1996

The Effect of Intraarticular Injection of Morphine following Knee Arthroscopy

Chandel Dietz

University of North Dakota

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The Effect of Intraarticular Injection of Morphine Following Knee Arthroscopy
by
Chandel Anne Dietz
Bachelor of Science in Physical Therapy
University of North Dakota, 1995

An Independent Study
Submitted to the Graduate Faculty of the
Department of Physical Therapy
School of Medicine
University of North Dakota
in partial fulfillment of the requirements
for the degree of
Master of Physical Therapy

Grand Forks, North Dakota
May
1996
This Independent Study, submitted by Chandel Anne Dietz in partial fulfillment of the requirements for the Degree of Master of Physical Therapy from the University of North Dakota, has been read by the Faculty Preceptor, Advisor, and Chairperson of Physical Therapy under whom the work has been done and is hereby approved.

(Faculty Preceptor)

(Graduate School Advisor)

(Chairperson, Physical Therapy)
PERMISSION

Title        The Effect of Intraarticular Injection of Morphine Following Knee Arthroscopy
Department   Physical Therapy
Degree       Masters of Physical Therapy

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Signature: Chandel Date

Date: 12-12-95
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ACKNOWLEDGEMENTS

I would like to express my immense gratitude to the following people who were instrumental in making this paper possible. First, I would like to thank Dr. Brian Briggs, Lori Klabunde, and Dr. Tom Mohr; this paper is but a small part of a project in which these people put a lot of time, talent, and interest in. In addition, I would like to thank Tom for not only being an outstanding instructor, but a mentor as well.

Many thanks also go out to my parents, Marvin and Jane, and all my friends at "the Hub" for their love and support.

Finally, I would like to thank my husband, Jay, for always being there, always listening, and being my best friend.
ABSTRACT

Postoperative pain is common following knee arthroscopy and has been typically controlled with opioids, the most popular of which is morphine. Morphine has been traditionally administered by intramuscular, intravenous, or epidural injections. These methods of administering morphine have been very effective in producing prolonged analgesia; however, they have also produce negative central nervous system side effects.

Recent research has suggested administering morphine via intraarticular injections to provide postoperative analgesia without the central nervous system side effects. However, there is little evidence to suggest that this method is effective. Therefore, the purposes of this randomized, double-blinded study were to 1) investigate the effects of intraarticular injections of morphine on pain, 2) determine the minimal effective dose of morphine, and 3) determine the effect of morphine on the need for supplemental analgesia (pain pills).

Seventy-six subjects participated in the study and were randomly injected with 0.0 mg, .25 mg, .50 mg, .75 mg, or 1.00 mg of
morphine. Pain was assessed at 1, 3, 6, and 24 hours postoperatively using a 100 mm visual analogue scale. Subject’s requests for supplemental analgesia were also recorded.

The results of this study found that any time interval $\geq 5$ hours resulted in a significant decrease in pain. The results of this study, however, did not find intraarticular injections of morphine to significantly reduce pain, or the need for supplemental analgesia.
CHAPTER 1
INTRODUCTION

Knee arthroscopy is currently the most common orthopaedic surgical procedure in the United States; 1.2 million are performed each year\(^1\). Forty-one percent of these patients report significant pain\(^2\), especially during the first twenty-four hours\(^3\). Therefore, postoperative pain is an important issue for physical therapists. Pain affects patient comfort, discharge status, and overall rehabilitation potential. Studies have shown that severe pain is difficult to treat\(^3\) and is frequently undermedicated\(^3-5\). Considering the volume of arthroscopic procedures and the frequency of pain, effective analgesics must be found.

Postoperative pain has been typically controlled with opioids, the most popular of which is morphine. Numerous studies have shown morphine to be very effective for pain, producing prolonged analgesia for 12 to 24 hours\(^3,5-9\). Morphine accomplishes this by blocking transmission of pain impulses, inhibiting afferent pain pathways while sparing efferent motor and proprioceptive functions\(^7\).
Opioid (or morphine) receptors are present at two sites:

1) The presynaptic endings of afferent pain fibers, or
2) The interneuronal level within the dorsal horn of the spinal cord.

Currently, the most popular method of administering morphine is epidurally. This method directly affects the opioid receptors at the interneuronal level in the spinal cord. This effectively inhibits pain throughout the central nervous system.

Along with its advantages, morphine has several drawbacks and some of them are severe (Table 1). Epidural and intravenous injections of morphine affect the central nervous system (CNS) and produce negative side effects. Research has documented that morphine can produce nausea, vomiting, sedation, delay in gastric emptying, anaphlaxis, pruritis, urinary retention, and even seizures. One study found that pruritis was prevalent in 5-10%, and urinary retention in 20-40% of all cases. The most severe side effect of morphine however, is delayed respiratory depression which can occur up to twenty-four hours later. Delayed respiratory depression has been documented in 4-7% of all cases, and is especially dangerous to patients with short hospital stays.
### TABLE 1
Central Nervous System Side Effects of Morphine

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Depression</td>
<td>4%-7%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pruritis</td>
<td>5%-10%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Urinary Retention</td>
<td>20%-40%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
</tr>
<tr>
<td>Sedation</td>
<td></td>
</tr>
<tr>
<td>Delay in Gastric Emptying</td>
<td></td>
</tr>
<tr>
<td>Anaphlaxis</td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Study by Gustafsson et al<sup>14</sup>
<sup>b</sup> Study by Sabbe et al<sup>11</sup>
<sup>c</sup> Prevalence when administered intratheca.
Study by Sabbe et al<sup>11</sup>
Recent research has explored alternative ways to administer morphine without these undesirable CNS effects\textsuperscript{16}. Opioid receptors outside of the CNS (or outside of the interneuronal level within the spinal cord) were sought out. Researchers have investigated opioid receptors that would provide localized pain relief without the side effects caused by affecting the central nervous system.

Interest began with a study by Stein et al\textsuperscript{17} which implied that “peripheral sites” of tissue could contain opioid receptors for morphine. Stein found peripheral opioid receptors in the hind paws of rats, and morphine injected into inflamed areas produced analgesia.

Further research by Stein and associates\textsuperscript{18} found similar results in humans. Stein found evidence of opioid receptors in the knee joint, and demonstrated effective postoperative analgesia with intraarticular injections of morphine. Stein also found that intraarticular injections of morphine gave significantly greater pain relief than intravenous injections, and decreased the need for supplemental analgesia (pain pills)\textsuperscript{18}. The maximal effect was 3-6 hours after injection\textsuperscript{18}. Furthermore, intraarticular injections of morphine were found to be safe, with none of the negative CNS side effects seen with epidural or intravenous morphine. Stein cited two
reasons for the lack of CNS side effects. First, pain was being blocked in the knee joint (i.e. at the presynaptic level) as opposed to the spinal cord level. Second, the low lipid solubility of morphine provided slow uptake out of the knee joint\textsuperscript{18,19}. Both of these factors reduced the CNS concentration of morphine providing pain relief without the side effects. Additional research done by Khoury et al\textsuperscript{20}, and Joshi et al\textsuperscript{20,21} supported Stein and found intraarticular morphine to significantly reduce pain without any side effects.

Contrasting studies performed by Raja et al\textsuperscript{23}, Ruwe et al\textsuperscript{24}, and Heard et al\textsuperscript{25} contradicted these results, finding no improvement in pain relief with intraarticular morphine. A study by Raja et al\textsuperscript{23}, found morphine to have no significant analgesic effect during the first two hours after surgery, similar to the observations reported by Stein\textsuperscript{18}. However, Raja failed to demonstrate any delayed analgesic effect of morphine. Ruwe et al\textsuperscript{24}, also reported that morphine was not beneficial for postoperative pain, even in combination with other opioids. Finally, Heard et al\textsuperscript{25} failed to find a significant benefit of morphine, even in larger volumes than used by Stein\textsuperscript{18}.

Other research has indicated another opioid, bupivacaine, which may have a positive impact on pain when injected in the knee joint. Bupivacaine is an opioid that has been used to provide local,
surgical anesthesia lasting up to eight hours\textsuperscript{26}. Numerous studies have found it to be safe, staying below toxic levels even with 100 mg injections\textsuperscript{23,25-29}. Bupivacaine also does not damage articular cartilage\textsuperscript{30}. Recently, studies\textsuperscript{20,23,25,31,32} have found bupivacaine to be effective in providing post-operative pain relief when injected into the knee joint. Khoury et al\textsuperscript{20} found that bupivacaine produced immediate, short-term pain relief. Raja et al\textsuperscript{23} also found it to be effective for a short period of time (two hours). Research by Heard et al\textsuperscript{25}, Chirwa et al\textsuperscript{31}, and Smith et al\textsuperscript{32} all reported both short-term and prolonged pain relief through bupivacaine. However, other studies\textsuperscript{2,22,24,26} conflicted with these findings, and failed to show any beneficial effect. Research by Khoury et al\textsuperscript{20}, and Joshi et al\textsuperscript{22} reported conflicting results on the effectiveness of bupivacaine; but both studies compared bupivacaine to morphine and found morphine to be more effective in relieving postoperative pain. Additional research on bupivacaine is needed, but for the purposes of this study; only the effect of morphine on pain relief was investigated.

Postoperative pain relief is an important issue, and the results of past studies are varied. Further research is needed to determine if intraarticular morphine is or is not an effective method of controlling postoperative pain. The purpose of this randomized,
double-blinded study was to compare morphine to a placebo injected into the knee after arthroscopic surgery. This study sought to determine if intraarticular morphine was an effective treatment for postoperative pain and if so, determine the minimal effective dose. The effect of intraarticular morphine on the need for supplemental analgesia (pain pills) was also recorded.
CHAPTER 2
METHODS

Patients
The study protocol was approved by the United Hospital (Grand Forks, ND) institutional research committee, prior to beginning the study (See Appendix A). Seventy-six subjects (fifty males and twenty-six females) between the ages of 15-55 participated in this study. Each patient underwent elective outpatient arthroscopic knee surgery performed by a single surgeon (Dr. Brian T. Briggs) at Grand Forks United Hospital. The surgical procedures included partial menisectomies, plicectomies, and grade(s) 1,2,3 chondromalacia. Patients were excluded from the study for the following reasons: an allergy or sensitivity to morphine, not completing all the necessary questionnaires, or undergoing procedures for grade 4 chondromalacia, lateral retinacular release, or osteochondritis dessicans.

Study Design
Preoperatively, all patients were educated with regard to postoperative pain measurements and the use of the Visual Analogue
Scale (VAS). General anesthesia was used in all cases, and no narcotics were administered intraoperatively. A tourniquet was applied ten minutes before the incision was made, and removed after the procedure, an average of 25-30 minutes later. At the conclusion of the surgery, a double-blinded procedure was used to randomly inject the patient with one of five solutions. A placebo or a solution containing morphine was injected directly into the knee joint. Group 1 (N=15) received an injection of 10 cc's normal saline. Group 2 (N=15) received 10 cc's of normal saline and 0.25 mg morphine. Group 3 (N=14) received 10 cc's of normal saline and 0.50 mg morphine. Group 4 (N=19) received 10 cc's of normal saline and 0.75 mg morphine. Group 5 (N=13) received 10 cc's of normal saline and 1.00 mg morphine. The injections were prepared by a pharmacist, randomized, and were revealed only at the completion of the study. The operating physician, the nursing staff, nor the patient were aware of the dosage.

Pain assessment

Postoperative pain was assessed with a 100-mm Visual Analogue Scale (VAS). Studies have shown the VAS to be simple\textsuperscript{33-36}, reliable\textsuperscript{33,37}, valid\textsuperscript{33-39}, and the most sensitive\textsuperscript{33,36-38} measure of pain. The scale ranged from no pain (0 mm), to excruciating or unbearable pain (100 mm) (Fig. 1). Subjects were asked to place
a vertical line on the scale to mark the pain they were feeling at that moment. VAS scores were recorded at 1, 3, 6, and 24 hours postoperatively. In addition, supplemental analgesia of Darvocet #100 and Tylenol #3 were made available to the patients and their use was documented.

**Statistical analysis**

The VAS score was obtained by measuring the distance in millimeters from zero (no pain) to the mark made by the patient. These measurements were taken by the same person to ensure consistent, reliable results. Comparisons of pain scores from the VAS and the need for supplemental analgesia were made using the Abstat Version 1.8 computer software (Anderson-Bell Corporation, Arvada, Co 80006). A two-way analysis of variance with repeated measures was used to analyze the relationship between morphine and pain. A one-way analysis of variance was used to compare the need for supplemental analgesia and pain.

A $p$ value of $< .05$ was considered to be statistically significant.
Figure 1. 100 mm visual analogue scale.
CHAPTER 3

RESULTS

One hundred patients received intraarticular injections, and seventy-six were included in this study. The other twenty-four patients were excluded due to incomplete questionnaires. There were no significant differences among the groups in regards to gender or type of surgical procedure.

There was a significant decrease in pain (i.e. lower VAS scores) within all groups over the twenty-four hour time period (Table 2) (Figure 2). Scheffe and Tukey post hoc tests found that any time interval $\geq 5$ hours resulted in significant decreases in pain. This held true for all groups regardless of morphine dose or number of pain pills taken. There were no significant differences between any of the five groups at any of the time intervals (1, 3, 6, or 24 hours post-operatively) (Table 2).

The most significant finding of this study was that intraarticular morphine injections did not significantly decrease VAS pain scores. A two-way ANOVA with replications indicated that there were no significant differences in pain between the control group (group 1), and any of the treatment groups (groups 2-5).
TABLE 2
Two Factor (Morphine Dose x Time) Analysis of Variance with Repeated Measures for One Factor (Time)

<table>
<thead>
<tr>
<th>Source</th>
<th>d</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Between Subjects</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine Dose</td>
<td>4</td>
<td>44.756</td>
<td>11.1891</td>
<td>.982</td>
<td>.4228</td>
</tr>
<tr>
<td>Error</td>
<td>71</td>
<td>808.660</td>
<td>11.3896</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Within Subjects</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time$^a$</td>
<td>3</td>
<td>141.419</td>
<td>47.1398</td>
<td>19.0772$^b$</td>
<td>.0000</td>
</tr>
<tr>
<td>Morphine Dose x Time</td>
<td>12</td>
<td>13.900</td>
<td>1.1583</td>
<td>.4688</td>
<td>.9313</td>
</tr>
<tr>
<td>Error</td>
<td>213</td>
<td>526.324</td>
<td>2.4710</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>303</td>
<td>1533.020</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Time of recording VAS score (VAS at 1, 3, 6, 24 hours)

$^b$ Significant at p < .05
Figure 2. Visual analogue scale score (in mm’s) over time for each treatment group; significant at p < .00001.
which had received morphine (Table 2). This table illustrates the variability of VAS results between each group. Figure 3 shows the visual analogue scores for each treatment group. Interestingly, while not significant, the control group (0.0 mg morphine) demonstrated the lowest VAS at 1, 3, 6, and 24 hours.

The presence or absence of morphine also did not have a significant impact on patient's requests for analgesics. Descriptive statistics on the amount of supplemental analgesics taken and the VAS for each treatment group are shown on Table 3. The number of pain pills taken was consistent across all five treatment groups (Figure 4).
Figure 3. Visual analogue scale score (in mm's) for each treatment group at 1, 3, 6, and 24 hours.
<table>
<thead>
<tr>
<th>Group</th>
<th>Amount of Morphine (mg)</th>
<th>0</th>
<th>.25</th>
<th>.5</th>
<th>.75</th>
<th>1.00</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS (mm’s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>2.302</td>
<td>3.010</td>
<td>3.147</td>
<td>2.955</td>
<td>2.314</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0.0 - 7.4</td>
<td>0.1 - 8.5</td>
<td>0.1 - 9.3</td>
<td>0.0 - 8.6</td>
<td>0.0 - 8.3</td>
<td></td>
</tr>
<tr>
<td># Pain Pills</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>2.533</td>
<td>3.333</td>
<td>3.357</td>
<td>3.316</td>
<td>1.538</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0.0 - 5.0</td>
<td>0.0 - 8.0</td>
<td>0.0 - 8.0</td>
<td>0.0 - 8.0</td>
<td>0.0 - 6.0</td>
<td></td>
</tr>
</tbody>
</table>
Figure 4. Average amount of supplemental analgesics taken by each treatment group.
CHAPTER 4

DISCUSSION

The results of this study found that intraarticular injections of morphine had no significant effect on postoperative pain or need for supplemental analgesia. These results support similar findings by Raja et al\textsuperscript{23}, Ruwe et al\textsuperscript{24}, and Heard et al\textsuperscript{25}.

The results were in disagreement with those reported by Stein et al\textsuperscript{18}, Khoury et al\textsuperscript{20}, and Joshi et al\textsuperscript{22}. Stein et al\textsuperscript{18} reported a significant reduction in pain with morphine; however, this effect was only at a single point in time (3 hours after injection). Additionally, Stein and associates\textsuperscript{18} did not report on patients in the control group of their study. The study performed by Khoury et al\textsuperscript{20} did not include a control or placebo group, and the results may have also been biased by the subject size (N=7). Results reported by Joshi et al\textsuperscript{22} were also compiled from a limited number of subjects (N=20).

There are other possible explanations for discrepancies with these studies. Joshi et al\textsuperscript{22} used a significantly higher dose of morphine (5 mg) when compared to the highest dose used in this study (1 mg). It is possible that higher doses of morphine will elicit
the desired analgesic effects. Also, in the study by Stein et al\textsuperscript{18}, patients received a larger volume of intraarticular injection (40 ml). This could have contributed significantly to the absorption of morphine and relief of pain.

This study may also have included other factors which affected the outcome. Pre-surgical pain scores were not obtained in this study. This is important as pain is a combination of both physiological and psychological factors\textsuperscript{37}. In fact, in studies by Ruwe et al\textsuperscript{24} and Henderson et al\textsuperscript{26}, pre-surgical pain scores were found to be the most significant indicator of post-surgical pain.

Another factor which may have affected the outcome was the variable length of tourniquet inflation. Studies by Joshi et al\textsuperscript{40} and Katz et al\textsuperscript{41} have reported that the tourniquet should be inflated a minimum of ten minutes after injection. This facilitates local tissue binding in the knee joint and increases the effect of morphine. In this study, the tourniquet was in place an average of 25-30 minutes total. However, the amount of time it was in place after injection was variable, which may have influenced the results.

This study also used general anesthesia as opposed to regional anesthesia. This could have been an additional factor as research by Heard and associates\textsuperscript{25} found significantly lower (p < .05) VAS scores
in patients who underwent regional anesthesia, regardless of post-operative pain treatments.

Finally, the method of pain interpretation or VAS also had it’s limitations. Numerous authors\textsuperscript{34,36-39,42} have stated that the VAS has two deficiencies; a source of error introduced with measurement of the patient’s slash mark, and the effect of age on validity. Research by Kremer et al\textsuperscript{42} found a significant correlation between the patient’s age and incorrect responses. Another author\textsuperscript{38} stated that the VAS “not be employed as a primary measure of pain intensity in adult clinical populations”. These findings and opinions certainly applied to this study as the patient population age was 15-55. However, I believe the benefits, reliability, and validity of the VAS far outweigh these proposed drawbacks.
The results of this study suggest that morphine injections into the knee joint after arthroscopic surgery do not significantly reduce pain. However, further research is needed. Additional studies are needed to address both the dosage and volume of morphine injections, psychological factors such as preoperative pain scores, tourniquet release time, mode of anesthesia, and alternative opioids such as bupivacaine. Additional research should also be performed following surgical procedures other than arthroscopy, as pain is a prevalent problem. For example, it has been reported that 75% of all TKA’s (total knee arthroplasties) have significant pain despite supplemental analgesics.

Comprehensive, double-blinded studies addressing these variables and areas for research would solidify previous conflicting results and add to the knowledge base. This would be a benefit to physicians, clinicians, and patients alike.
APPENDIX A

Human Subjects Review Form.................................................................24
Information and Consent Form.............................................................28
Postoperative pain is a major complaint of many patients following surgery. According to some studies, the pain is not only severe but is often under medicated. With the increased use of outpatient surgery, such as arthroscopy, the need for an effective analgesic has become more apparent. The greatest demand for analgesics comes during the first 2-4 hours postoperatively. Arthroscopy patients are often released from the hospital within 4-6 hours following surgery.

The use of opioids to control postoperative pain is widespread with few side effects provided the patient is properly attended in the postoperative period. Opioid drugs have been previously administered postoperatively by intramuscular injection, intravenous infusion, and epidural catheters. However, some of these methods of administration do not lend themselves well to the arthroscopy patient who is released from the hospital within a few hours of surgery. In addition, the traditional administration of opioid analgesics causes the drugs to work on the central nervous system which can increase the side effects of the medication.

Recent evidence has shown the presence of opioid receptors in peripheral joints. If that evidence holds true, then peripheral administration of opioid drugs could be used which would block the pain, but may not produce such undesirable central nervous system effects as respiratory depression and sedation. These side effects are particularly unwanted in the patient who is to be released from the hospital within hours after surgery.

There is limited research which has found the use of intraarticular morphine to be useful in controlling pain in post knee arthroscopy patients. Unfortunately the full details of these studies have not been published. Furthermore, the researchers have not established an effective dosage for the medication; and have arbitrarily used either a 0.5 or 1.0 mg. dose of morphine sulfate. Thus the establishment of a minimal effective dosage would be desirable to reduce the side effects.

The purpose of this study is twofold: 1) to determine if intraarticularly administered morphine reduces postoperative pain in comparison to a placebo, and 2) attempt to determine a minimal effective dosage. Because we want to test the evidence from previous studies, and establish a clinical dosage of the medication, the use of human subjects is required.
The purpose of this study is to examine the effects of morphine injected into the knee on postoperative pain in individuals undergoing knee arthroscopy.

Informed Consent

Postoperative pain will be decreased with intraarticular morphine. Tissue effects will be reduced compared to narcotics used systemically.

Participants

Individuals between the ages of 15-60 (male and female), who are not allergic or sensitive to morphine and who have been recommended to undergo knee arthroscopy to help treat their knee condition, will be invited to participate. Refusal by the patient to participate in the study will in no way affect the quality of orthopedic care they receive. Participants will receive no compensation for their participation.

Consent Form

A thorough explanation of the study will be provided by Dr. Briggs prior to surgery, and the patient will be asked to read and sign a consent form (enclosed).

Procedures

All surgeries will be performed at the United Hospital by Dr. Brian T. Briggs, Orthopedic Surgeon. Postoperative assessments will be under the direction of Lori Klabunde, Nurse Practitioner. All patients will be educated about the postoperative pain assessments and the use of the Visual Analogue Scale prior to surgery (enclosed).

Participants will be randomized into one of five groups as follows:

- Intraarticular injection of 10 cc's normal saline
- Intraarticular injection of 10 cc's normal saline + 0.25 mg. morphine
- Intraarticular injection of 10 cc's normal saline + 0.50 mg. morphine
- Intraarticular injection of 10 cc's normal saline + 0.75 mg. morphine
- Intraarticular injection of 10 cc's normal saline + 1.00 mg. morphine

Using a double-blinded system, once arthroscopy is completed, each patient will be injected with one of the above solutions. The patient will be asked to complete the Visual Analogue Scale at 1 hour postoperatively, 2 hours postoperatively, 3 hours postoperatively and 6 hours postoperatively. They will also be sent home with a scale to fill out approximately 24 hours after the surgery. These scales are completed by simply placing a vertical line on a scale to mark the degree of pain they're experiencing. The patient will be given supplemental analgesia as it is required in the form of intramuscular injections and/or oral agents. All supplemental analgesics will be documented and used in the evaluation process.

Morphine is a Schedule II narcotic medication commonly used to relieve pain. When administered intramuscularly, intravenously, or by mouth, the standard recommended dose is between 10-20 mg. every 4-6 hours. Given by the above mentioned routes, morphine acts upon the central nervous system to produce pain relief without loss of sensation or consciousness. Morphine is well accepted by the FDA and has been used for many years.

Potential side effects of morphine include respiratory depression, nausea and vomiting, itching, urinary retention, and a sense of euphoria. An allergic reaction to morphine may also occur in those not aware of a previous allergy.

The medication will be prepared in the United Hospital Pharmacy under the direction of Dr. Bill Reay, Pharmacy Director. All patients will be randomized and sent to surgery prior to each arthroscopy.

Patients will be closely monitored by specially trained nurses postoperatively for side effects. Medications will be available to help with side effects.
If total knee arthroscopies are performed on an outpatient basis, pain is present postoperatively which requires some form of pain medication. Morphine is a very effective medication used to control pain. The side effects of morphine are caused by affect on the central nervous system. By directly injecting morphine into the joint, the central nervous system is not affected and the side effects are reduced. Research has proven that there are special receptors present within the joint that will react to pain medication when injected and, therefore, relieve pain.

Studies have also proven that low dose morphine injected into the joint provides safe, effective pain relief devoid of side effect. Because patients return home so quickly after surgery (often within 4-6 hours), it is imperative that adequate pain control is accomplished, and helpful if this can be done with few side effects.

Risks: (Describe the risks to the subject and precautions that will be taken to minimize them. The concept of risk goes beyond physical risk and includes risks to the subject's dignity and self respect, as well as psychological, emotional, or behavioral risk. If data are collected which could prove harmful or embarrassing to the subject if associated with him or her, then describe the methods to be used to insure the confidentiality of data obtained, including plans for final disposition or destruction, debriefing procedures, etc.)

The potential side effects of morphine are well-documented when it is given by traditional routes. These include respiratory depression, nausea and vomiting, itching, somnolence, and an allergic reaction.

Each patient is closely monitored by specially trained professionals after surgery. Vital signs are measured every 15-30 minutes and each patient is carefully assessed for any complications. Medications may be given to help control side effects.

All patient files and hospital records will be kept confidential. Once completed, files containing study information will be kept in a confidential file by Lori Klabunde at the Grand Forks Clinic.
A copy of the CONSENT FORM to be signed by the subject (if applicable) and/or any statement to be read to the subject should be attached to this form. If no CONSENT FORM is to be used, document the procedures to be used to assure that infringement upon the subject's rights will not occur.

Describe where signed consent forms will be kept and for what period of time.

For FULL review forward a signed original and 12 copies of this completed form and, where applicable, 12 copies of the proposed consent form, questionnaires, etc., and any supporting documentation to:

Eleanor Tuell
1000 South Columbia Road
Grand Forks, ND 58201

For EXEMPT or EXPEDITED REVIEW forward a signed original and a copy of the consent form, questionnaires, etc., and any supporting documentation to the address above.

The policies and procedures on Use of Human Subjects in Medical Park Institutions apply to all activities involving use of human subjects performed by personnel conducting such activities. No activities are to be initiated without prior review and approval of the Medical Park Institutional Review Committee.

SIGNED:

__________________________________________  DATE: _____________
Principal Investigator

__________________________________________  DATE: _____________
Project Director

__________________________________________  DATE: _____________
Student Adviser (where applicable)
INFORMATION AND CONSENT FORM

The Effect of Intra-articular Morphine on Post-arthroscopy Pain

You are being invited to participate in a study being conducted by Dr. Brian Briggs and his staff regarding the use of morphine to control postoperative pain. One goal of this study is to determine if an injection of morphine directly into the knee joint following your arthroscopic surgery will affect the amount of postoperative pain you experience. The other goal is to determine a proper dosage for the morphine injection. Only subjects who were normal and healthy prior to their knee problem will be included in this study.

Prior to your surgery you will be given instructions on the pain testing procedures that will be done after surgery. For the testing, you will be asked to rate your pain on a scale which varies from a response of "no pain" to "unbearable pain". In addition an examiner will ask you to bend your knee, and then that examiner will measure the distance you moved your knee. These same measurements will be conducted at 1, 3 and 6 hours after your surgery. In addition, you will be asked to fill out a short questionnaire after 24 hours at home. You will be instructed on how to fill out the questionnaire.

As a participant in this study you will be randomly assigned to one of five (5) treatment groups. Four of those groups will be given different dosage levels of morphine, and the other group will be given a placebo injection. It is not clear at the present time which of the treatment programs would be better for you. For this reason, the treatment plan which is offered to will be based upon a method of randomization. Randomization means selection of a treatment by chance. This is predetermined by the doctor's staff, and selection of treatment for each patient is done in a sequential manner. This is equivalent to flipping a coin to select one of two treatments.

The actual testing procedure will only take approximately 5 to 10 minutes of your time. The testing procedure should not cause you any discomfort or inconvenience over and above the standard post-operative procedures.

As with the administration of any medication, there are some risks involved with the administration of morphine. Although the dosages of the drug used are well within normal clinical guidelines, the use of morphine does carry some risk. Because morphine is used on a routine basis, we do not anticipate any problems. However, potential risks may include respiratory depression (i.e. difficulty breathing), allergic reaction, nausea, vomiting, itching and drowsiness. While you are in the hospital following your surgery, you will be under the direct care of the hospital physician and nursing staff to monitor your progress and intervene should you experience any problems.

The benefits to you as a participant include enhanced control of post-operative pain without the standard repeated drug injections which can increase the side effects of the pain medication. A more effective means of controlling pain will ultimately lead to decreased post-operative pain, better joint movement and less weakness.
Any information that is obtained in connection with the study and that can be identified with you will remain confidential and will be disclosed only with your permission. The data collected will be identified by a number known only by the investigators. You will not be assessed any additional cost as a study participant.

Your decision whether or not to participate in this study will not prejudice your future relationship with your doctor or with the United Hospital staff. If you decide to participate, you are free to discontinue participation at any time without prejudice.

The investigators involved are available to answer any questions you have concerning this program. In addition, you are encouraged to ask any questions concerning this program that you may have in the future. Questions may be asked by calling Lori Klabunde at 780-6112. A copy of this consent is available to participants in this study.

In the event that this research activity results in a physical injury, and the project is being conducted in a health care facility, medical treatment will be available, including first aid, emergency treatment, and follow up care as needed. Payment for any such treatment must be provided by you and your third party payor, if any.

"ALL OF MY QUESTIONS HAVE BEEN ANSWERED AND I AM ENCOURAGED TO ASK ANY QUESTIONS THAT I MAY HAVE CONCERNING THIS STUDY IN THE FUTURE."

I have read all of the above and willingly agree to participate in this study explained to me by _____________________________.

________________________

Patient's Signature Date Parent or Legal Guardian's Date

Signature

________________________

Witness (not the investigator) Date

I have explained fully to the patient the above objective of this study, what is to be expected, and the possible complications.

________________________

Counseling Physician's Signature Date
REFERENCES


