Long-Term Outcomes Following High-Energy Orthopaedic Trauma (Pain Study). *Journal of Orthopaedic Trauma*, **31**, S71-S77. https://doi.org/10.1097/BOT.0000000000000793

[3] Ricci, W.M., Black, J.C., McAndrew, C.M. and Gardner, M.J. (2015) Specialty Update: What's New in Orthopaedic Trauma. *The Journal of Bone and Joint Surgery*, **97**, 1200-1206. https://doi.org/10.2106/JBJS.O.00259

[4] Apfelbaum, J.L., Chen, C., Mehta, S.S. and Gan, T.J. (2003) Postoperative Pain Experience: Results from a National Survey Suggest Postoperative Pain Continues to Be Undermanaged. *Anesthesia & Analgesia*, **97**, 534-540. https://doi.org/10.1213/01.ANE.0000068822.10113.9E

[5] James, S.L., *et al.* (2018) Global, Regional, and National Incidence, Prevalence, and Years Lived with Disability for 354 Diseases and Injuries for 195 Countries and Territories, 1990-2017: A Systematic Analysis for the Global Burden of Disease Study 2017. *The Lancet*, **392**, 1789-1858. https://doi.org/10.1016/S0140-6736(18)32279-7

[6] Fuzier, R., Rousset, J., Bataille, B., Salces-y-Nédéo, A. and Maguès, J.P. (2015) One

Half of Patients Reports Persistent Pain Three Months after Orthopaedic Surgery. *Anaesthesia Critical Care & Pain Medicine*, **34**, 159-164. https://doi.org/10.1016/j.accpm.2014.09.006

[7] Edgley, C., Hogg, M., De Silva, A., Braat, S., Bucknill, A. and Leslie, K. (2019) Severe Acute Pain and Persistent Post-Surgical Pain in Orthopaedic Trauma Patients: A Cohort Study. *British Journal of Anaesthesia*, **123**, 350-359. https://doi.org/10.1016/j.bja.2019.05.030

[8] Kampo, S., Han, J., Ziem, J.B., Mpemba, F., Gao, P. and Wen, Q.P. (2013) Intraoperative Pain Assessment: The Use of an Anaesthetized Patient Pain Scale and Cerebral State Monitor. *Journal of Anesthesiology*, **1**, 15-20.

[9] Pogatzki-Zahn, E.M., Segelcke, D. and Schug, S.A. (2017) Postoperative Pain—From Mechanisms to Treatment. *Pain Reports*, **2**, e588. https://doi.org/10.1097/PR9.0000000000000588

[10] Maier, C., *et al.* (2010) Qualität der schmerztherapie in Deutschen krankenhäusern. *Deutsches Ärzteblatt*, **107**, 607-614.

[11] Koneti, K.K. and Jones, M. (2016) Management of Acute Pain. *Surgery*, **34**, 84-90. https://doi.org/10.1016/j.mpsur.2015.11.008

[12] Gousheh, M., Akhondzadeh, R., Rashidi, M., Olapour, A. and Moftakhar, F. (2019) Comparison of Dexmedetomidine and Morphine as Adjuvants to Bupivacaine for Epidural Anesthesia in Leg Fracture Surgery: A Randomized Clinical Trial. *Anesthesiology and Pain Medicine*, **9**, e91480. https://doi.org/10.5812/aapm.91480

[13] Edinoff, A.N., *et al.* (2021) Adjuvant Drugs for Peripheral Nerve Blocks: The Role of Nmda Antagonists, Neostigmine, Epinephrine, and Sodium Bicarbonate. *Anesthesiology and Pain Medicine*, **11**, e117146. https://doi.org/10.5812/aapm.117146

[14] Prabhakar, A., *et al.* (2019) Adjuvants in Clinical Regional Anesthesia Practice: A Comprehensive Review. *Best Practice & Research Clinical Anaesthesiology*, **33**, 415-423. https://doi.org/10.1016/j.bpa.2019.06.001

[15] Mehta, N. and tu Nisa Qazi, A.S. (2020) Adjuvant Drugs to Local Anesthetics. In: Whizar-Lugo, V.M. and Hernández-Cortez, E., Eds., *Topics in Local Anesthetics*, IntechOpen, London, UK, 1-15. https://doi.org/10.5772/intechopen.91980

[16] Parvizi, J., Porat, M., Gandhi, K., Viscusi, E.R. and Rothman, R.H. (2009) Postoperative Pain Management Techniques in Hip and Knee Arthroplasty. *Instructional Course Lectures*, **58**, 769-779.

[17] Hughes, M.J., Ventham, N.T., McNally, S., Harrison, E. and Wigmore, S. (2014) Analgesia after Open Abdominal Surgery in the Setting of Enhanced Recovery Surgery: A Systematic Review and Meta-Analysis. *JAMA Surgery*, **149**, 1224-1230. https://doi.org/10.1001/jamasurg.2014.210

[18] Khalili, G., Salimianfard, M. and Zarehzadeh, A. (2016) Comparison between Paracetamol, Piroxicam, Their Combination, and Placebo in Postoperative Pain Management of Upper Limb Orthopedic Surgery (A Randomized Double Blind Clinical Trial). *Advanced Biomedical Research*, **5**, 114. https://doi.org/10.4103/2277-9175.184310

[19] Honarmand, A., Kashefi, P. and Safavi, M. (2012) Effects of Preemptive Analgesia with Celecoxib or Acetaminophen on Postoperative Pain Relief Following Lower Extremity Orthopedic Surgery. *Advanced Biomedical Research*, **1**, 66. https://doi.org/10.4103/2277-9175.100197

[20] Bhure, A., Kalita, N., Ingley, P. and Gadkari, C.P. (2012) Comparative study of intrathecal hyperbaric Bupivacaine with Clonidine , Fentanyl and Midazolam for Qual-

ity of Anaesthesia and Duration of Post Operative Pain Relief in Patients Undergoing Elective Caesarean Section. *People's Journal of Scientific Research*, **5**, 19-23.

[21] Visser, E., *et al.* (2017) Postoperative Pain Management after Esophagectomy: A Systematic Review and Meta-Analysis. *Diseases of the Esophagus*, **30**, 1-11. https://doi.org/10.1093/dote/dox052

[22] Kokki, H., Tuovinen, K. and Hendolin, H. (1998) Spinal Anaesthesia for Paediatric Day-Case Surgery: A Double-Blind, Randomized, Parallel Group, Prospective Comparison of Isobaric and Hyperbaric Bupivacaine. *British Journal of Anaesthesia*, **81**, 502-506. https://doi.org/10.1093/bja/81.4.502

[23] Karaman, S., Günüsen, I., Uyar, M., Biricik, E. and Firat, V. (2011) The Effects of Morphine and Fentanyl Alone or in Combination Added to Intrathecal Bupivacaine in Spinal Anesthesia for Cesarean Section. *Agriculture*, **23**, 57-63.

[24] Machino, M., *et al.* (2010) A Prospective Randomized Study for Postoperative Pain Relief of Lower Extremity Fractures: Efficacy of Intrathecal Morphine Administration. *Nagoya Journal of Medical Science*, **72**, 145-150.

[25] Kona-Boun, J.J., Cuvelliez, S. and Troncy, E. (2006) Evaluation of Epidural Administration of Morphine or Morphine and Bupivacaine for Postoperative Analgesia after Premedication with an Opioid Analgesic and Orthopedic Surgery in Dogs. *Journal of the American Veterinary Medical Association*, **229**, 1103-1112. https://doi.org/10.2460/javma.229.7.1103

[26] Sarotti, D., Rabozzi, R. and Franci, P. (2013) A Retrospective Study of Efficacy and Side Effects of Intrathecal Administration of Hyperbaric Bupivacaine and Morphine Solution in 39 Dogs Undergoing Hind Limb Orthopaedic Surgery. *Veterinary Anaesthesia and Analgesia*, **40**, 220-224. https://doi.org/10.1111/j.1467-2995.2012.00787.x

[27] Köse Tamer, L., and Sucu Dağ, G. (2020) The Assessment of Pain and the Quality of Postoperative Pain Management in Surgical Patients. *SAGE Open*, **10**, 1-10. https://doi.org/10.1177/2158244020924377

[28] Menlah, A., Garti, I., S. Amoo, A., Atakro, C.A., Amponsah, C. and Agyare, D.F. (2018) Knowledge, Attitudes, and Practices of Postoperative Pain Management by Nurses in Selected District Hospitals in Ghana. *SAGE Open Nursing*, **4**, 1-11. https://doi.org/10.1177/2377960818790383

[29] Bijur, P.E., Silver, W. and Gallagher, E.J. (2001) Reliability of the Visual Analog Scale for Measurement of Acute Pain. *Academic Emergency Medicine*, **8**, 1153-1157. https://doi.org/10.1111/j.1553-2712.2001.tb01132.x

[30] Myles, P.S., *et al.* (2017) Measuring Acute Postoperative Pain Using the Visual Analog Scale: The Minimal Clinically Important Difference and Patient Acceptable Symptom State. *The British Journal of Anaesthesia*, **118**, 424-429. https://doi.org/10.1093/bja/aew466

[31] Kjeldsen, H.B., Klausen, T.W. and Rosenberg, J. (2016) Preferred Presentation of the Visual Analog Scale for Measurement of Postoperative Pain. *Pain Practice*, **16**, 980-984. https://doi.org/10.1111/papr.12344

[32] Thokchom, M. and Khoirom, S. (2020) To Compare the Effect of Intrathecal Morphine and Hyperbaric Bupivacaine by Using Different Techniques of Administration in Lower Limb Orthopaedics Surgeries. *Journal of Dental and Medical Sciences*, **19**, 27-31.

[33] Lautenbacher, S., Peters, J.H., Heesen, M., Scheel, J. and Kunz, M. (2017) Age Changes in Pain Perception: A Systematic-Review and Meta-Analysis of Age Effects on Pain and Tolerance Thresholds. *Neuroscience & Biobehavioral Reviews*, **75**, 104-113. https://doi.org/10.1016/j.neubiorev.2017.01.039

[34] Hayek, S.M., Veizi, I.E., Narouze, S.N. and Mekhail, N. (2011) Age-Dependent Intrathecal Opioid Escalation in Chronic Noncancer Pain Patients. *Pain Medicine*, **12**, 1179-1189. https://doi.org/10.1111/j.1526-4637.2011.01188.x

[35] Pizz, L.T., *et al.* (2012) Relationship between Potential Opioid-Related Adverse Effects and Hospital Length of Stay in Patients Receiving Opioids after Orthopedic Surgery. *Pharmacotherapy*: *The Journal of Human Pharmacology and Drug Therapy*, **32**, 502-514. https://doi.org/10.1002/j.1875-9114.2012.01101.x

[36] Wong, J.Y., Carvalho, B. and Riley, E.T. (2013) Intrathecal MorphAine 100 and 200μg for Post-Cesarean Delivery Analgesia: A Trade-Off between Analgesic Efficacy and Side Effects. *International Journal of Obstetric Anesthesia*, **22**, 36-41. https://doi.org/10.1016/j.ijoa.2012.09.006

[37] Basnet, U. (2018) A Comparative Study of Intrathecal Hyperbaric Bupivacaine with or without Morphine for Post-Operative Analgesia in Hysterectome. *Nepal Journal of Obstetrics and Gynaecology*, **13**, 20-23.

[38] Gehling, M.H.G., Luesebrink, T., Kulka, P.J. and Tryba, M. (2009) The Effective Duration of Analgesia after Intrathecal Morphine in Patients without Additional Opioid Analgesia: A Randomized Double-Blind Multicentre Study on Orthopaedic Patients. *European Journal of Anaesthesiology*, **26**, 683-688. https://doi.org/10.1097/EJA.0b013e328329b045

[39] Krishna Prasad, G.V., Khanna, S. and Jaishree, S. (2020) Review of Adjuvants to Local Anesthetics in Peripheral Nerve Blocks: Current and Future Trends. *Saudi Journal of Anaesthesia*, **14**, 77-84. https://doi.org/10.4103/sja.SJA_423_19

[40] El-shmaa, N.S., El-Kashlan, M. and Salama, E.R.(2018) The Impact of Two Different Doses of Dexmedetomidine to Local Anesthetic Mixture on the Quality of Single Injection Peribulbar Block in Vitreoretinal Operations. *International Journal of Clinical Anesthesia and Research*, **2**, 1-8. https://doi.org/10.29328/journal.ijcar.1001005

[41] David Cosgrave, N.C. (2017) Intrathecal Opioids. *Pain Revolution*, **1**, 295-307.

[42] Shim, J.W., *et al.* (2021) Analgesic Efficacy of Intrathecal Morphine and Bupivacaine during the Early Postoperative Period in Patients Who Underwent Robotic-Assisted Laparoscopic Prostatectomy: A Prospective Randomized Controlled Study. *BMC Urology*, **21**, Article No. 30. https://doi.org/10.1186/s12894-021-00798-4

[43] Ashok Jadon, A.K.P. and Mayur Motka, N.S. (2016) Postoperative Analgesia by Transmuscular Quadratus Lumborum Block Catheters. *Journal of Anesthesia and Intensive Care Medicine*, **1**, e555562. https://doi.org/10.19080/JAICM.2016.01.555562

[44] Wagner, P.J. and Sharrock, N.E. (1998) Update in Regional Anesthesia for Shoulder Surgery. *Current Opinion in Anaesthesiology*, **11**, 503-506. https://doi.org/10.1097/00001503-199810000-00009

[45] Barbosa, M.H., de Araújo, N.F., da Silva, J.A.J., Corrêa, T.B., Moreira, T.M. and Andrade, É.V. (2014) Pain Assessment Intensity and Pain Relief in Patients Post-Operative Orthopedic Surgery. *Escola Anna Nery Revista de Enfermagem*, **18**, 143-147. https://doi.org/10.5935/1414-8145.20140021

[46] Akmaz, H.E., Uyar, M., Kuzeyli Yıldırım, Y. and Akın Korhan, E. (2018) Validity and Reliability of the Turkish Chronic Pain Acceptance Questionnaire. *Balkan Medical Journal*, **35**, 238-244. https://doi.org/10.4274/balkanmedj.2016.1998

[47] Abouleish, E., Rawal, N., Fallon, K. and Hernandez, D. (1988) Combined Intrathecal Morphine and Bupivacaine for Cesarean Section. *Anesthesia & Analgesia*, **67**, 370-374. https://doi.org/10.1213/00000539-198804000-00014

[48] Meco, B.C., Bermede, O., Vural, C., Cakmak, A., Alanoglu, Z. and Alkis, N. (2016) A Comparison of Two Different Doses of Morphine Added to Spinal Bupivacaine for Inguinal Hernia Repair. *Brazilian Journal of Anesthesiology* (*English Edition*), **66**, 140-144. https://doi.org/10.1016/j.bjane.2014.08.002

[49] Koning, M.V., *et al.* (2020) The Effect of Intrathecal Bupivacaine/Morphine on Quality of Recovery in Robot-Assisted Radical Prostatectomy: A Randomised Controlled Trial. *Anaesthesia*, **75**, 599-608. https://doi.org/10.1111/anae.14922

List of Abbreviations

NRS—Numerical Rating Scale

PONV—Postoperative nausea and Vomiting

IT—Intrathecal

CSF—Cerebrospinal fluid