Anesthesiology 2003; 99:160–5

Postoperative Morphine Consumption in the Elderly Patient

Frédéric Aubrun, M.D., Dorothea Bunge, M.D.,* Olivier Langeron, M.D. Ph.D.,* Gérard Saillant, M.D.,† Pierre Coriat, M.D.,‡ Bruno Riou, M.D., Ph.D.§*

Background: **It has been suggested that the dose of intravenous morphine used during postoperative titration is not modified by aging. The authors therefore studied morphine requirements in patients undergoing total hip replacement.**

Methods: **Intravenous morphine titration was administered as boluses, then subcutaneous morphine was administered every 4 h over 24 h. Pain was assessed by use of the visual analog scale (0 to 100), and the threshold required to administer morphine was 30. Young and elderly (≥70 yr old) patients were compared. Data are mean ± SD or odds ratio (OR) [95% CI].**

Results: **Two hundred twenty-four patients (68%) were young and 105 (32%) were elderly. The initial visual analog scale was not significantly different between groups. The dose of intravenous morphine in the postanesthesia care unit was not significantly different between young and elderly patients (0.15 ± 0.11 *vs.* 0.14 ± 0.10 mg/kg, P = NS), in contrast to the dose of subcutaneous morphine (0.18 ± 0.18 *vs.* 0.11 ± 0.11 mg/kg, $P < 0.001$) in the ward. Only severe pain (visual analog scale of 70 or greater; OR, 10.5 [4.5–24.8]) was significantly associated with a high dose (greater than 0.15 mg/kg) of intravenous morphine, whereas severe pain (OR, 2.5 [1.6–4.0]), age less than 60 yr (OR, 2.3 [1.4–3.8]), and absence of a nonsteroidal antiinflammatory drug (OR, 1.9 [1.2–3.1]) were significantly associated with a high dose (greater than 0.12 mg/kg) of subcutaneous morphine.**

Conclusions: **The dose of intravenous morphine during titration is not modified in elderly patients, in contrast to the dose administered subcutaneously over a prolonged period.**

ELDERLY patients undergo surgery with increased frequency, and this trend will be enhanced in the near future as a result of demography and an increase in life expectancy in developed countries.[1] Aging is associated with a variety of changes, such as diminished functional status and chronic diseases.[2] Postoperative analgesia is associated with potential adverse effects or complications that might be more pronounced and/or more frequent in elderly patients.[3] Conversely, inadequate analgesia has been reported to be more frequent in elderly patients.[4–6] In elderly patients, a decrease in the dose of opioids is usually recommended because of changes in pharmacodynamics and pharmacokinetics.[2,7–9] In a recent study,[10] we demonstrated that intravenous morphine titration can be administered safely in elderly patients by use of the same protocol as that used in young patients. Moreover, in that study, we also observed that the dose of morphine during intravenous titration in the postanesthesia care unit (PACU) was not significantly decreased in elderly patients.[10] Titration is performed over a very short period during which age-related changes in pharmacodynamics and pharmacokinetics might be less important. However, we failed to reach a conclusion on this important issue, primarily because of the possible bias in the type of surgery that young and elderly patients experienced and because important information was lacking, such as American Society of Anesthesiologists status and intraoperative data.[10]

Thus, we conducted a prospective study to compare postoperative morphine consumption in young and elderly patients undergoing the same surgical procedure. We chose total hip replacement because it is a relatively standardized and painful surgery that is performed in both young and elderly patients. We proposed the hypothesis that the morphine dose during intravenous titration is not significantly modified by aging, whereas the morphine dose administered subcutaneously over the first 24 h is significantly decreased.

This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 5A.

Materials and Methods

This study was approved by the hospital's ethical committee (Comité de Protection des Personnes se Prêtant à la Recherche Biomédicale Pitié-Salpêtrière, Paris, France). Because data were recorded without any intervention and according to a protocol already used routinely in our PACU,[11] authorization was given to waive informed consent.

Nurse Training

All nurses in the PACU and in the wards have been trained to assess pain by use of unidimensional scales and to perform morphine titration (PACU) and subcutaneous administration (PACU and wards). They used the visual analog scale (VAS) (0 to 100, hand-held slide-rule type).[12] When patients had difficulties in manipulating the VAS, nurses were allowed to use a numerical rating scale (from 0 to 100),[13] because these two methods are equivalent.[14]

* Staff Anesthesiologist, † Professor of Orthopedic Surgery and Chairman of the Department of Orthopedic Surgery and Trauma, ‡ Professor of Anesthesiology and Chairman of the Department of Anesthesiology, § Professor of Anesthesiology and Chairman of the Department of Emergency Medicine and Surgery.

From the Department of Anesthesiology and Critical Care, the Department of Emergency Medicine and Surgery, and the Department of Orthopedic Surgery and Trauma, Groupe hospitalier Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Université Pierre et Marie Curie, Paris, France. Submitted for publication September 3, 2002. Accepted for publication March 12, 2003. Support was provided solely by departmental sources.

Address reprint requests to Dr. Aubrun: Département d' Anesthésie-Réanimation, Centre Hospitalier Universitaire Pitié-Salpêtrière, 47 Boulevard de l' Hôpital, 75651 Paris Cedex 13, France. Address electronic mail to: frederic.aubrun@psl.ap-hop-paris.fr.

Regimen of Morphine Administration

A strict protocol of intravenous morphine titration was implemented in the PACU after a previous study had determined the optimal regimen of morphine titration.[11] This protocol defined the dose of intravenous boluses of morphine, the interval between boluses, the absence of limitation on the total dose, the VAS threshold required to administer morphine, and the criteria to stop titration. Immediately after the patients were tracheally extubated and awake, they were questioned as to the presence of pain in the PACU (at least every 15 min before the onset of morphine titration) and were asked to rate pain intensity on a scale (VAS). When the pain increased to more than 30, intravenous morphine was titrated every 5 min by 3-mg increments (2 mg in patients weighing 60 kg or less), and pain was assessed every 5 min until pain relief, defined as a VAS of 30 mm or less. When the patient was asleep, no attempt was made to wake him or her, and the patient was considered as having pain relief. When pain was too severe to obtain a VAS (patient refusal), it was scored 100. The delay to morphine titration was defined as time elapsed between the arrival in the PACU and onset of intravenous morphine titration. Clinical monitoring included respiratory rate measurements, pulse oximetry (Spo_2), sedation according to the Ramsay score,[15] arterial blood pressure, and heart rate. All patients received oxygen supplementation. Morphine titration was stopped if the patient had a respiratory rate lower than 12 breaths/min and/or an Spo_2 lower than 95% and/or experienced a serious adverse event related to morphine administration (allergy, vomiting, severe pruritus). In case of severe ventilatory depression (respiratory rate $<$10 breaths/min), naloxone (intravenous bolus of 0.04 mg) was administered until the respiratory rate was greater than 12 breaths/min, and this was defined as a severe morphine-related adverse effect. Severe postoperative pain was defined as an initial VAS of 70 or more, as reported previously.[16] A high dose of intravenous morphine was defined as a dose of 0.15 mg/kg or more, as reported previously.[16]

A strict protocol of subcutaneous administration of morphine has been implemented in the PACU and in the wards. Subcutaneous morphine could be started 2 h after the end of intravenous morphine titration, either in the PACU or in the ward. Subcutaneous morphine was administered every 4 h, and the dose was adjusted according to the VAS and the patient's weight. The subcutaneous dose was 10 mg when VAS was 60 or greater (7.5 mg in patients weighing 60 kg or less) and 7.5 mg when VAS was lower than 60 (5 mg in patients weighing 60 kg or less). No morphine was administered when VAS was lower than 30. A high dose of subcutaneous morphine was defined as a dose of 0.12 mg/kg or more, because this threshold was the median dose administered in a previous study in our center that used the same protocol.[16]

During the data collection period, consecutive patients who fulfilled the criteria of (1) total hip replacement and (2) understanding of the unidimensional methods were included. Thus, patients with delirium or dementia or who were non-French speaking were not included in the study.

During the study, the anesthesiologists could decide to administer propacetamol and/or nonsteroidal antiinflammatory drugs (NSAIDs), but these prescriptions were also included in the protocol routinely used in our center. Vials containing 2 g of propacetamol (Pro-Dafalgan®, Laboratoires UPSA, Rueil-Malmaison, France), yielding 1 g of paracetamol, were administered intravenously within 15 min. The first administration was performed at the beginning of skin closure in the operating room, as described previously.[17] The dose regimen was 2 g of propacetamol every 6 h. Ketoprofen (Profenid®, Laboratoire Aventis, Paris, France) was used because it is the sole intravenous NSAID available in France. The first administration was also performed at the beginning of skin closure. The dose regimen was 100 mg of ketoprofen every 8 h, as described previously.[18]

Endpoints

Patients were divided into two groups according to age: young and elderly ($\geq$70 yr old), as described previously.[10] The primary endpoint was the dose of intravenous morphine during titration in the PACU. The secondary endpoint was the dose of subcutaneous morphine administered over the first 24 h. The following adverse effects were noted over the first 24 h: ventilatory depression, defined as a respiratory rate below 10 breaths/min and/or the need for naloxone administration; nausea and vomiting; pruritus; retention of urine requiring drainage in the PACU; bradycardia; bronchospasm; and cutaneous rash or other allergic events. Sedation was defined as a Ramsay score[15] greater than 3 but was not considered an adverse effect. However, the percentage of sedated patients during morphine titration was also recorded.

The decision to leave the PACU was made by the anesthesiologist after the nurse had checked that the patient fulfilled the Aldrete criteria[19] and did not suffer from emesis, severe pain, or major postoperative bleeding. Like the nurses, the anesthesiologists were not aware of the data collecting period.

The main characteristics of the patients were recorded, including the preoperative use of analgesics. The analgesic drugs used by the patient were classified according to the World Health Organization classification: level 1 (paracetamol), level 2 (dextropropoxyphen, codeine, tramadol), and level 3 (major opioids).[20] Moreover, the use of antiinflammatory drugs (NSAIDs or corticosteroids) was also recorded. The main characteristics of surgery were recorded, including indication for surgery, type of surgery, surgical approach, experience of

the surgeon (less than or more than 5 yr), postoperative drainage, and early (less than 24 h) postoperative mobilization.

Statistical Analysis

Data are expressed as means ± SD or medians and their 95% CIs in nongaussian variables (time delay and duration). The main endpoint being the dose of intravenous morphine during titration, we assumed that this dose was 0.15 ± 0.10 mg/kg in young patients, as reported previously,[10] and that elderly patients represent 30% of patients undergoing total hip replacement in our center. We estimated that at least 310 patients would be needed for the study to be able to detect a 25% difference with 90% certainty ($1-\beta$) and a two-sided 5% significance level (α) (NQuery 3.0, Statistical Solutions Ltd., Cork, Ireland). Therefore, we decided to include up to 340 patients, excluding those who were removed from the study (a maximum of 8% of patients in this class was expected). Student *t* test and repeated-measures ANOVA were used for continuous gaussian variables. The Mann–Whitney U test was used to compare two medians. The chi-square test or Fisher's exact method were used for categorical variables. Correlation between two variables was performed by use of the least-squares method. For multivariate analysis, a forward step-by-step logistic regression was used, and odds ratios with their 95% CIs were calculated. All comparisons were two-tailed, and a value of $P < 0.05$ was needed to rule out the null hypothesis. Statistical analysis was performed with a computer and NCSS 6.0 software (Statistical Solutions Ltd.).

Results

Three hundred forty patients were included in the study over an 18-month period. Eleven patients were excluded because some data were lacking. Thus, 329 patients were analyzed. Mean age was 62 ± 13 yr, 153 patients (46%) were male, and 176 (54%) were female. Two hundred twenty-four patients (68%) were young, and 105 (32%) were age 70 yr or older. The main characteristics of the two groups of patients are summarized in table 1. Before surgery, elderly patients took corticosteroids more often than young patients (table 1), but the proportion of patients receiving antiinflammatory drugs (NSAIDS or corticosteroids) was not significantly different between young and elderly patients (22 *vs.* 28%, P = NS). The main characteristics of surgery and anesthesia in the two groups were comparable. Only the indication for surgery differed slightly between groups (table 2).

The VAS was not significantly different in the two groups during and at the end of morphine titration (fig. 1). The total dose of intravenous morphine administered

Table 1. Main Characteristics of Young and Elderly Patients

	Young Patients (n = 224)	Elderly Patients (n = 105)	*P* Value
Age, yr	55 ± 11	76 ± 5	—
Male	108 (48%)	45 (43%)	NS
Female	116 (52%)	60 (57%)	
Weight, kg	73 ± 14	67 ± 13	0.002
ASA class			
I	99 (44%)	12 (11%)	
II	98 (44%)	63 (60%)	<0.001
III	25 (11%)	29 (28%)	
IV	2 (1%)	1 (1%)	
No preoperative analgesic	82 (37%)	36 (34%)	NS
Preoperative analgesics			
WHO level 1	23 (10%)	9 (9%)	NS
WHO level 2	100 (45%)	32 (30%)	0.02
Opioids	17 (8%)	5 (5%)	NS
NSAIDs	18 (8%)	4 (4%)	NS
Corticosteroids	31 (14%)	25 (23%)	0.03

Data are means ± SD or number (percentages). Because of rounding, adding percentages may not sum to 100%. ASA = American Society of Anesthesiologists; NS = not significant; NSAIDs = nonsteroidal antiinflammatory drugs; WHO = World Health Organization.

Table 2. Comparison of Surgery and Anesthesia in Young and Elderly Patients

	Young Patients (n = 224)	Elderly Patients (n = 105)	*P* Value
Indication for surgery			
Hip arthrosis	148 (66%)	69 (66%)	
Redo surgery	35 (16%)	23 (22%)	
Osteonecrosis	32 (14%)	5 (5%)	0.03
Fracture	5 (2%)	6 (6%)	
Others	4 (2%)	2 (2%)	
Total hip replacement	215 (96%)	104 (99%)	NS
Surgical approach			
Anteroexternal	169 (75%)	74 (70%)	
Posteroexternal	33 (15%)	19 (18%)	NS
Anterior	22 (10%)	12 (11%)	
Experienced surgeon (>5 yr)	154 (69%)	67 (64%)	NS
Duration of surgery, min	139 ± 55	129 ± 57	NS
>1 postoperative drain	127 (57%)	48 (46%)	NS
Regional anesthesia	27 (13%)	11 (11%)	NS
General anesthesia	198 (88%)	93 (89%)	NS
Dose of sufentanil, μg	67 ± 30	57 ± 21	0.01
Dose of sufentanil, $\mu g \cdot kg^{-1} \cdot h^{-1}$	0.44 ± 0.20	0.46 ± 0.21	NS
Postoperative temperature, °C	35.3 ± 0.9	35.2 ± 1.0	NS
Delay to extubation, min	80 [70–90]	100 [90–130]	0.001
Delay to titration, min	60 [50–75]	105 [60–120]	0.005
Duration of PACU stay, min	250 [240–280]	330 [300–360]	<0.001
Early mobilization	189 (84%)	94 (89%)	NS

Data are means ± SD, medians [95% CI], or number (percentages). Because of rounding, adding percentages may not sum to 100%.

NS = not significant; PACU = postanesthesia care unit.

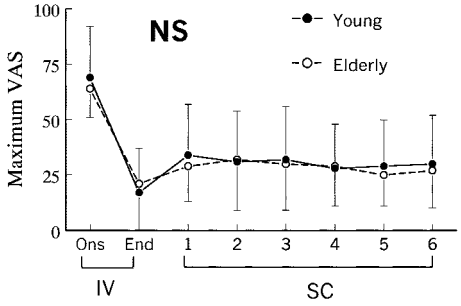

Fig. 1. Comparison of the visual analog pain score (VAS, mean ± SD) in young (n = 224) and elderly (n = 105) patients. VAS corresponds to the maximum value recorded just before morphine administration (IV = intravenous; SC = subcutaneous, every 4 h, from 1 to 6). End = end of morphine titration; Ons = onset of morphine titration. *P* values refer to between-groups comparison. NS = not significant.

during titration was lower in elderly patients, but the body weight was also significantly lower in this group (table 3). When the dose was normalized for body weight, no significant difference was observed between groups (table 3). No significant differences in morphine-related adverse effects were observed between the two groups (table 3). No patient required naloxone administration. The number of sedated patients and the number of patients requiring termination of morphine titration were not significantly different between groups. Elderly patients exhibited significantly longer delay in morphine titration and duration of stay in the PACU than young patients (table 3). The use of NSAIDS in the postoperative period was more frequent in young patients (table 3). Even when excluding patients receiving NSAIDS, we did not observe a significant difference between young (n = 118) and elderly (n = 82) patients in the dose of intravenous morphine administered during titration (0.15 ± 0.12 *vs.* 0.14 ± 0.09 mg/kg, *P* = NS), in contrast to the dose of subcutaneous morphine (0.19 ± 0.16 *vs.* 0.13 ± 0.11 mg/kg, $P < 0.001$) administered later.

Table 3. Comparison of Morphine Dose and Adverse Effects and Analgesic Drugs

	Young Patients (n = 224)	Elderly Patients (n = 105)	*P* Value
Dose of IV morphine, mg	10.3 ± 7.5	8.9 ± 6.9	NS
Dose of IV morphine, mg/kg	0.15 ± 0.11	0.14 ± 0.10	NS
Number of morphine boluses	3 [3–4]	3 [2–3]	NS
Titration stopped	27 (12%)	13 (12%)	NS
Sedated patients	92 (41%)	31 (29%)	NS
Dose of SC morphine, mg	12.5 ± 12.0	7.3 ± 7.1	<0.001
Dose of SC morphine, mg/kg	0.18 ± 0.18	0.11 ± 0.11	<0.001
Minor analgesics	174 (78%)	81 (78%)	NS
NSAIDs	106 (47%)	23 (22%)	<0.001
Adverse effects			
Nausea/vomiting	18	8	
Ventilatory depression	0	0	
Pruritus	0	0	
Urinary retention	7	3	
Allergy	2	1	
Total*	29 (13%)	14 (13%)	NS

Data are means ± SD, medians [95% confidence interval], or number (percentages).

* The total is the number of patients with at least one side effect. One patient may have suffered several different side effects.

IV = intravenous; NS = not significant; NSAID = nonsteroidal antiinflammatory drugs; SC = subcutaneous.

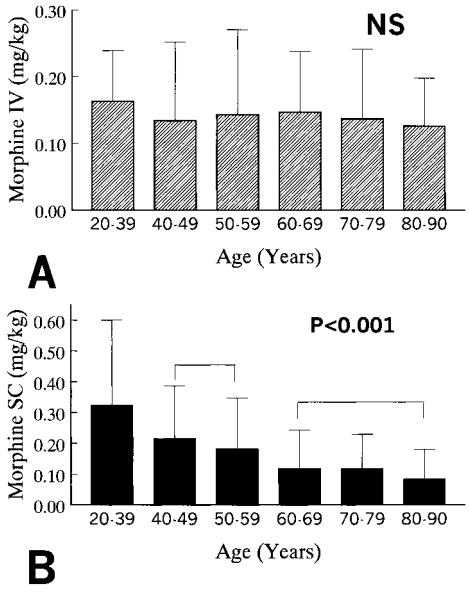

Fig. 2. Doses of intravenous (*IV*) morphine during titration (*A*) and subcutaneous (*SC*) morphine administered over the first 24 hours after surgery (*B*) in patients according to their age. The *P* value corresponds to the global analysis by ANOVA. Brackets indicate groups of means that were not significantly different (*NS*) (Newman–Keuls test).

When patients were grouped in decades of age, no significant differences in the postoperative dose of intravenous morphine during titration were observed (fig. 2). In contrast, elderly patients required a significantly lower subcutaneous dose of morphine in the postoperative period (fig. 2).

We looked for variables associated with the requirement of a high dose of intravenous morphine. By univariate analysis, patients requiring a high dose of intravenous morphine (n = 131, 40%) experienced severe pain more frequently (VAS of 70 or more, 82 *vs.* 35%, $P < 0.001$) and had a higher initial VAS (81 ± 16 *vs.* 58 ± 22, $P < 0.001$) and a lower weight (69 ± 14 *vs.* 72 ± 14 kg, $P = 0.02$). The mean age was lower (60 ± 14 *vs.* 63 ± 13 yr, $P < 0.05$), but the proportion of elderly patients (28 *vs.* 38%, *P* = NS) was not significantly different. However, by multivariate analysis, only severe pain was significantly associated with a high dose of intravenous morphine (table 4).

We looked for variables associated with the requirement of a high dose of subcutaneous morphine. By univariate analysis, patients requiring a high dose of

Table 4. Identification of Risk Factors for Requiring a High Dose of Intravenous Morphine during Titration (≥0.15 mg/kg) or a High Dose of Subcutaneous Morphine (≥0.12 mg/kg) (n = 329)

Variable	Odds Ratio (95% CI)	*P* Value
High intravenous morphine dose		
Initial VAS ≥70	10.5 (4.5–24.8)	<0.001
High subcutaneous morphine dose		
Initial VAS ≥70	2.5 (1.6–4.0)	<0.001
Age <60 yr	2.3 (1.4–3.8)	<0.001
No NSAIDs	1.9 (1.2–3.1)	0.01

NSAIDs = nonsteroidal antiinflammatory drugs; VAS = visual analog pain score.

subcutaneous morphine (n = 167, 51%) experienced severe pain more frequently (VAS 70 or greater, 65 *vs.* 42%, $P < 0.001$) and had a higher initial VAS (71 ± 15 *vs.* 63 ± 23, $P = 0.002$), a lower age (59 ± 14 *vs.* 65 ± 12 yr, $P < 0.001$), and a longer duration of surgery (144 ± 62 *vs.* 128 ± 47 min, $P = 0.007$). The proportion of patients less than 60 yr old was higher (48 *vs.* 31%, $P = 0.002$), as was the proportion of patients receiving no NSAIDs (67 *vs.* 55%, $P = 0.04$) and no minor analgesic drugs (28 *vs.* 17%, $P = 0.02$). However, by multivariate analysis, only severe pain, age less than 60 yr, and no NSAIDs were significantly associated with a high dose of subcutaneous morphine (table 4).

The dose of intravenous morphine titration was not significantly correlated to age ($R = 0.06$, P = NS). In contrast, the dose of subcutaneous morphine titration was significantly correlated with age ($R = 0.15$, $P < 0.009$).

Discussion

The main finding of our study is that the dose of intravenous morphine during postoperative titration (*i.e.*, acute administration) was not significantly modified in elderly patients, in contrast to the dose of subcutaneous morphine administered over the first 24 postoperative hours (*i.e.*, subacute administration).

Elderly patients have been noted to be more susceptible to the effects of opioid analgesic than young patients,[2,21] because aging affects some phases of pharmacokinetics, including distribution, metabolism, and elimination.[22–24] For any given weight-adjusted dose of an opioid, elderly patients have been shown to have higher blood levels and more pronounced pharmacologic effects than young patients.[6,8] In elderly patients, the morphine volume of distribution is approximately half that of young patients, probably because of a decreased cardiac output.[25] Plasma clearance of morphine is also lower in the elderly.[26] Moreover, renal failure is more frequent in elderly patients and can induce an accumulation of morphine metabolites (morphine-3-glucuronide and morphine-6-glucuronide), which explains its prolonged effect in the elderly patients.[27]

Previous studies have found a significant correlation between the dose of opioid required in the postoperative period and the patient's age.[28–30] Nevertheless, these studies assessed the variables influencing morphine requirements over a large time period (the initial 24 h). In our previous study,[10] we observed no significant difference in the dose of intravenous morphine during titration between young and elderly patients. However, we could draw no definite conclusions, because these two populations differed in many respects (type of surgery undertaken, duration of anesthesia, and surgery) that were potential and important biases for this comparison. In the present study, we included only patients undergoing total hip replacement, generating approximately the same surgical trauma and postoperative pain complaints. As expected, the two populations were not completely comparable in American Society of Anesthesiologists status, delay for tracheal extubation, and weight (tables 1 and 2). However, age was not a significant variable associated with the requirement of a high dose of intravenous morphine when assessed by multivariate analysis (tables 3 and 4). Moreover, these differences between young and elderly patients are thought to decrease the dose of morphine and not potentially to mask a difference.

There is an important discrepancy between our present and past studies[10] and the well-accepted concept that opioids are more potent in the elderly. We suggest that the influence of pharmacokinetic variables may not be so important during intravenous morphine titration. Nevertheless, because the dose of intravenous morphine was carefully adapted to pain, we cannot completely rule out the hypothesis that differences in pain intensity (or pain sensitivity to morphine) occur between young and elderly patients. Indeed, although the prevalence of painful conditions in the elderly patient is greater than it is in the young,[31] pain complaints are less frequent in the elderly.[2] Some studies have shown that pain tolerance is slightly increased in elderly patients,[32] whereas others did not.[33] Our study may lack sufficient power to detect a significant difference between groups. However, the small difference observed (−8%) (table 3) should not be considered clinically significant. Our results are strengthened by the significant decrease (−36%) in the dose of subcutaneous morphine we observed in elderly patients, which is consistent with the 41% decrease reported previously over the first postoperative day.[34] After remifentanil anesthesia, Minkowitz *et al.*[35] also observed that total morphine requirements in the 24-h postoperative period was almost halved in patients older than 65 yr. Thus, in contrast to intravenous morphine titration, the dose and the rate of morphine administration after titration should be adjusted according to age, as demonstrated by numerous studies.[26,28,30,34,35]

We did not observe a significant decrease in the dose of sufentanil required during surgery. This result contrasts with the 50% decrease in opioid requirements

reported previously during the intraoperative period.[36,37] Several methodologic issues preclude any valid comparison between the two groups in our study: (1) sufentanil was usually administered as fixed boluses of 10 μg, decreasing the probability of observing a difference over a short period, and (2) opioid requirements were not validated by a precise technique such as electroencephalographic recording.

Some remarks must be included to assess the limitations of our study. First, nurses were not blinded to patient age and thus might have behaved differently in the two groups. Despite this, pain relief was similar in the two groups (fig. 1) because of the strict protocol implemented in our PACU. Moreover, in our previous study,[10] we observed that protocol violations occurred rarely, were minor in most cases, and did not occur more frequently in elderly patients. Second, polypharmacy occurs very often in the elderly population. In addition to age-related changes in either the pharmacokinetics or the pharmacodynamics of the opioids, further studies are necessary to assess interactions, accumulation, and toxicity risks between analgesics and other drugs used before prescription of the pain treatment. Third, the reliability of the pain measurement tools might be affected by age.[38,39] We limited this problem by excluding severely cognitively impaired patients, but we cannot rule out the hypothesis that a subtle difference occurs. Fourth, further studies are necessary in the very elderly population (greater than 90 yr old), which was not included in our study, primarily because total hip replacement is rarely performed at these advanced ages.

In conclusion, we confirm that the dose of intravenous morphine during postoperative titration is not significantly modified in elderly patients, in contrast to the dose of morphine administered subcutaneously over a more prolonged period.

The authors thank the nurses of the postanesthesia care unit (Department of Anesthesiology, Centre Hospitalier Universitaire [CHU] Pitié-Salpêtrière, Paris) for their work on this study and David Baker, D.M., F.R.C.A. (Department of Anesthesiology, CHU Necker-Enfants Malades, Paris), for reviewing the manuscript.

References

1. Clergue F, Auroy Y, Pequignot F, Jougla E, Lienhart A, Laxenaire MC: French survey of anesthesia in 1996. ANESTHESIOLOGY 1999; 91:1509–20
2. Wall RT: Use of analgesics in the elderly. Clin Geriatr Med 1990; 6:345–64
3. Etches RC: Respiratory depression associated with patient-controlled analgesia: A review of eight cases. Can J Anaesth 1994; 41:125–132
4. Portenoy RK, Kanner RM: Patterns of analgesic prescription and consumption in a university-affiliated community hospital. Arch Intern Med 1985; 145: 439–41
5. Faherty BS, Grier MR: Analgesic medication for elderly people post-surgery. Nurs Res 1984; 33:369–72
6. Egbert AM: Postoperative pain management in the frail elderly. Clin Geriatr Med 1996; 12:583–99
7. Singleton MA, Rosen JI, Fisher DM: Pharmacokinetics of fentanyl in the elderly. Br J Anaesth 1988; 60:619–22
8. Gordon M, Preiksaitis HG: Drugs and the aging brain. Geriatrics 1988; 43:69–88
9. Richardson J, Bresland K: The management of postsurgical pain in the elderly population. Drugs Aging 1998; 13:17–31
10. Aubrun F, Monsel S, Langeron O, Coriat P, Riou B: Postoperative titration of intravenous morphine in the elderly. ANESTHESIOLOGY 2002; 96:17–23
11. Aubrun F, Monsel S, Langeron O, Coriat P, Riou B: Postoperative titration of intravenous morphine. Eur J Anaesthesiol 2001; 18:159–65
12. Huskisson EC: Measurement of pain. Lancet 1974; 2:1127–31
13. Jensen MP, Karoly P, Braver S: The measurement of clinical pain intensity: A comparison of six methods. Pain 1986; 27:117–26
14. DeLoach LJ, Higgins MS, Caplan AB, Stiff JL: The visual analog scale in the immediate postoperative period: Intrasubject variability and correlation with a numeric scale. Anesth Analg 1998; 86:102–6
15. Ramsay MA, Savege TM, Simpson BR, Goodwin R: Controlled sedation with alphaxalone-alphadolone. BMJ 1974; 2:656–9
16. Aubrun F, Langeron O, Quesnel C, Coriat P, Riou B: Relationships between measurement of pain using visual analog score and morphine requirements during intravenous morphine titration. ANESTHESIOLOGY 2003; 98:1415–21
17. Aubrun F, Kalfon F, Mottet P, Bellanger A, Langeron O, Coriat P, Riou B: Adjunctive analgesia with intravenous propacetamol does not reduce morphine-related adverse effects. Br J Anaesth 2003; 90:314–19
18. Aubrun F, Langeron O, Heitz D, Coriat P, Riou B: Randomised, placebo-controlled study of the postoperative analgesic effects of ketoprofen after spinal fusion surgery. Acta Anaesthesiol Scand 2000; 44:934–9
19. Aldrete JA, Kroulik D: A postanesthetic recovery score. Anesth Analg 1970; 49:924–34
20. World Health Organization Expert Committee: Cancer pain relief. (Technical Report Series). Geneva: World Health Organization 1986
21. Bellville JW, Forest WH, Miller E, Brown BW: Influence of age on pain relief from analgesics: A study of postoperative patients. JAMA 1971; 217:1835–41
22. Kaiko RF: Age and morphine analgesia in cancer patients with postoperative pain. Clin Pharmacol Ther 1980; 28:823–26
23. Greenblatt DJ, Sellers EM, Shader RI: Drug therapy: Drug disposition in old age. N Engl J Med 1982; 306:1081–108
24. Owen JA, Sitar DS, Berger L, Brownell L, Duke PC, Mitenko PA: Age-related morphine kinetics. Clin Pharmacol Ther 1983; 34:364–368
25. Upton RN, Huang YF: Influence of cardiac output, injection time and injection volume on the initial mixing of drugs with venous blood after i.v. bolus administration to sheep. Br J Anaesth 1993; 70:333–8
26. Burns JW, Hodsman NB, McLintock TT, Gillies GW, Kenny GN, McArdle CS: The influence of patient characteristics on the requirements for postoperative analgesia: A reassessment using patient-controlled analgesia. Anaesthesia 1989; 44:2–6
27. Chauvin M, Sandouk P, Scherrmann JM, Farinotti R, Strumza P, Duvaldestin P: Morphine pharmacokinetics in renal failure. ANESTHESIOLOGY 1987; 66:327–31
28. Gil KM, Ginsberg B, Muir M, Sykes D, Williams DA: Patient-controlled analgesia in postoperative pain: The relation of psychological factors to pain and analgesic use. Clin J Pain 1990; 6:137–42
29. Macintyre PE, Jarvis DA: Age is the best predictor of postoperative morphine requirements. Pain 1996; 64:357–64
30. Egbert AM, Parks LH, Short LM, Burnett ML: Randomized trial of postoperative patient-controlled analgesia vs intramuscular narcotics in frail elderly men. Arch Intern Med 1990; 150:1897–903
31. Harkins SW, Warner MH: Age and pain. Annu Rev Gerontol Geriatr 1980; 1:121–31
32. Sherman ED, Robillard E: Sensitivity to pain in the aged. Can Med Assoc J 1960; 83:944–7
33. Woodrow KM, Friedman GD, Siegelaub AB, Collen MF: Pain tolerance: Differences according to age, sex and race. Psychosom Med 1972; 34:548–56
34. Gagliese L, Jackson M, Ritvo P, Wowk A, Katz J: Age is not an impediment to effective use of patient-controlled analgesia by surgical patients. ANESTHESIOLOGY 2000; 93:601–10
35. Minkowitz HS and the Multicentre Investigator Group: Postoperative pain management in patients undergoing major surgery after remifentanil vs fentanyl anesthesia. Can J Anaesth 2000; 47:522–8
36. Scott JC, Stanski DR: Decreased fentanyl and alfentanil dose requirements with age: A simultaneous pharmacokinetic and pharmacodynamic evaluation. J Pharmacol Exp Ther 1987; 240:159–66
37. Minto CF, Schnider TW, Egan TD, Youngs E, Lemmens HJ, Gambus PL, Billard V, Hoke JF, Moore KH, Hermann DJ, Muir KT, Mandema JW, Shafer SL: Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanil: I. Model development. ANESTHESIOLOGY 1997; 86:10–23
38. Herr KA, Mobily PR: Complexities of pain assessment in the elderly: Clinical considerations. J Gerontol Nurs 1991; 17:12–9
39. Krulewitch H, London MR, Skakel VJ, Lundstedt GJ, Thomason H, Brummel-Smith K: Assessment of pain in cognitively impaired older adults: A comparison of pain assessment tools and their use by nonprofessional caregivers. J Am Geriatr Soc 2000; 48:1607–11