



## Intrathecal Morphine Following Lumbar Fusion: A Randomized, Placebo-Controlled Trial

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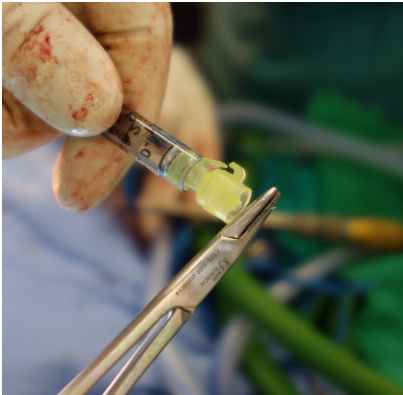


**Introduction:** Despite the potential for faster postoperative recovery and the ease of direct intraoperative injection into the exposed dura, intrathecal morphine is rarely provided in lumbar spine surgery.

**Methods:** In this double-blind trial, we randomly assigned 150 patients undergoing instrumented lumbar fusion for degenerative indications to receive a single intrathecal injection of morphine (0.2 mg) or placebo (normal saline) immediately prior to wound closure. An oblique injection technique was used to reduce the risk of precipitating a cerebrospinal fluid leak. The primary outcome was pain measured on the visual-analogue scale during the first 24 hours after surgery. Secondary outcomes included respiratory depression and treatment-related side effects. An intention-to-treat, repeated-measures analysis was used to estimate outcomes.

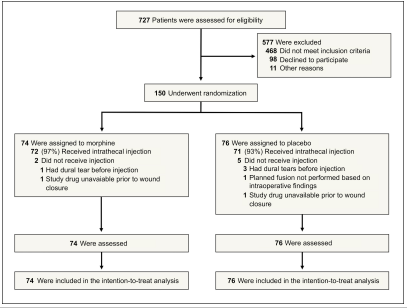
**Results:** The baseline characteristics of the groups were similar. Intrathecal morphine reduced pain both at rest (32% area under the curves [AUCs] difference,  $P<0.002$ ) and with movement (22% AUCs difference,  $P<0.02$ ) during the initial 24 hours after surgery.

**Figure 1. Oblique intrathecal injection**

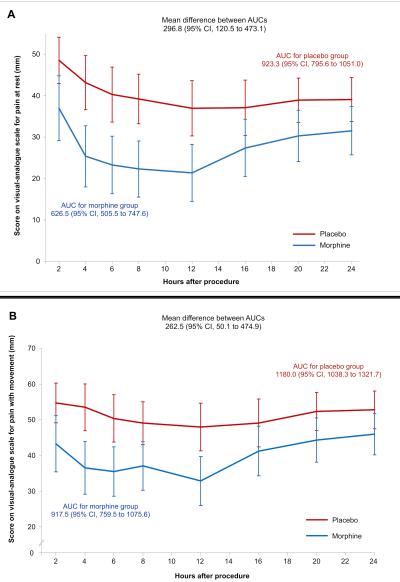


Oblique intrathecal injection was performed using a 30-gauge needle bent 60° towards the open bevel.

**Figure 2. Enrollment, randomization, and follow-up**



**Figure 3. Mean postoperative pain**

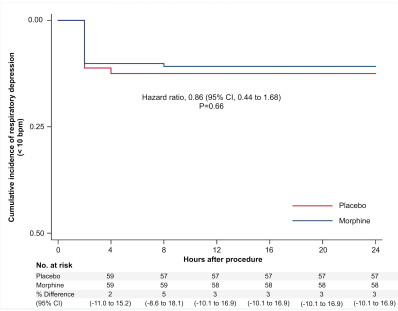


Pain scores on a 100 mm visual-analogue scale at rest (A) and with movement (B) in the 24 hours after surgery are shown.

Vertical bars indicate 95% confidence intervals (CIs). Area under the curves (AUCs) were determined through a repeated-measures analysis. Differences in the AUCs were significant both at rest ( $P<0.002$ ) and with movement ( $P<0.02$ ).

**Results (cont.):** The risk of respiratory depression was not increased by intrathecal morphine (hazard ratio, 0.86; 95% confidence interval, 0.44 to 1.68;  $P=0.66$ ).

**Figure 4. Risk of respiratory depression**



The number of patients with respiratory depression are shown. The cumulative probability of respiratory depression did not differ between groups ( $P=0.66$ ). The risk of respiratory depression remained similar after adjustment in proportional-hazard models for age ( $P=0.65$ ), gender ( $P=0.64$ ), and pre-existing pulmonary disease ( $P=0.66$ ).

**Figure 5. Treatment-related side effects**

Outcome	Proportion of Patients (%) <sup>a</sup>		Hazard Ratio (95% CI) <sup>b</sup>	P Value
	Morphine	Placebo		
Nausea	73	68	1.2 (0.8 - 1.8)	0.27
Emesis	32	32	1.2 (0.6 - 2.1)	0.62
Antiemetic given	30	26	1.3 (0.7 - 2.5)	0.38
Pruritus	45	45	1.2 (0.7 - 1.9)	0.56
Antihistamine given	23	18	1.8 (0.7 - 3.2)	0.25
Urinary retention	24	17	1.5 (0.7 - 3.0)	0.29
Intermittent catheterization	22	11	2.1 (0.9 - 4.9)	0.09
Constipation	34	39	1.0 (0.7 - 1.4)	0.99
Laxative given	46	46	1.1 (0.7 - 1.7)	0.78

(a) Proportion of patients with adverse event during hospital stay in a single-failure-per-subject analysis.(b) Hazard ratios and 95% confidence intervals (CIs) from Cox proportional-hazard models adjusted for age and gender.

**Conclusions:** A single intrathecal injection of 0.2 mg of morphine safely reduces postoperative pain following lumbar fusion. (Funded by the Alberta Spine Foundation; ClinicalTrials.gov number, NCT01053039.)