

A RANDOMIZED EVALUATION

THE EFFECT OF SEDATION ON DIAGNOSTIC VALIDITY OF FACET JOINT NERVE BLOCKS: AN EVALUATION TO ASSESS SIMILARITIES IN POPULATION WITH INVOLVEMENT IN CERVICAL AND LUMBAR REGIONS (ISRCTNo:76376497)

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Background: Zygapophysial or facet joint pain in patients suffering with chronic spinal pain without disc herniation or radiculopathy may be diagnosed with certainty by the use of controlled diagnostic blocks. But, in patients suffering with either lumbar or cervical facet joint pain, even this diagnostic approach may be confounded by false-positives when using a single diagnostic block. It may also be confounded by the administration of anxiolytics and narcotics prior to, or during, the controlled diagnostic facet joint blocks. The effect of sedation on the validity and potential differential results in patients suffering with combined cervical and lumbar facet joint pain has not been evaluated.

Objective: To assess the effects of midazolam and fentanyl on the diagnostic validity of facet joint blocks in patients suffering with both cervical and lumbar facet joint pain.

Study Design: Randomized, double-

blind, placebo-controlled study.

Methods: The design consisted of a placebo group receiving a sodium chloride solution and two experimental groups receiving either midazolam or fentanyl. Patients included in the study had been diagnosed with facet joint pain using controlled comparative local anesthetic blocks of the medial branches and L5 dorsal rami. They had been treated with lumbar and cervical facet joint nerve blocks and experienced good pain relief; and were presenting for repeat treatment after a period of symptom relief.

The study was performed in an interventional pain management practice in the United States; a total of 60 patients participated with 20 patients randomly allocated into each group. Outcome measures included numeric pain scores, proportion of pain relief, and ability to perform prior painful movements.

Outcome Measures: Outcomes were assessed at baseline and after the adminis-

tration of 1 of the 3 solutions (Group I, sodium chloride solution; Group II, midazolam; or Group III, fentanyl).

Results: Overall, 50% of the patients were relaxed or sedated in the placebo group, while 100% of the patients in the midazolam and fentanyl groups were relaxed or sedated. As many as 10% of the patients reported significant relief ($\geq 80\%$) with the ability to perform prior painful movements.

Conclusions: Perioperative administration of sodium chloride, midazolam, or fentanyl can confound results in the diagnosis of combined cervical and lumbar facet joint pain. False-positive results with placebo or sedation may be seen in a small proportion of patients.

Key Words: Spinal pain, facet joint pain, controlled comparative local anesthetic blocks, false-positives, confounding factors, analgesia

Based on the present literature, two separate controlled, diagnostic blocks – local anesthetic or placebo-controlled blocks – are the only means of confirming the diagnosis of zygapophysial or facet joint pain in the spine (1-28). However, a significant proportion of patients (22% to

63%) may present with false-positive results (5,9,18-30). Further, despite the well-established validity of facet or zygapophysial joint blocks, multiple other confounding factors (psychological and sedation) may affect the diagnostic results (31-33).

Two randomized trials (32,33) (ISRCTN23482653 and ISRCTN52746887) have evaluated the role of the administration of anxiolytics and narcotics with results differing in the cervical and lumbar spine. An evaluation of the effect of sedation as a confounding factor in the diagnostic validity of lumbar facet joint pain (32) concluded that employing strict criteria – including significant pain relief of at least 50% with the ability to perform prior painful movements – as the standard for evaluating the effect of controlled local anesthetic blocks, would preserve the diagnostic validity of lumbar facet joint

nerve blocks. However, in a study of the effect of sedation on the diagnostic validity of cervical facet joint blocks for the diagnosis of cervical facet joint pain (33), it was concluded that the diagnostic validity of cervical facet joint nerve blocks may be preserved if 80% or more pain relief with the ability to perform prior painful movements is used as the standard for evaluating the effect of controlled local anesthetic blocks. Thus, there were differences observed in patients suffering with lumbar facet joint pain as compared to cervical facet joint pain.

In the United States, facet joint interventions are one of the most commonly performed interventional pain management procedures, ranking just behind epidural steroid injections (34). If the validity of diagnostic blocks is compromised, it may lead to substantial waste and unne-

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essary treatment in managing spinal pain (32-35). Further, combined pain problems are commonly seen in spinal pain syndromes in general and in interventional pain management settings in particular (36,37). Consequently, it is essential to have knowledge of the influence of confounding factors in patients suffering with a combined problem of chronic neck and low back pain secondary to facet joint involvement.

This study sought to evaluate the effect of placebo, midazolam, or fentanyl on the validity of diagnosis of lumbar and facet joint pain in patients with combined neck and low back pain of facet joint origin. Those patients included were proven to have a combination of lumbar and cervical facet joint pain as demonstrated by fluoroscopically-directed, controlled, comparative local anesthetic blocks of medial branches and L5 dorsal rami. Their response was good to therapeutic measures involving facet joint nerve blocks, and they were returning for a repeat treatment after a significant period of symptom relief.

METHODS

The protocol was approved by the institutional review board (IRB) of the ambulatory surgery center and interventional pain management practice (a private practice specialty referral center in the United States) where the study was conducted. The design consisted of a control group (Group I) receiving sodium chloride solution, Group II receiving midazolam, and Group III receiving fentanyl.

Informed Consent

All patients were provided with an informed consent document approved by the IRB for this study. The informed consent document described the details of the trial, inclusion, and exclusion criteria. Patients for the study were identified and recruited from the existing patients of the interventional pain management practice. All patients had a proven diagnosis of combined lumbar and cervical facet joint pain as determined by the use of controlled comparative local anesthetic blocks of medial branches and L5 dorsal rami. In the past, patients had been treated with therapeutic cervical and lumbar facet joint nerve blocks and were presenting for repeat treatment after a significant period of symptom relief. Consequently, patients were participating in the study

prior to undergoing facet joint nerve blocks. They all understood the nature of the study, and that they would receive either a placebo or one of two drugs provided for sedation. Patients also understood that their participation in the study would not affect the type or amount of sedation provided during the actual facet joint nerve blocks in the operating room.

Inclusion Criteria

Patients included were between the ages of 18 and 90 years, had a history of chronic neck and low back pain of at least two year's duration, and had confirmed evidence of facet joint pain in the neck and low back by the use of controlled, comparative, local anesthetic blocks and therapeutic medial branch blocks. Further, the patients included demonstrated ability to understand the investigation, were cooperative with the investigational procedures, and were willing to participate in the clinical trial.

Exclusion Criteria

Excluded from the trial were patients without confirmed facet joint pain either in neck or low back. Even though they had neck and low back pain, patients excluded from the study were those with uncontrolled major depression or other psychiatric disorders, pregnant or lactating women, patients with multiple complaints involving other problems with overlapping pain complaints, patients unable to understand the informed consent and protocol, those with a history of adverse reaction to either midazolam or fentanyl, or those unwilling to participate in the study.

Evaluation

Evaluation of all the patients included in the study consisted of the following: 1) demographic data; 2) routine physical and medical evaluation; 3) confirmed evidence of cervical and lumbar facet joint pain by controlled comparative local anesthetic blocks of medial branches or L5 dorsal rami; 4) significant symptom relief following facet joint nerve blocks in both cervical and lumbar spine, and necessity for repeat treatment; 5) pain assessment by numeric pain scores; and 6) identification of painful movements.

Study Design and Investigation

The study was the holding area of the ambulatory surgery center where registered nurses experienced in the evalua-

tion, administration, and monitoring of sedatives and narcotics conducted the initial portion of the study. Patients agreeing to participate in the study were brought to the holding area of the surgery center where they signed the IRB-approved consent. Patients were allocated into one of the three groups based on a computer generated randomization scheme.

Identical preparation was provided to patients in the three groups. All patients were administered identical volumes of drugs via unlabeled syringes.

All patients rated their lumbar and cervical spine pain separately based on a numeric pain rating scale of 0 to 10, with a score of 0 being no pain and 10 being the worst possible pain. The evaluation also identified painful movements both in the neck and the low back. Based on randomization, over a period of 5-10 minutes, each patient received one of the three solutions in incremental doses of 1 ml with a maximum of 5 ml of NAACL in Group I, 1 mg of midazolam per ml (5 mg per 5 ml) in Group II, or 50 mcg of fentanyl per ml (250 mcg per 5 ml) in Group III. Patients and the investigator(s) were blinded to the randomized allocation as well as to the solution administered.

The solutions were administered slowly in increments of 1 ml while simultaneously judging the patient's response. The response was evaluated with assessment of relaxation and drowsiness over a period of 5 to 20 minutes after the initiation of each solution's administration. Once the patient was found to be relaxed or drowsy, further administration of the solution was stopped. The maximum solution administered in each group was 5 ml. After patients experienced either relaxation or drowsiness, or after a waiting period following administration of maximum dosage of the solution, an assessment of pain was conducted. Patients were asked to rate their current pain on a numeric pain score. Subsequently, patients were also assessed for their ability to perform painful movements and all results were appropriately documented. After completion of the evaluation, unblinding was carried out and the amount of sedation administered to each patient in Group II and Group III was noted on the record.

Outcomes Assessment

Assessments of pain and ability to perform painful movements were per-

formed at baseline prior to, and after, administration of the solution. Multiple parameters included numeric pain scores, proportion of pain relief, and ability to perform prior painful movements.

Statistical Methods

Chi-squared test was used to evaluate the differences in proportions. One-way analysis of variance was used for comparison of means between groups. The least significant difference (LSD) pair-wise multiple comparison test was used to test the difference between means. A paired t test was used to compare pre- and post-treatment results for individual patients within the group. Results were considered statistically significant if the P value was less than 0.05.

RESULTS

The study was performed over a period of six months extending from May 2004 through October 2004. From a sample of 76 eligible patients, 60 patients were randomized and 20 patients assigned to each group. Sixteen patients were excluded for various reasons.

Demographic Characteristics

As illustrated in Table 1, no significant differences were noted between the groups with regards to gender, age, height,

weight, and post surgery status.

Study Characteristics

Characteristics of the administration of drugs and their effects are illustrated in Table 2. There were no differences noted in the times required for relaxation following administration of sedatives. However, the amount of solution or drug dosage in ml was significantly less in Group II and Group III as compared to Group I, with no difference noted between groups II and III. Relaxation status was significantly different in Group II and Group III as compared to Group I (100% vs 50%).

Pain Relief

Table 3 illustrates pre- and post-injection comparisons of pain status by numeric pain scores, relaxation status, and ability to perform movements painful prior to injection of solution. Baseline pain scores were similar in all three groups and in both regions. Post-study follow-up pain scores were also similar. Pre-study and post-study changes in pain scores were significantly different in all three groups.

Combined pain relief of ≥ 80% and relaxation status, plus the ability following injection to perform movements that were painful prior to the injection of solution, was seen in the same number of pa-

tients presenting with ≥ 80% pain relief, regardless of group.

Complications

There were no adverse events or complications noted during the study.

DISCUSSION

In this randomized, placebo-controlled, double-blind evaluation, 50% to 100% of the patients reported relaxation, and as many as 10% of the patients experienced significant pain relief (80% or greater) and were able to perform movements that were painful prior to the administration of intravenous sodium chloride, midazolam, or fentanyl. There were no significant differences noted either among the groups or between regions (cervical vs. lumbar). Significant differences were noted only with regards to relaxation status, with 50% reported in Group I, and 100% in groups II and III. Thus, overall this study showed no significant differences in any of the groups between pain relief or the ability to perform painful movements and the type of sedation.

The results of this study once again confirm that some patients may obtain relaxation and pain relief with the ability to perform prior painful movements with placebo, midazolam, or fentanyl. Consequently, placebo, midazolam, or fentanyl occasionally may produce false-positive results and may dilute the diagnostic value of controlled, comparative, local anesthetic blocks. This may also apply to placebo-controlled blocks.

Conclusion

This placebo-controlled, double-blind evaluation showed that the administration of sedation with midazolam or fentanyl could be a confounding factor in the diagnosis of facet joint pain in the neck or low back in a small proportion of patients with a combination of chronic low back and neck pain. This study also showed that an intravenous sedative dose of fentanyl or midazolam is no more likely to cause a small proportion of patients to report false-positive pain relief with active motion testing than does a placebo.

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Table 1. Demographic Characteristics

		Group I	Group II	Group III
Gender	Male	35% (7)	35% (7)	25% (5)
	Female	65% (13)	65% (13)	75% (15)
Age (yrs)	Range	29 – 73	25 – 61	27 – 68
	Mean ± SD	50 ± 11.6	43 ± 10.6	46 ± 10.6
Height (inches)	Mean ± SD	67 ± 4.4	66 ± 3.4	65 ± 3.5
Weight (lbs)	Mean ± SD	199 ± 49.7	192 ± 53.5	173 ± 45.8
Post Surgery	Cervical	10% (2)	20% (4)	15% (3)
	Lumbar	35% (7)	20% (4)	25% (5)

Table 2. Characteristics of administration of drugs and their effect

		Group I	Group II	Group III	P Value
Time required for relaxation (in minutes)	Mean ± SD	9.0 ± 3.4	8.9 ± 2.8	9.5 ± 2.6	0.789
	Range	5 – 20	4 – 13	5 – 13	
Amount of solution or drug dosage (in ml)	1 ml	5% (1)	-	-	-
	2 ml	10% (2)	25% (5)	15% (3)	
	3 ml	10% (2)	30% (6)	50% (10)	
	4 ml	10% (2)	20% (4)	15% (3)	
	5 ml	65% (13)	25% (5)	20% (4)	
	Mean ± SD	4.2 ± 13	3.5* ± 1.2	3.4* ± 1.0	0.055
Relaxed Patients		50% (10)	100%* (20)	100%* (20)	0.000

* Indicates significant difference with Group I (Numbers in parentheses are actual patient numbers)

Table 3. Comparison of pain status by numeric pain scores, relaxation status, and, following the injection, the ability to perform movements that were painful prior to the injection of solution.

Numeric Pain Score	Group I		Group II		Group III	
	Cervical	Lumbar	Cervical	Lumbar	Cervical	Lumbar
Baseline pain score (Mean ± SD)	7.3 ± 1.6	7.8 ± 1.5	7.8 ± 2.0	7.9 ± 1.8	7.8 ± 1.9	8.2 ± 1.8
Post-study follow-up (Mean ± SD)	6.3 ± 2.1	6.7 ± 1.6	6.1 ± 2.9	6.8 ± 2.3	5.7 ± 3.0	6.9 ± 2.4
Change in pain status (Mean ± SD)	1.0* ± 1.4	1.1* ± 1.8	1.7* ± 2.4	1.1* ± 1.6	2.1* ± 2.4	1.3* ± 1.9
Relaxed patients	50% (10)	50% (10)	100% (20)	100% (20)	100% (20)	100% (20)
Pain relief of ≥ 50%	5% (1)	5% (1)	15% (3)	5% (1)	15% (3)	10% (2)
Pain relief of ≥ 80%	5% (1)	5% (1)	10% (2)	5% (1)	10% (2)	0%
Significant pain relief with relaxation	5% (1)	5% (1)	15% (3)	5% (1)	15% (3)	10% (2)
Ability to perform painful movements	5% (1)	5% (1)	15% (3)	5% (1)	15% (3)	10% (2)
Pain relief of ≥ 50% and ability to perform painful movements	5% (1)	5% (1)	15% (3)	5% (1)	15% (3)	10% (2)
Pain relief of ≥ 80% and ability to perform painful movements	5% (1)	5% (1)	10% (2)	5% (1)	10% (2)	0%

*Indicates significant difference between pre- and post-study follow-up. (Numbers in parentheses are actual patient numbers)

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