Intraoperative *vs* postoperative morphine improves analgesia without increasing PONV on emergence from ambulatory surgery

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Purpose: To compare the timing of administration of morphine in patients undergoing painful ambulatory surgical procedures to determine whether there was a difference in postoperative nausea or vomiting (PONV), quality of analgesia, and recovery profile.

Methods: In a double-blinded, placebo-controlled, prospective study, 70 ASA I-II patients were randomized to receive 0.1 $mg \cdot kg^{-1}$ morphine intraoperatively (Iop) (n=35), or postoperatively (Pop) (n=35). The severity of nausea and pain were measured using visual analog scales (VAS).

Results: There was no difference between the groups in postoperative nausea scores or the incidence of PONV. Upon awakening, patients who received Pop morphine had higher pain VAS scores with movement (7.6 ± 2 *vs* 5.4 ± 3, $P < 0.003$) and at rest (6.9 ± 3 *vs* 5.1 ± 3, $P < 0.013$) than the Iop morphine group. The total number of PCA attempts and analgesic requirements were similar. Patients who received Pop morphine were able to drink sooner than the Iop group (90 ± 34 *vs* 111 ± 38 min, $P < 0.05$). All other recovery milestones were similar. Times to discharge from hospital were similar.

Conclusions: Administration of 0.1 $mg \cdot kg^{-1}$ morphine *iv* intraoperatively improves postoperative analgesia upon emergence from painful ambulatory surgical procedures without increasing the incidence of PONV. There was no increase in PONV when morphine was administered intraoperatively rather than postoperatively.

Objectif : Vérifier si l'incidence de nausées et de vomissements postopératoires (NVPO), la qualité d'analgésie et le profil de récupération est différente selon le moment choisi pour l'administration de morphine lors d'une intervention chirurgicale ambulatoire algique.

Méthode : Une étude prospective et à double insu contre placebo a été menée auprès de 70 patients d'état physique ASA I-II. On a procédé à l'administration peropératoire (PER) ou postopératoire (POST) de 0,1 $mg \cdot kg^{-1}$ (n = 35 dans chaque groupe). La sévérité des nausées et des douleurs a été mesurée par l'échelle visuelle analogique (EVA).

Résultats : On n'a pas noté de différence intergroupe du score de nausées postopératoires ou d'incidence de NVPO. Au réveil, les patients du groupe POST, comparés à ceux du groupe PER, ont présenté des scores de douleurs plus élevés à l'EVA lors de mouvement ($7,6 \pm 2$*vs* $5,4 \pm 3$, $P < 0,003$) et au repos (6.9 ± 3*vs* $5,1 \pm 3$, $P < 0,013$). Le nombre total de recours à l'ACP et de demandes d'analgésiques a été similaire. Les patients du groupe POST ont pu boire plus tôt que ceux du groupe PER (90 ± 34 *vs* 111 ± 38 min, $P < 0,05$). Les autres étapes de la récupération étaient semblables et le congé a été accordé après un temps de récupération similaire pour tous.

Conclusion : L'administration peropératoire, comparée à l'administration postopératoire, de 0,1 $mg \cdot kg^{-1}$ de morphine *iv* améliore l'analgésie postopératoire au réveil d'une intervention chirurgicale ambulatoire algique sans augmenter l'incidence de NVPO.

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ORTHOPEDIC ambulatory surgical procedures are often associated with moderate to severe postoperative pain that may require morphine for analgesia.[1,2]

Inadequate analgesia may delay or prevent discharge or result in unanticipated hospitalization. However, one of the side effects of morphine is postoperative nausea or vomiting (PONV).[3,4] There is no evidence whether intraoperative morphine improves postoperative analgesia or influences the incidence of side effects, although previous studies have favoured administering morphine postoperatively to reduce PONV.[5,6]

The hypothesis of this study was that postoperative morphine would result in less PONV than intraoperative morphine. The primary objective was to determine whether there was a difference in the incidence of PONV. The secondary objectives were to determine if there was a difference in quality of analgesia or recovery.

Methods

After Ethics Committee approval 70 consenting ASA I-II patients between 18-65 yr of age undergoing painful ambulatory procedures were studied.[1] Exclusion criteria were: history of severe PONV, drug abuse, psychiatric illness, morphine allergy, severe asthma, analgesic use in the preceding eight hours, anticipated difficult airway, morbid obesity.

Patients were randomized prospectively to two groups in a double-blind, placebo controlled fashion. The sample size estimate of 70 patients was based on a 60% incidence of PONV with morphine given intraoperatively, a standard deviation of 3.5%, a 50% reduction in PONV was considered significant, with an alpha error of 0.05, and beta error of 0.2.

Two syringes; one containing 0.1 $mg \cdot kg^{-1}$ morphine and the other containing an equivalent volume of saline 0.9%, were prepared and supplied by pharmacy. The intraoperative morphine (Iop) group (n=35) received 0.1 $mg \cdot kg^{-1}$ morphine *iv* intraoperatively, five minutes after skin incision. The postoperative morphine (Pop) group (n= 35) received an equivalent volume of saline 0.9% *iv* intraoperatively five minutes after skin incision. No intra-articular local anesthetic or local anesthetic technique was used. A standardized general anesthetic was given.

In the PACU, the Iop morphine group received an equivalent volume of saline 0.9% *iv* over five minutes, and the Pop morphine group received 0.1 $mg \cdot kg^{-1}$ morphine *iv*.

Pain intensity was assessed with a VAS on a verbal ordinal scale from 0 to 10 (0 = no pain, 10 = worst pain imaginable) and the requirement of analgesics. The VAS for pain was measured at 15 min intervals for the first hour and then at 30 min intervals up to four hours. At the same time intervals, nausea and vomiting were assessed with a VAS for nausea (0 = no nausea, 10 = severe nausea); number of episodes of PONV and treatment required. Management of postoperative pain and PONV was standardized.

Readiness for discharge from PACU was determined by the Aldrete score[7] and discharge from the Ambulatory Surgical Unit (ASU) was determined by the Post Anesthesia Discharge Score (PADS).[8] The times to sit unaided, void, drink, eat, ambulate, qualification for and actual discharge from ASU were recorded.

A standardized telephone questionnaire was conducted 24 hr after surgery and patients were given a diary to complete for pain and PONV for the first three postoperative days.

Demographic data between the two groups were compared by Student's t test or Chi square test when appropriate. The severity of nausea, and pain measured by VAS were analyzed by repeat measures analysis of variance (RMANOVA). The total dose of morphine, time to reach an Aldrete score ≥ 9 and PADS ≥ 9 were analyzed by Student's t test.

Results

The demographic data were similar (Table I). There was no difference in the mean doses of intraoperative anesthetic drugs except for a higher propofol dose in the Iop *vs* the Pop morphine group (Table II).

Upon emergence, the Pop morphine group had higher pain VAS scores with movement (7.6 ± 2 *vs* 5.4 ± 3 *vs*, $P < 0.003$) and at rest (6.9 ± 3 *vs* 5.1 ± 3, $P < 0.013$) than the Iop morphine group (Figure 1). However, this difference in overall pain scores did not persist. The time to first analgesic was similar for the Iop and Pop morphine group (8 ± 6 min *vs* 8 ± 6 min).

The total number of patient controlled analgesia (PCA) attempts, total PCA morphine requirements, number of acetaminophen with 60 mg codeine tablets on the first three postoperative days were similar (Table II).

There was no difference in the incidence of PONV between the two groups in PACU, ASU, and after discharge (Table III). The mean nausea and sedation VAS scores postoperatively and after discharge were similar at all times except for increased sedation at 60 min in the Iop group (Figure 2). A similar number of patients received medication for PONV in the Iop and Pop morphine groups (19 *vs* 17). The Pop morphine group was able to drink sooner than the Iop morphine group (90 ± 34 min *vs* 111 ± 38 min, $P < 0.02$).

TABLE I Patient characteristics

	Intraop. morphine (n=35)	*Postop. morphine (n=35)*
Age, yr	38 ± 12	38 ± 14
Weight, kg	86 ± 15	80 ± 16
Sex, male/female	31 / 4	29 / 6
ASA, I/II	31 / 4	32 / 3
Duration of surgery, min	59 ± 18	59 ± 24
Type of surgery		
Shoulder arthroscopy	27	28
Elbow arthroscopy	1	1
Hardware removal	3	2
Knee arthroscopy	1	0
Ankle arthroscopy	0	2
Exostosis foot	0	1
Augm. mammoplasty	2	1
Partial mastectomy	1	0

Values are expressed as mean ± SD, where applicable.

TABLE II Drugs

	Intraop. morphine (n=35)	*Postop. morphine (n=35)*
Alfentanil, µg	1429 ± 246	1372 ± 447
Propofol, mg	228 ± 34*	198 ± 47
Vecuronium, mg	7.5 ± 3 (n=32)	6.7 ± 3 (n=33)
Succinylcholine, mg	30 ± 60 (n=9)	21 ± 47 (n=11)
Rocuronium, mg	3.8 ± 11 (n=8)	7.5 ± 24 (n=10)
Neostigmine, mg	2.5 ± 1 (n=31)	2.3 ± 1 (n=32)
Glycopyrrolate, mg	0.5 ± 0.2 (n=30)	0.5 ± 0.3 (n=32)
PCA morphine, mg	6.4 ± 4	7.0 ± 4
PCA no. of attempts	7.5 ± 10	8.1 ± 6
Acetaminophen + 60 mg codeine, same day, no. of tab.	3.4 ± 3	2.7 ± 3
Acetaminophen + 60 mg codeine, 1st day, no. of tab.	3.2 ± 3	3.2 ± 3
Acetaminophen + 60 mg codeine, 2nd day, no. of tab.	2.6 ± 3	2.5 ± 3
Acetaminophen + 60 mg codeine, 3rd day, no. of tab.	1.4 ± 3	1.7 ± 3

Values are expressed as mean ± SD. Number in brackets indicates the number of patients receiving that drug, if no number specified, n=35. *$P < 0.004$

TABLE III Frequency of PONV

	Intraop. morphine (n=35)	*Postop. morphine (n=35)*
PACU	12 (34%)	8 (23%)
ASU	12 (34%)	14 (40%)
After discharge	17 (49%)	16 (46%)
Antiemetic administered	19 (54%)	17 (49%)

However, there were no differences in the other recovery milestones.

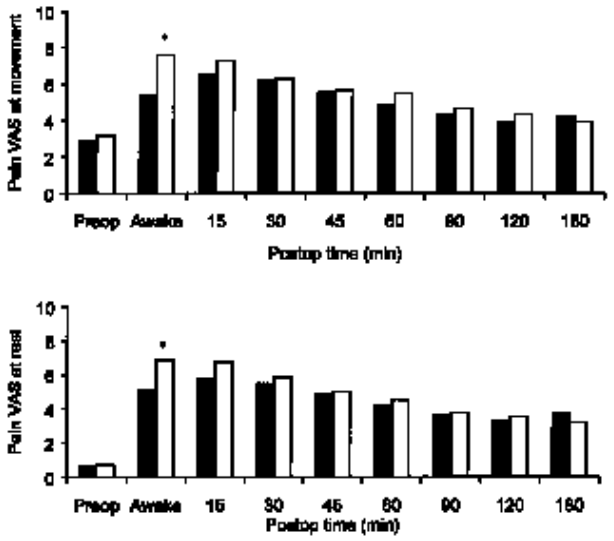

FIGURE 1 Mean pain VAS scores at movement and at rest. Solid bars: patients receiving morphine intraoperatively; Open bars: patients receiving morphine postoperatively. *$P < 0.05$.

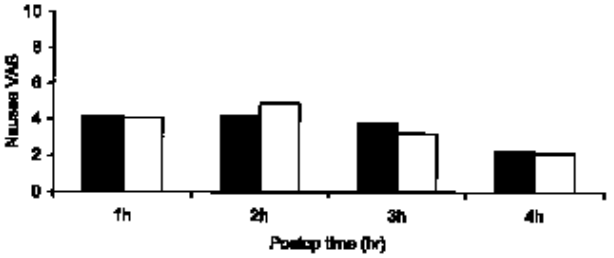

FIGURE 2 Nausea VAS including only patients with nausea; After discharge (Solid bars: intraop. morphine; Open bars: postop. morphine)

Sixty-five patients (93%) participated in the 24 hr postoperative questionnaire, 35/35 (100%) of the Iop morphine group and 30/35 (85%) of the Pop morphine group. Of these, 86% in the Iop morphine group, and 69% in the Pop morphine group were highly satisfied with their anesthetic care. Return to normal functional activity occurred sooner than or as expected in 83% of the Iop morphine group and 80% of the Pop morphine group. The daily living function level of activity was similar in the Iop and Pop morphine groups (4.8 ± 2 *vs* 4.4 ± 2). There were no unanticipated admissions to hospital for any adverse events.

Discussion

Intraoperative morphine administration improved analgesia upon emergence in patients undergoing painful ambulatory procedures. There was no difference in the frequency of PONV. The relatively slow onset time of morphine likely accounts for the improved pain scores on emergence in the Iop morphine group.[9] Patients in the Pop morphine group were able to drink sooner than the Iop morphine group; this may be secondary to the higher sedation score at 60 min in the Iop morphine group.

The 30% incidence of PONV in our study was consistent with a previous study of postoperative morphine for ambulatory surgical patients.[10] The higher incidence of PONV after discharge in both studies may be attributable to the continued effect of morphine stimulation of the vestibular apparatus with the increase in activity after discharge home.[11]

The incidence of PONV varies in previous studies of perioperative morphine. In gynecological patients, 10 mg morphine *im* administered preoperatively resulted in a 9-15% incidence of nausea and a 3-45% incidence of vomiting.[5,12] Postoperative morphine use was associated with a 19% incidence of nausea with 5 mg *iv* and a 23% incidence with 10 mg *iv*.[3] Inpatient gynecological patients experienced an 85% incidence of 24 hr PONV with 0.3 $mg \cdot kg^{-1}$ morphine *iv* given on induction of anesthesia compared with 67% with 0.15 $mg \cdot kg^{-1}$ *iv* given upon closure of the wound.[13]

A limitation of our study is that multi-modal analgesic techniques were not used. The high incidence of PONV found in our study, particularly after discharge, suggests that morphine is not an ideal opioid for painful ambulatory surgical procedures.

In conclusion, the timing of administration of 0.1 $mg \cdot kg^{-1}$ morphine *iv* does not influence the incidence of PONV in patients undergoing painful ambulatory surgical procedures. Intraoperative morphine administration improved analgesia only on emergence from anesthesia. Patients who received postoperative morphine were able to drink sooner, although, analgesic requirements, time to achieve recovery milestones, and discharge times were similar. The high incidence of PONV suggests that alternative adjunctive analgesics may be beneficial and/or a prophylactic antiemetic should be administered when morphine is given for painful ambulatory surgical procedures.

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