Cardiothoracic Anesthesia, Respiration and Airway

A background infusion of morphine does not enhance postoperative analgesia after cardiac surgery

[Une perfusion de morphine de base n'améliore pas l'analgésie postopératoire en cardiochirurgie]

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Purpose: To compare the effects of patient-controlled analgesia (PCA), with or without a background infusion of morphine on postoperative pain relief and stress response after cardiac anesthesia.

Methods: With University Ethics approval, 35 consenting adults undergoing elective open-heart surgery were randomly assigned preoperatively in a double-blind fashion to receive either morphine PCA alone (Group I, $n = 15$) or morphine PCA plus a continuous basal infusion (Group II, $n = 14$) for 44 hr postoperatively. Pain scores with visual analogue scale (VAS) at rest, deep inspiration and with cough, sedation scores, stress hormone levels [cortisol, adrenocorticotropin (ACTH) and growth hormone (GH)] and morphine consumption were assessed, and serum morphine levels were measured at four, 20, 28 and 44 hr after surgery. Adverse effects including nausea, vomiting, constipation, urinary retention and pruritus were noted. Total blood, fluid requirements, drainage and urinary output were recorded.

Results: Postoperative morphine consumption at 44 hr was less in Group I (29.43 ± 12.57 mg) than in Group II (50.14 ± 16.44 mg), $P = 0.0006$. There was no significant difference between groups in VAS scores, GH levels, blood levels of morphine and adverse effects. While VAS scores, ACTH and GH levels decreased significantly in both groups, plasma cortisol levels increased significantly in Group I only at four hours. In Group II, ACTH and cortisol were higher at four and 44 hr respectively.

Conclusion: PCA with morphine effectively controlled postoperative pain after cardiac surgery. The addition of a background infusion of morphine did not enhance analgesia and increased morphine consumption.

Objectif : *Comparer les effets de l'analgésie autocontrôlée (AAC), avec ou sans une perfusion de morphine de base, sur l'analgésie postopératoire et la réaction de stress à la suite d'une anesthésie cardiaque.*

Méthode : *Notre étude a été menée en double aveugle, avec l'accord du comité d'éthique de l'université, auprès de 35 adultes consentants devant subir une opération à cœur ouvert réglée. Les patients ont reçu, soit de la morphine en AAC seule (Groupe I, n = 15), soit de la morphine en AAC plus une perfusion de base continue (Groupe II, n = 14) pendant 44 h après l'opération. Nous avons évalué : la douleur, au repos, pendant l'inspiration profonde et la toux, selon une échelle visuelle analogique (EVA), la sédation, les niveaux d'hormones de stress [cortisol, les hormones adrénocorticotropes (ACTH) et de croissance (GH)] et la consommation de morphine, ainsi que les niveaux sériques de morphine à quatre, 20, 28 et 44 h après l'opération. Les effets indésirables, incluant les nausées, les vomissements, la constipation, la rétention urinaire et le prurit ont été notés. Le sang total, les besoins liquidiens, le débit de drainage et la diurèse ont été enregistrés.*

Résultats : *À 44 h, la consommation de morphine postopératoire était plus faible dans le Groupe I (29,43 ± 12,57 mg) que dans le Groupe II (50,14 ± 16,44 mg), P = 0,0006. Il n'y avait pas de différence intergroupe significative des scores à l'EVA, des niveaux de GH, des niveaux sanguins de morphine et d'effets indésirables. Les scores à l'EVA, les niveaux d'ACTH et de GH ont diminué significativement dans les deux groupes, mais le cortisol plasmatique a augmenté de façon significative dans le Groupe I, à quatre heures seulement. Dans le Groupe II, l'ACTH et le cortisol étaient respectivement plus élevés à quatre et 44 h.*

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Conclusion : *L'AAC avec de la morphine réduit efficacement la douleur postopératoire en cardiochirurgie. L'ajout d'une perfusion de base de morphine n'améliore pas l'analgésie, mais augmente la consommation de morphine.*

PAIN that also augments the neurohumoral response is an important problem for patients who undergo cardiothoracic surgery.[1] Therefore methods for effective pain control are required.

Patient-controlled analgesia (PCA) was used either alone or in addition to continuous basal infusion in different clinical trials.[2–6] In a series of postoperative studies, PCA plus continuous infusion resulted in better analgesia than PCA alone. However other studies demonstrate no benefit in adding a continuous infusion to PCA therapy and claim increased drug utilization without an increase in analgesia.[7–9]

In this double-blinded prospective clinical study, the effects of a continuous infusion of morphine in addition to PCA on postoperative pain and stress hormones in patients undergoing open heart surgery were evaluated.

Methods

After Ethics Committee approval, a prospective double-blind study was conducted. ASA II–III patients younger than 70 yr of age undergoing an elective open-heart surgery were included.

Patients with a left ventricular ejection fraction less than 45% and with abnormal hepatic or renal functions and diabetes were excluded. Patients that necessitated a reoperation or intraaortic balloon pump, and patients with agitation or neurological complications that impaired the proper use of the PCA pump were excluded from the study.

Patients provided informed consent and were randomly allocated into the PCA alone (Group I) or PCA plus continuous basal infusion (Group II) groups. They were informed on the role and function of PCA and use of the pump.

A standard anesthetic technique was used. Diazepam 10 mg *po* was administered as premedication. Anesthesia was induced with diazepam 5–10 mg, fentanyl 5 $\mu g \cdot kg^{-1}$, etomidate 0.3 $mg \cdot kg^{-1}$ and vecuronium bromide 0.08 $mg \cdot kg^{-1}$ and was maintained with isoflurane 0.5–1%, N_2O in oxygen. Additional fentanyl was given as required for the operative period. Cardiopulmonary bypass was standardized. Patients

TABLE I Patient and perioperative characteristics

	Group I (n = 15)	*Group II (n = 14)*
Age (yr)	49.53 ± 14.26	45.86 ± 9.83
Sex (M/F)	7/8	10/4
Height (cm)	1.68 ± 0.06	1.66 ± 0.07
Weight (kg)	71.23 ± 8.78	68.36 ± 9.54
Type of surgery (CABG/valve)	11/4	10/4
Duration of surgery (hr)	3.23 ± 0.32	3.46 ± 0.41
Cross-clamp time (min)	39.73 ± 15.45	40.71 ± 21.57
Total by-pass time (min)	64.73 ± 20.5	63.21 ± 22.41
Intraoperative fentanyl (mg)	0.46 ± 0.14	0.42 ± 0.12

Mean ± SD or number, *n* = number of patients; PCA = patient-controlled analgesia; Group I = PCA alone; Group II = PCA plus continuous basal infusion.

TABLE II Serum morphine + morphine glucuronide concentrations and total morphine consumption

Blood morphine concentrations ($ng \cdot mL^{-1}$)	*Postop. four hours*	*Postop. 20 hr*	*Postop. 28 hr*	*Postop. 44 hr*
Group I *n* = 15	80.20 ± 0	86.814 ± 43.1	114.48 ± 49.8	103.73 ± 36.6
Group II *n* = 14	86.11 ± 30.1	119.06 ± 66.5	153.12 ± 76.7	124.63 ± 66.5
P	1.000	0.2295	0.3431	0.9372
Total morphine consumption (mg)				
Group I *n* = 15	2.13 ± 1.25	11.60 ± 6.99	18.47 ± 7.90	29.43 ± 12.57
Group II *n* = 14	2.69 ± 1.11	22.68 ± 10.66	32.84 ± 12.85	50.14 ± 16.44
P	0.2172	0.0023*	0.0001*	0.0006 *

Mean ± SD. *$P < 0.05$ Group I *vs* II. PCA = patient-controlled analgesia; Group I = PCA alone; Group II = PCA plus continuous basal infusion.

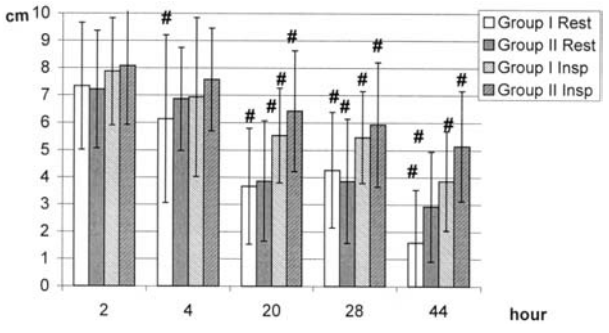

FIGURE 1 Pain scores as measured by visual analogue scale at rest and at inspiration at predetermined times after surgery. Mean ± SD. #$P < 0.05$ *vs* baseline. Group I = patient-controlled analgesia (PCA) alone; Group II = PCA plus continuous basal infusion.

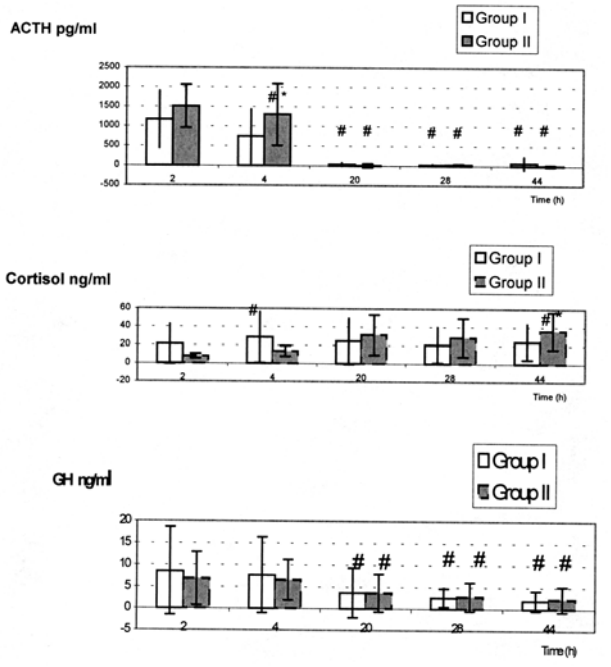

FIGURE 2 Adrenocorticotropin (ACTH), cortisol and growth hormone (GH) concentrations (mean ± SD). Group I = patient-controlled analgesia (PCA) alone; Group II = PCA plus continuous basal infusion. *$P < 0.05$ Group I *vs* II; #$P < 0.05$ *vs* baseline.

were extubated in the operating room and transferred to the intensive care unit for the first 24 hr and treated in an intermediate care unit after the first 24 hr.

Postoperative analgesia was provided by *iv* PCA with morphine and was started on the second postoperative hour. No additional analgesic drugs were given in the first two hours after extubation. PCA included a loading dose of 3 mg, and a bolus dose of 1 mg, with a 15-min lockout period in both groups. The continuous infusion was set at 0.5 $mg \cdot hr^{-1}$ in Group II. Pain was evaluated with a visual analogue scale (VAS) at rest, deep inspiration and with coughing. Blood samples were obtained for measurements of adrenocorticotropin (ACTH), growth hormone (GH), cortisol, and morphine levels two hours before PCA (baseline) and four, 20, 28 and 44 hr after the operation. Postoperative pain was evaluated in these two groups by a standard 10-cm VAS with one end representing "no pain" (0 cm) and the other "most severe pain" (10 cm). An anesthesiologist blinded to group assignment recorded pain and sedation scores. The sedation score was assessed using a four-point scale as follows: 0 = awake; 1 = easy awakening; 2 = awaken by physical stimulation; 3 = difficult to awake by physical stimulation.[2] VAS and sedation scores, and morphine consumption were assessed at the same time intervals. Serum morphine concentrations were measured by chemiluminescence. Adverse effects including nausea, vomiting, constipation, urinary retention and pruritus were also noted. Total blood and fluid requirement, drainage and urinary output were recorded. Heart rate, arterial pressure, oxygen saturation, central venous pressure and ventilatory frequency were monitored continuously.

The primary measures (dependent variable) of treatment efficacy were VAS scores and stress response. Measurements at five time points were analyzed in a repeated measures analysis of Wilcoxon matched pairs test. T test was used for demographic data. Intragroup comparisons were performed by Mann-Whitney U test and *P* values less than 0.05 were considered to be statistically significant.

Results

Thirty-five patients were enrolled in the study and six patients, three in each group, were excluded because of reoperation, late extubation or missing data. The two groups were similar for demographic data, surgical procedures and anesthesia regimen (Table I).

All patients reported less pain at rest at all evaluations after the initiation of PCA (Figure I). The differences between the basal values (before the initiation of PCA) at rest and deep inspiration were found to be significant in both groups ($P < 0.05$; Figure 1). While VAS scores with cough were significantly different at the 28th and 44th hr ($P < 0.05$) in Group I, the difference was significant only at the 44th hr ($P < 0.05$) in Group II.

There was no statistically significant difference between the sedation scores of the groups.

GH, ACTH and cortisol levels were similar in both groups during the study period (Figure II). The decrease in ACTH level was more pronounced at the fourth hour in Group I and cortisol levels of groups were significantly different at the 44th hr ($P < 0.05$; Figure 2).

Morphine consumption was significantly higher in Group II ($P < 0.05$; Table II) and was not associated with weight, age and sex. Serum morphine measurements are listed in Table II.

None of the patients required reintubation and neither excessive sedation nor significant respiratory depression was encountered. There were no differences between the groups with regard to various adverse effects, chest drainage, urinary output, fluid and blood requirement.

Discussion

Despite impaired cardiopulmonary and hepatic functions, patients undergoing open-heart surgery are required to awaken rapidly after surgery. These conditions render pain control and sedation more difficult. Checketts *et al.* suggested that PCA techniques could be used successfully by adult cardiac surgical patients.[10] Our study is in agreement and shows that PCA alone or with an additional basal infusion of morphine at the suggested minimal dosage[1] effectively controls pain after cardiac operations.

While cortisol concentrations did not differ, ACTH and GH concentrations decreased in both groups. However, decreases were similar in both groups, irrespective of pain management.

The addition of a continuous basal infusion of morphine to morphine PCA does not result in superior pain control or an improved neurohumoral response, but increases morphine consumption. PCA alone should be preferred for pain control in patients who have undergone open-heart surgery.

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