



## Original article

# Immediate postoperative pain level from lumbar arthrodesis following epidural infiltration of morphine sulfate<sup>☆</sup>



Carlos Alexandre Botelho do Amaral\*, Tertuliano Vieira, Edgar Taira Nakagawa, Eduardo Aires Losch, Pedro José Labronici

Prof. Dr. Donato D'Ângelo Orthopedics and Traumatology Service, Hospital Santa Teresa, Petrópolis, RJ, Brazil

## ARTICLE INFO

## Article history:

Received 15 December 2013

Accepted 24 February 2014

Available online 19 February 2015

## Keywords:

Morphine

Epidural analgesia

Postoperative pain

Arthrodesis

Vertebral fusion

## ABSTRACT

**Objective:** To evaluate the pain level in patients treated with epidural infusion of morphine sulfate in a single dose, after a surgical procedure to perform lumbar arthrodesis.

**Methods:** Forty patients underwent posterolateral lumbar arthrodesis or intersomatic lumbar arthrodesis via a posterior route at one, two or three levels. They were prospectively randomized into two groups of 20. In the first group (study group), 2 mg of morphine sulfate diluted in 10 mL of physiological serum was infiltrated into the epidural space, through the laminectomy area. The second group (controls) did not receive analgesia. The patients were asked about their pain levels before and after the operation, using a visual analog scale (VAS).

**Results:** It was found that the patients presented a significant diminution of pain as shown by the VAS. From before to after the operation, it decreased by an average of 4.7 points ( $p=0.0001$ ), which corresponded to 53.2% ( $p=0.0001$ ).

**Conclusion:** Application of 2 mg of morphine sulfate in a single epidural dose was shown to be a good technique for pain therapy following lumbar spinal surgery.

© 2015 Sociedade Brasileira de Ortopedia e Traumatologia. Published by Elsevier Editora Ltda. All rights reserved.

## Nível de dor no pós-operatório imediato de artrodese lombar após infiltração epidural com sulfato de morfina

## RESUMO

**Objetivo:** avaliar o nível de dor em pacientes tratados com infusão epidural de sulfato de morfina em Dose única, após procedimento cirúrgico de artrodese lombar.

**Métodos:** Foram submetidos à artrodese lombar posterolateral ou artrodese lombar intersomática por via posterior, em um, dois ou três níveis, 40 pacientes, divididos, prospectivos

## Palavras-chave:

Morfina

Analgesia epidural

Dor pós-operatória

<sup>☆</sup> Work developed at the Prof. Dr. Donato D'Ângelo Orthopedics and Traumatology Service, Hospital Santa Teresa, and in the Petrópolis School of Medicine, Petrópolis, RJ, Brazil.

\* Corresponding author.

E-mail: [carlosaba@oi.com.br](mailto:carlosaba@oi.com.br) (C.A.B. Amaral).

<http://dx.doi.org/10.1016/j.rboe.2015.02.005>

2255-4971/© 2015 Sociedade Brasileira de Ortopedia e Traumatologia. Published by Elsevier Editora Ltda. All rights reserved.

Artrodese  
Fusão vertebral

e randomizados em dois grupos de 20. No primeiro grupo (de estudo) foram infiltrados no espaço epidural, através da área da laminectomia, 2 mg de sulfato de morfina diluídos em 10 mL de soro fisiológico. O segundo grupo (controle) não recebeu analgesia. Os pacientes foram interrogados quanto ao nível de dor, no pré e pós-operatório, com o uso da escala visual analógica (EVA).

**Resultados:** Verificou-se que os pacientes apresentaram uma queda significativa da dor pela EVA. A dor entre o pré e o pós-operatório diminuiu em média 4,7 pontos ( $p=0,0001$ ), o que corresponde a 53,2% ( $p=0,0001$ ).

**Conclusão:** Aplicação de 2 mg de sulfato de morfina, em dose única epidural, demonstrou ser uma boa técnica na terapia da dor após cirurgia na coluna lombar.

© 2015 Sociedade Brasileira de Ortopedia e Traumatologia. Publicado por Elsevier Editora Ltda. Todos os direitos reservados.

## Introduction

Despite advances in the treatments for postoperative pain, a large number of patients still suffer after spinal surgery. Most of these surgical procedures cause intense pain during the immediate postoperative period, and this may last for at least three days.<sup>1-5</sup> This pain may increase morbidity and the incidence of complications, along with delaying rehabilitation. Furthermore, postoperative pain is a risk factor, given that it may give rise to development of chronic pain syndromes.<sup>6</sup>

Safe and efficient methods for postoperative analgesia are therefore essential following vertebral arthrodesis procedures. Parenterally administered opioids are most frequently indicated for analgesia among patients who have undergone lumbar arthrodesis by means of a posterior route.<sup>7</sup> Epidural analgesia has been used in some procedures in the lumbar spine, such as vertebral arthrodesis, laminectomy, discectomy, hemilaminectomy and foraminectomy.<sup>8-10</sup> However, administration of opioids intravenously or intramuscularly is generally done at doses that may cause side effects, such as respiratory depression, nausea, vomiting, sedation, urine retention, pruritus and paralytic ileus.<sup>7</sup> Other possible causes of pain may include the patient's positioning over the perioperative period; prolonged anesthesia; long posterior surgical incisions, which give rise to discomfort in the postoperative position of dorsal decubitus; large detachment of the paravertebral musculature, which is necessary for surgical access; and long periods of use of surgical retractors.<sup>7</sup> Since the dural sac is dissected during this procedure, morphine can easily and safely be injected into the epidural region, by the surgeon during the procedure.<sup>8,10-16</sup>

This randomized prospective study had the objectives of comparing patients who underwent posterior arthrodesis of the lumbar spine with untreated patients and ascertaining the efficacy of a single dose of epidural morphine sulfate during the immediate postoperative period.

## Methods

Between June 2008 and January 2010, 40 patients who underwent intersomatic lumbar arthrodesis via a posterior route in one, two or three levels were evaluated. These patients, who had diagnoses of degenerative disk disease or stenosis of

the lumbar spinal canal, were operated under general anesthesia at Hospital Santa Teresa, Petrópolis. Approval for this study was obtained from the institution's ethics committee and informed consent was obtained from all the patients. Patients were excluded if they presented the following criteria: ASA > III, allergy or intolerance to morphine, pregnancy, previous opioid use, preoperative pain other than in the lumbar spine or previous lumbar spine surgery. After the surgical procedure, patients in Group 1 (study group) underwent in situ epidural infiltration through the laminectomy area, consisting of 2 mg of morphine sulfate diluted in 10 mL of 0.9% physiological serum. Group 2 (controls) did not undergo infiltration. Both groups were evaluated regarding pain levels 24 h before the surgical procedure and 18–24 h after the surgery, by means of a visual analog scale (VAS). This scale formed an instrument for measuring the evolution of the pain levels (Table 1).

## Statistical methodology

The data observed were analyzed descriptively and presented in the form of a table showing frequencies ( $n$ ) and percentages (%) for the categorical data and the mean  $\pm$  standard deviation and medians for the numerical data.

The statistical analysis was composed of the following methods:

- To ascertain whether there were any significant differences in the numerical variables between the two groups (study and control), Student's  $t$  test for independent samples or the Mann-Whitney test was used for nonparametric variables, and the Chi-square test ( $\chi^2$ ) was used for comparing categorical data (qualitative variables).
- To analyze the change in the pain scale from before to after the operation, the Wilcoxon signed rank test was used (nonparametric variables).

Nonparametric methods were used because some variables (pain scale and deltas) did not present normal distribution (Gaussian distribution), because of the dispersion of the data and rejection of the hypothesis of normality according to the Kolmogorov-Smirnov test. The criterion adopted for determining significance was the 5% level. The statistical analysis was processed by means of the SAS® System

**Table 1 – General description of the baseline numerical variables.**

Variable	Study group (n = 20)	Control group (n = 20)
Female sex, n (%)	12 (60.0%)	11 (55.0%)
Male sex, n (%)	8 (40.0%)	9 (45.0%)
Disk hernia, n (%)	10 (50.0%)	11 (55.0%)
Vertebral canal stenosis, n (%)	10 (50.0%)	9 (45%)
Age (years)	52.1 ± 11.2	51.1 ± 13.7

Source: Hospital Santa Teresa, Petrópolis, RJ.

statistical software, version 6.11 (SAS Institute, Inc., Cary, North Carolina, USA).

## Results

The first objective was to ascertain whether there was any significant difference in the baseline variables between the two groups (study and control).

Table 2 presents the frequencies (n) and percentages (%) relating to sex and pathological condition, and the mean ± standard deviation relating to age and the corresponding descriptive level (p-value) of the statistical test. The statistical analysis was composed of the  $\chi^2$  test for categorical data (sex and pathological condition) and Student's t test for independent samples (age).

It was observed that there were no significant differences in the baseline variables between the two groups, at the 5% level.

The second objective was to ascertain whether there was any significant change on the pain scale from before to after the operation. Tables 3 and 4 present the means, standard deviations (SD) and medians on the pain scale before and after the operation, the corresponding absolute delta (points) and relative delta (%) and the descriptive level (p value) of the Wilcoxon test, separately for the study group (in situ infiltration with morphine sulfate) and control group, respectively.

The absolute delta of the pain scale from before to after the treatment was given by the formula:

$$\text{Delta(points)} = (\text{preoperative pain} - \text{postoperative pain})$$

**Table 2 – Baseline variables according to the group.**

Variable	Study (n = 20)	Control (n = 20)	p Value <sup>a</sup>
Female sex, n (%)	12 (60%)	11 (55%)	0.74
Pathological condition of disk hernia, n (%)	10 (50%)	11 (55%)	0.75
Age (years)	52.1 ± 11.2	51.1 ± 13.7	0.79

Source: Hospital Santa Teresa, Petrópolis, RJ.

The pathological condition of disk hernia was compared with stenosis of the vertebral canal (arthrosis).

<sup>a</sup> Descriptive level of the  $\chi^2$  or Mann-Whitney test.

**Table 3 – Preoperative and postoperative pain scales in the study group (n = 20).**

Variable	Mean	SD	Median	p Value <sup>a</sup>
Preoperative pain scale (points)	8.8	0.9	9	
Postoperative pain scale (points)	4.1	1.4	4	
Absolute delta (points)	-4.7	1.6	-4	0.0001
Relative delta (%)	-53.2	15.6	-50.0	0.0001

Source: Hospital Santa Teresa, Petrópolis, RJ.

SD, standard deviation.

<sup>a</sup> Wilcoxon signed rank test.

The relative delta of the pain scale from before to after the treatment was given by the formula:

$$\text{Delta(points)} = (\text{preoperative pain} - \text{postoperative pain}) / \text{preoperative pain} \times 100$$

It was found that in the study group, there was a significant decline on the pain scale after the operation, comprising a mean of 4.7 points ( $p = 0.0001$ ), which corresponded to 53.2% ( $p = 0.0001$ ).

It was found that in the control group, there was a significant decline on the pain scale after the operation, comprising a mean of 2.7 points ( $p = 0.0001$ ), which corresponded to 28.8% ( $p = 0.0001$ ).

The third objective was to ascertain whether there was any significant difference on the pain scale and in the respective deltas (absolute and relative) between the study and control groups.

Table 5 presents the means, standard deviations (SD) and medians of the pain scale and the respective deltas (absolute and relative) according to the group (study or control) and the corresponding descriptive level (p value) of the Mann-Whitney test.

It was found that the postoperative declines for the study group were significantly greater than those of the control group; such a relative decline was approximately twice as much, with regard to the pain scale ( $p = 0.0001$ ), absolute delta ( $p = 0.0001$ ) and relative delta ( $p = 0.0001$ ).

There was no significant difference between the two groups on the pain scale before the operation, at the 5% level ( $p = 0.086$ ).

**Table 4 – Preoperative and postoperative pain scales in the control group (n = 20).**

Variable	Mean	SD	Median	p Value <sup>a</sup>
Preoperative pain scale (points)	9.3	0.7	9	
Postoperative pain scale (points)	6.6	1.2	7	
Absolute delta (points)	-2.7	0.9	-2.8	0.0001
Relative delta (%)	-28.8	9.7	-29.7	0.0001

Source: Hospital Santa Teresa, Petrópolis, RJ.

SD, standard deviation.

<sup>a</sup> Wilcoxon signed rank test.

**Table 5 – Pain scale and respective deltas according to the groups.**

Variable	Study (n=20)		Control (n=20)		p Value <sup>a</sup>
	Mean ± SD	Median	Mean ± SD	Median	
Preoperative pain scale (points)	8.8 ± 0.9	9	9.3 ± 0.7	9	0.086
Postoperative pain scale (points)	4.1 ± 1.4	4	6.6 ± 1.2	7	0.0001
Absolute delta (points)	-4.7 ± 1.6	-4.0	-2.7 ± 0.90	-2.8	0.0001
Relative delta (%)	-53.2 ± 15.6	-50	-28.8 ± 9.7	-29.7	0.0001

Source: Hospital Santa Teresa, Petrópolis, RJ.

SD, standard deviation.

<sup>a</sup> Descriptive level of the Mann-Whitney test.

## Discussion

Perioperative analgesia remains a great challenge for surgeons, in treating patients through complex spinal surgery.<sup>17</sup> Since the discovery of opioid receptors in the spinal cord in 1970, many studies have proven the efficacy of epidural morphine.<sup>18-20</sup> Surgery on the posterior region of the spine may lead to intense postoperative pain because of the extensive dissection of soft tissues and the detachment of the paravertebral musculature to obtain adequate exposure of the lamina, facets and transverse processes.<sup>17,21-23</sup>

O'Neill et al.<sup>8</sup> observed that there was a significant reduction in the need for additional analgesic among patients who underwent lumbar spinal procedures after 1 mg of epidural morphine had been administered. However, these authors warned about side effects. Blacklock et al.<sup>12</sup> studied five patients who underwent lumbar surgery after receiving 1 mg of morphine epidurally, in comparison with a control group. Although the authors observed that there was superior analgesia in the study group over the first 24 h, they reported that there was a rebound effect with intense pain, such that treatment with opioids was required between two and five days after the operation. The authors concluded that the pain might have been triggered by early movement of the patient or through reduction in endorphin production. France et al.<sup>13</sup> used a mean epidural morphine dose of 0.91 mg (range: 0.4-1.2 mg). The patients had a high level of analgesia over the first 24 h after the surgery, with significantly lower use of analgesics than what was observed in the placebo group. They also reported that there was a rebound effect after the second postoperative day. Urban et al.<sup>15</sup> analyzed the use of two morphine doses (0.7 and 1.4 mg) in comparison with a control group that did not receive epidural infiltration. Both groups presented superior analgesia in relation to the control group. These authors concluded that the best results were obtained among patients treated with high doses of morphine (1.4 mg).

Techanivate et al.<sup>16</sup> conducted a placebo-controlled randomized prospective study involving 40 patients who underwent lumbar laminectomy and fusion. They observed that the group treated with morphine presented significantly lower pain over the first 48 h after the operation, according to the VAS scoring, than what was observed in the placebo group.

Wu et al.<sup>24</sup> demonstrated that low morphine doses (1 mg) administered epidurally were sufficient for controlling the pain after decompression surgery and posterior fusion of the short segment of the spine. These authors observed that low

doses resulted in fewer side effects than were seen with intravenous injection of analgesia controlled by the patient, or with injection of meperidine.

Our study demonstrated that the two groups did not present any significant difference ( $p=0.086$ ) in relation to preoperative pain, according to the VAS scoring. This indicates that the patients in the two groups had similar intensities of pain. However, after the study group had been treated with an application of 2 mg of morphine sulfate in the peridural region, it was seen after the end of the surgical procedure that the pain level in this group was significantly lower, according to the VAS scoring. From before to after the operation, the pain level decreased by a mean of 4.7 points ( $p=0.0001$ ), corresponding to 53.2% ( $p=0.0001$ ), in the study. As shown by the results, both groups presented significant declines in pain after the treatment, but in a differentiated manner, i.e. the group treated with morphine sulfate showed a substantial improvement in relation to the untreated group.

The positive aspect of this study was that it demonstrated the efficacy of using morphine sulfate, administered in a single dose, to significantly reduce the pain during the immediate postoperative period. We believe that the negative aspect of this study was the lack of follow-up on the evolution of the pain and any side effects that might have occurred.

## Conclusion

Application of 2 mg of morphine sulfate in a single dose with epidural infiltration was shown to be a good technique for pain therapy following posterior arthrodesis of the lumbar spine. This resulted in high satisfaction among the patients.

## Conflicts of interest

The authors declare no conflicts of interest.

## REFERENCES

- Bianconi M, Ferraro L, Ricci R, Zanoli G, Antonelli T, Giulia B, et al. The pharmacokinetics and efficacy of ropivacaine continuous wound instillation after spine fusion surgery. *Anesth Analg.* 2004;98(1):166-72.
- Cohen BE, Hartman MB, Wade JT, Miller JS, Gilbert R, Chapman TM. Postoperative pain control after lumbar spine fusion. *Patient-controlled analgesia versus continuous*

- epidural analgesia. *Spine (Phila PA 1976)*. 1997;22(16):1892-6.
3. Gottschalk A, Freitag M, Tank S, Burmeister MA, Kreil S, Kothe R, et al. Quality of postoperative pain using an intraoperatively placed epidural catheter after major lumbar spinal surgery. *Anesthesiology*. 2004;101(1):175-80.
  4. Blumenthal S, Min K, Nadig M, Borgeat A. Double epidural catheter with ropivacaine versus intravenous morphine: a comparison for postoperative analgesia after scoliosis correction surgery. *Anesthesiology*. 2005;102(1):175-80.
  5. Lowry KJ, Tobias J, Kittle D, Burd T, Gaines RW. Postoperative pain control using epidural catheters after anterior spinal fusion for adolescent scoliosis. *Spine (Phila PA 1976)*. 2001;26(11):1290-3.
  6. Perkins FM, Kehlet H. Chronic pain as an outcome of surgery. A review of predictive factors. *Anesthesiology*. 2000;93(4):1123-33.
  7. Raw DA, Beattie JK, Hunter JM. Anaesthesia for spinal surgery in adults. *Br J Anaesth*. 2003;91(6):886-904.
  8. O'Neill P, Knickenberg C, Bogahalanda S, Booth AE. Use of intrathecal morphine for postoperative pain relief following lumbar spine surgery. *J Neurosurg*. 1985;63(3):413-6.
  9. Blackman RG, Reynolds J, Shively J. Intrathecal morphine: dosage and efficacy in younger patients for control of postoperative pain following spinal fusion. *Orthopedics*. 1991;14(5):555-7.
  10. Ross DA, Drasner K, Weinstein PR, Flaherty JF, Barbaro NM. Use of intrathecally administered morphine in the treatment of postoperative pain after lumbar spinal surgery: a prospective, double-blind, placebo-controlled study. *Neurosurgery*. 1991;28(5):700-4.
  11. Ziegeler S, Fritsch E, Bauer C, Mencke T, Müller BI, Soltesz S, et al. Therapeutic effect of intrathecal morphine after posterior lumbar interbodyfusion surgery: a prospective, double-blind, randomized study. *Spine (Phila PA 1976)*. 2008;33(22):2379-86.
  12. Blacklock JB, Rea GL, Maxwell RE. Intrathecal morphine during lumbar spine operation for postoperative pain control. *Neurosurgery*. 1986;18(3):341-4.
  13. France JC, Jorgenson SS, Lowe TG, Dwyer AP. The use of intrathecal morphine for analgesia after posterolateral lumbar fusion: a prospective, double-blind, randomized study. *Spine (Phila PA 1976)*. 1997;22(19):2272-7.
  14. Boezaart AP, Eksteen JA, Spuy GV, Rossouw P, Knipe M. Intrathecal morphine double-blind evaluation of optimal dosage for analgesia after major lumbar spinal surgery. *Spine (Phila PA 1976)*. 1999;24(11):1131-7.
  15. Urban MK, Jules-Elysee K, Urquhart B, Cammisa FP, Boachie-Adjei O. Reduction in postoperative pain after spinal fusion with instrumentation using intrathecal morphine. *Spine (Phila PA 1976)*. 2002;27(5):535-7.
  16. Techanivate A, Kiatgungwanglia P, Yingsakmongkol W. Spinal morphine for post-operative analgesia after lumbar laminectomy with fusion. *J Med Assoc Thai*. 2003;86(3):262-9.
  17. Gottschalk A, Durieux ME, Nemerbut EC. Intraoperative methadone improves postoperative pain control in patients undergoing complex spine surgery. *Anesth Analg*. 2011;112(1):218-23.
  18. Rathmell JP, Lair TR, Nauman B. The role of intrathecal drugs in the treatment of acute pain. *Anesth Analg*. 2005;101 5 Suppl.:S30-43.
  19. Koulousakis A, Kuchta J, Bayarassou A, Sturm V. Intrathecal opioids for intractable pain syndromes. *Acta Neurochir Suppl*. 2007;97(Pt 1):43-8.
  20. Greenberg HS, Taren J, Ensminger WD, Doan K. Benefit from and tolerance to continuous intrathecal infusion of morphine for intractable cancer pain. *J Neurosurg*. 1982;57(3):360-4.
  21. Ray CD, Bagley R. Indwelling epidural morphine for control of post-lumbar spinal surgery pain. *Neurosurgery*. 1983;13(4):388-93.
  22. Greenbarg PE, Brown MD, Pallares VS, Tompkins JS, Mann NH. Epidural anesthesia for lumbar spine surgery. *J Spinal Disord*. 1988;1(2):139-43.
  23. Johnson RG, Miller M, Murphy M. Intraspinous narcotic analgesia. A comparison of two methods of postoperative pain relief. *Spine (Phila PA 1976)*. 1989;14(4):363-6.
  24. Wu MH, Wong CH, Niu CC, Tsai TT, Chen LH, Chen WJ. A comparison of three types of postoperative pain control after posterior lumbar spinal surgery. *Spine (Phila PA 1976)*. 2011;36(25):2224-31.