The purpose of this study was to analyze postoperative pain differences in patients undergoing peripheral arm surgery. Differences between patients' perceived pain who received 2 mg of morphine sulfate added to the standard Bier block solution and the standard Bier block solution without morphine were studied.

A quasi-experimental nonequivalent control group design was utilized. Thirty adult subjects (22 men and 8 women) ages 21 to 76 years constituted the convenience sample. Pain scores were measured by a verbal descriptor scale at the following times: upon admission to the postanesthesia care unit, at 30 minutes and 60 minutes after surgery, and at 24 hours postoperatively. A two-tailed Mann-Whitney U test was used to analyze pain scores for the two groups (P < .05).

No statistically significant differences were found in postoperative pain between the group receiving a Bier block solution with 2 mg of morphine sulfate and the group with a standard Bier block solution without morphine sulfate. The mean scores for the morphine sulfate group were lower in each time period measured.

This study suggests a questionable benefit for adding 2 mg of morphine sulfate to a Bier block solution. A larger sample may have yielded different results. Many issues remain undecided regarding the potential role of opioids in various regional anesthetic techniques. Further studies are warranted to investigate the peripheral effects of opioids and to understand the mechanisms of action of opioid analgesics at peripheral sites.

Key words: Arm surgery, Bier block, opioid receptors, pain.

Introduction

Today's healthcare concerns center on decreasing costs, shortening hospital stays, and facilitating the patient's return to normal activities. Therefore, the ideal regional anesthetic technique would offer rapid onset of surgical anesthesia, dissipation of motor block upon the completion of surgery, and prolonged analgesic effects without the necessity for postoperative analgesic medications.

Postoperatively, pain may be the factor most responsible for slowing the patient's return to daily activities. Pain awareness involves a complex pathway that often starts with noxious stimuli applied to peripheral pain receptors called nociceptors. The cell bodies of these primary pain receptors are located in the dorsal root ganglia and trigeminal nucleus and synapse on second-order neurons in the spinal cord dorsal horn. When noxious stimuli arrive at the spinal cord, they are modified by ultimately stimulating ascending pathways in the central nervous system where identification of the noxious stimuli takes place. Modification of pain perception is achieved through the use of opioid agonists.
Several studies have indicated prolonged analgesia with the addition of opioids, such as morphine sulfate and fentanyl to regional anesthetic solutions, including the brachial plexus block, \(^2,3\) stellate ganglion block, \(^4\) and intra-articular \(^5\) and perineural \(^6,5\) administration. Consequently, some anesthesia care providers are adding morphine sulfate to the standard Bier block solution for use in selected upper extremity surgeries.

Fields et al found that opiates act directly on opioid receptors on terminals of C fibers and exert a selective inhibitory response in nociceptor input to dorsal horn neurons. \(^8\) Class C fibers are small unmyelinated or thinly myelinated fibers. They are composed of preganglionic autonomic and pain fibers. \(^9\) The literature also suggests that there are peripheral opioid receptors that modify central nervous system pain perception. \(^10,14\) Evidence for the existence of peripheral opioid receptors suggests that pain impulses may be blocked before transmission to the dorsal horn of the spinal cord. This would prevent the perception and/or realization of pain at the supraspinal level.

Erciyes et al studied 20 subjects who received intravenous (IV) regional anesthesia with 6 mg of morphine sulfate added to a prilocaine solution. \(^15\) They found that the morphine-added group had a significantly faster onset of anesthesia and analgesia, and the recovery from anesthesia and analgesia was significantly slower. They concluded that 6 mg of morphine affected the peripheral nervous system. \(^15\) A similar study by Gupta et al found no effect on postoperative pain or analgesic requirements when 1 mg of morphine was added to prilocaine during IV regional anesthesia. \(^16\)

Subjects undergoing peripheral arm surgery experience postoperative pain. Morphine sulfate (MSO\(_4\)) is being added to the standard Bier block solution in peripheral arm surgery. This study measured the effects of the addition of an opioid receptor agonist (MSO\(_4\)) to a standard Bier block solution on postoperative pain as measured by a verbal descriptor scale (VDS).

**Material and methods**

Approval was granted by the institutional review boards at a southwestern Army Medical Center and the University of Texas-Houston Health Science Center. Informed consent was obtained from the subjects scheduled for peripheral arm surgery under Bier block anesthesia. Instruction concerning the VDS was given during the preoperative assessment. Privacy was assured as subject identification was coded. Only the investigators maintained a record of subject identification. To strengthen reliability of data collection, the four coprincipal investigators obtained the informed consent, performed the Bier blocks, and administered the VDS.

The sample consisted of 30 subjects who were English speaking, ASA physical status I or II, 18 years or older, within 30% of their ideal body weight, and without history of peripheral neuropathy or prior peripheral arm surgery under Bier block technique. Pregnant subjects were excluded. If subjects received additional intraoperative analgesics, they were eliminated from the study.

Group assignment was based on the last digit of the subjects' social security number. Subjects with odd numbers were placed in the standard Bier block solution group (group 1) and those with even numbers were placed in the morphine-added Bier block solution group (group 2). The subjects were unaware of group assignment.

After informed consent was obtained in the preoperative area, the maintenance IV line was established, and midazolam was titrated intravenously. The subject was taken into the operating room and appropriately prepared for the peripheral arm surgery and Bier block procedure to include the application of all routine monitors. A double pneumatic tourniquet was applied. Oxygen was administered at 2 L/min by nasal cannula, and the subject was given additional midazolam intravenously before the initiation of the Bier block procedure. The dose of midazolam was titrated to decrease the subject's anxiety. Anxiety levels were assessed by asking the subjects if they needed any more medication to help them relax or by clinical signs, such as resting with their eyes closed.

An IV catheter was placed in a vein on the dorsum of the hand of the surgical arm and taped securely. The subject's arm was elevated above the head, and exsanguination was accomplished by a two-step technique: gravity for 2 minutes and Esmarch bandage. The proximal and distal compartments of a two-compartment pneumatic tourniquet were inflated to 250 mmHg. The distal compartment was then deflated. The cuff pressure was continuously monitored on an automatic tourniquet insufflator. The Esmarch bandage was then removed.

The 0.5% lidocaine preservative-free solution was slowly injected while assessing the competency of the tourniquet and the subject's sensation at the site. The block was evaluated to ensure that analgesia had developed. The IV catheter was then removed and a pressure dressing applied.

During the operation, the proximal compartment of the tourniquet was kept inflated above the patient's systolic pressure. If the patient began to complain of discomfort, the distal compartment,
which was over the analgesic part of the arm, was inflated and the proximal compartment deflated to relieve discomfort related to ischemia. At the end of the operation, the tourniquet was released and reinflated immediately to release a “test dose” of solution into the general circulation. The patient was monitored for toxic reactions to the local anesthetic as it was released into the systemic circulation. Then the tourniquet was deflated for 5 seconds and reinflated for 45 seconds. This cycle was repeated four to five times and the tourniquet was removed.\(^{17}\)

If the subject was in group 2, 2 mg of MSO\(_4\) were added to the standard Bier block solution and the same procedure was followed. If the subjects received any additional intraoperative opioids or analgesics, they were eliminated from the sample.

Once the surgical procedure was completed and approximately 10 minutes after tourniquet release, the subject was taken to the postanesthesia care unit (PACU). In the PACU, vital signs and the intensity of postoperative pain as rated by the patient using the VDS (Table I) were obtained during the initial patient assessment, at 30 minutes, and 60 minutes into the recovery phase. The VDS was administered again telephonically 24 hours postoperatively by the researcher who performed the Bier block. In 1948, Keele established the most commonly used words patients used to describe the severity of pain.\(^{19}\) In 1975, Melzack used the McGill Pain Questionnaire for patients to rate their pain on a scale from 1 to 5.\(^{20}\) Littmen et al found that performance of three types of pain scales—visual analogue, verbal descriptor, and visual pain relief—correlated strongly with one another (\(r = 0.89\) to 0.93) and had minimal differences in sensitivity.\(^{20}\) Many authors agree that using a VDS is a valid measurement of an individual’s subjective rating of the intensity of pain.\(^{20-22}\) The VDS has the advantages of brevity, ease of administration and completion, and ease of scoring. It also is indicated in conditions of impaired mobility of the upper extremities, as the subject may not be able to write if his or her dominant hand is affected by the surgical procedure.

The mean pain scores for each group and comparison of the pain scores between the two groups at each specified time period were analyzed for statistical significance by using the two-tailed Mann-Whitney \(U\) test (\(P < .05\)). Descriptive statistics and a two-sample \(t\) test were used to describe and measure equivalence of the two groups by sex, ASA classification, age, weight, tourniquet time, midazolam dose, mean arterial blood pressure, and heart rate.

**Results**

The sample consisted of 22 male and 8 female subjects with a mean age of 42 years. Seven subjects were classified as ASA physical status I and 23 as ASA physical status II; in group 1, there were 2 ASA physical status I (14%) and 12 ASA physical status II (86%) subjects; and in group 2, 5 ASA physical status I (31%) and 11 ASA physical status II (69%) subjects. The mean ± SD weight for the subjects in group 1 was 81 ± 10.8 kg, and for group 2 was 78 ± 13.4 kg. Group 1 received midazolam doses that ranged from 1.5 mg to 6 mg with a mean of 4 mg administered. The intraoperative midazolam dose for group 2 ranged from 1 mg to 6 mg with a mean dose of 3.4 mg (Tables II and III). The mean arterial blood pressure and heart rate were recorded at the initial postoperative assessment, at 30 minutes, and 60 minutes after surgery. Figures 1 and 2 show the mean arterial pressure and heart rate changes for both groups.

Age, ASA classification, weight, tourniquet time, sex, midazolam dose, mean arterial pressure, and heart rate (taken initially, at 30 minutes, and 60 minutes) did not differ significantly between the two groups (two-sample \(t\) test, \(P < .05\)).

Pain was measured by using the VDS on each patient initially after surgery and at 30 minutes, 60 minutes, and 24 hours postoperatively. The pain scores for each time period were lower in group 2 and are listed in Table IV.

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**Table I**

Verbal descriptor scale for postoperative pain management

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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<tbody>
<tr>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
</tr>
<tr>
<td>5</td>
<td>Unbearable</td>
</tr>
</tbody>
</table>

**Table II**

Gender and ASA physical status of the study groups*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 14)</th>
<th>Group 2 (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>8 (57)</td>
<td>14 (88)</td>
</tr>
<tr>
<td>Women</td>
<td>6 (43)</td>
<td>2 (12)</td>
</tr>
<tr>
<td>ASA physical status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>2 (14)</td>
<td>5 (31)</td>
</tr>
<tr>
<td>II</td>
<td>12 (86)</td>
<td>11 (69)</td>
</tr>
</tbody>
</table>

*Group 1 received a plain Bier block solution; group 2 received a Bier block solution with 2 mg of morphine sulfate added. Data are given as number (percentage).
Subjects’ pain scores were then averaged for each group. Group 1 had a mean pain score of 2.4, and group 2 had a mean pain score of 2.0 for the four time periods at which pain was measured. This difference was most pronounced at 30 minutes when group 1 had a pain score of 2.57 and group 2 had a pain score of 1.81 for a P value of .052. However, there was no statistically significant difference in the postoperative pain scores between the two groups at 30 minutes, 60 minutes, and 24 hours by the two-tailed Mann-Whitney U test (P< .05). Figure 3 compares the mean scores on the VDS for both groups.

Five (33%) of the 15 patients who received MSO₄ added to the Bier block solution reported itching. This itching was reported in the PACU and confined to the surgical arm. There were no reports of itching in group 1. No treatment was required for the itching.

Discussion
The theoretical framework for this research was based on the gate control theory of pain by
Melzack and Wall, and the peripheral opioid receptor hypothesis was based on the works of Fields et al. and others. Melzack and Wall succinctly summarized the sequence of events of the gate control theory of pain. Peripheral nerves convey the presence of an injury to the central nervous system. Certain small-diameter nerve fibers respond only to injury. Others with lower threshold potential increase their discharge frequency when the stimulus reaches noxious levels.

The literature review examined current empirical evidence supporting and refuting the peripheral opioid receptor hypothesis. The results of this research, designed to test the effects of the addition of 2 mg of MSO₄ to a local anesthetic solution on postoperative pain, support the findings of several previous studies. Racz et al. found the addition of MSO₄ to a local anesthetic solution of 1% lidocaine and 0.5% bupivacaine for axillary blocks did not improve the quality of postoperative pain relief. Similarly, Arthur et al. reported no significant difference in analgesia and anesthesia when adding fentanyl to lidocaine in a Bier block.

A study by Gupta et al. showed no effect on postoperative pain or analgesic requirements when 1 mg of morphine was added to prilocaine during IV regional anesthesia.

Many studies also report findings supporting the addition of opioids to local anesthetics for the management of pain. Erciyes et al. found that 6 mg of morphine added to a 1% prilocaine Bier block solution had a statistically significant faster onset of anesthesia and analgesia and a statistically significant slower recovery from anesthesia and analgesia. They concluded that 6 mg of morphine affected the peripheral nervous system. Mays et al. reported that MSO₄ provided more profound pain relief than the local anesthetic alone when administered to the stellate ganglion. Stein et al. concluded that low doses of intra-articular MSO₄ significantly reduced postoperative pain after arthroscopic knee surgery by its action on local opioid receptors. Bourke and Furman found that addition of MSO₄ to a local anesthetic for an axillary block provided improved postoperative analgesia compared with blocks without MSO₄.

The present study found no statistically significant differences between a group with and a group without an opioid added to a Bier block. Differences in the findings of this and other reported studies may be due to variability in method and design, such as a small sample (n < 20), type of surgery, sites of opioid administration, types of opioids, and opioid dosages.

Group 2 reported less pain at the surgical site compared with group 1. The greatest difference between the groups occurred at 30 minutes postoperatively, group 2 reported a mean pain score of 1.81 and group 1 reported a mean pain score of 2.57 (P = .052). The study showed no statistically significant difference in postoperative pain with the addition of 2 mg of MSO₄ to a lidocaine Bier block solution.

Morphine sulfate is being used in clinical practice with standard Bier block solutions. The findings of the present study and other research do not support the use of MSO₄ in Bier block procedures.

In group 2, 5 (33%) of the 15 subjects reported itching. This itching was reported while subjects were in the PACU, and it was confined to the surgical arm. There were no reports of itching in group 1. Arthur et al. also found an increase in itching in subjects receiving fentanyl added to Bier block solution. This incidental observance may or may not be related to the addition of MSO₄ in a lidocaine Bier block solution.

The use of MSO₄ in Bier block anesthesia has been advocated by some anesthesia providers, but its effectiveness has not been substantiated suffi-
ciently with empirical data. Educating anesthesia providers about the use of MSO₄ in Bier block anesthesia and the known side effect (itching) may influence current clinical practice.

This research should be replicated in a multi-center study with a large sample to avoid type I error and to provide evidence of statistical differences in pain between groups with and without MSO₄ added to a Bier block. Power analysis was not performed because the sample size was restricted due to a selected population at a teaching hospital and the adherence to the thesis study time lines. Authors of similar studies with sample sizes of less than 20 did not cite a type I error as a concern.⁷,⁸-²⁷

A double-blind design with random sampling, varying doses of MSO₄ added to the Bier block solution, and standardization of the operative pain medication and type of surgery is suggested. The dose used in this study may have been too small to exhibit potential benefits of the addition of MSO₄ to Bier block solutions. However, larger doses may cause concerns about the systemic effects of MSO₄ when the tourniquet is released. If higher doses are studied, a control group that receives IV MSO₄ to assess for differences in systemic effects between the two groups would address this concern. The VDS should be used in further studies in this area of research because of its established validity and reliability.²⁸-³²

Conclusion

The present study and other studies do not support the addition of an opioid (morphine sulfate) to Bier block anesthesia to extend analgesia. However, it is difficult to explain the results obtained with opioids in Bier block anesthesia studies²⁵-²⁷ and the positive findings obtained in other studies evaluating peripheral opioid administration (e.g., brachial plexus block, intra-articular).²⁸,³⁹ One factor may be the sample size. The studies that showed an increase in pain relief with the addition of opioids had sample sizes greater than 40, while those with no increase in pain relief were usually studies with a sample size less than 20. Many issues remain unresolved regarding the potential role of opioids in various regional anesthetic techniques. Further studies are warranted to investigate the peripheral effects of opioids and to understand the mechanisms of action of opioid analgesics at peripheral sites.

REFERENCES


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