J Shoulder Elbow Surg (2021) 30, 250–257

ELSEVIER

Journal of Shoulder and Elbow Surgery

www.elsevier.com/locate/ymse

Multimodal oral analgesia strategy after ambulatory arthroscopic shoulder surgery: case series using adaptive therapeutic approaches by sequential analysis

Benjamin Garnaud, MD[a,b], Olivier Mares, MD[b,c], Joel L'hermite, MD[a,b], Nathalie Vialles, MD[a,b], Yann Gricourt, MD[a,b], Ariane Lannelongue, MD[a,b], Jean Yves Lefrant, MD, PhD[a,b], Philippe Cuvillon, MD, PhD[a,b,*]

[a]*Department of Anesthesiology and Pain Management, Centre Hospitalo-Universitaire (CHU) Carémeau, Nîmes, France*
[b]*Medical Department, Montpellier University 1, Montpellier, France*
[c]*Department of Traumatology and Orthopedic Surgery, Centre Hospitalo-Universitaire (CHU) Carémeau, Nîmes, France*

Background: Pain control and quality of recovery (QoR) at home remains a challenge after ambulatory shoulder arthroscopy. This study aims to assess the QoR and pain relief using a sequential implementation strategy for rescue analgesic drugs.

Methods: After institutional review board approval, patients (>18 years, American Society of Anesthesiology [ASA] score 1-3 stable) scheduled for ambulatory surgery under general anesthesia with a single-shot interscalene nerve block were enrolled. After discharge, patients received standard information regarding the postoperative recovery and care consisting of a multimodal analgesic regime (acetaminophen and ketoprofen for 5 days). The first 48 postoperative hours allowed us to compare 3 different rescue drug regimes with a control group, in sequential order: tramadol (control group), tramadol + nefopam, immediate-release oxycodone (IR), and extended-release oxycodone (ER). The primary endpoint was the QoR 40 score at 48 hours after surgery. Secondary endpoints were pain relief and adverse events over a 7-day period. An intention-to-treat statistical analysis was performed with sequential analysis (as an interim analysis) every 20 patients. Results were recorded as medians and interquartiles (25-75).

Results: We analyzed 109 patients with similar characteristics among groups. The QoR 40 scores were similar for the tramadol group (168 [161-172]), the tramadol + nefopam group (161 [151-173], $P = .09$), and the IR group (164 [153-169], $P = .17$), but higher for the ER group (176 [167-181], $P = .03$). Concerning adverse events, drugs were interrupted more frequently in the tramadol + nefopam group (36 %). In the ER group, a higher quality of postoperative relief was attained in the domains of pain and sleep.

Conclusion: The present study shows that a combination of IR and ER oxycodone over a short period of time (<48 hours) is associated with a better QoR at home after ambulatory shoulder surgery.

Level of evidence: Level II; Prospective Cohort Design; Treatment Study

Keywords: Shoulder; analgesia; surgery; oxycodone; nefopam; tramadol

According to French law, the present study was approved by the Institutional Human Investigation Committee (Comité de Protection des Personnes, CPP, Nîmes, France: 2017-A01316-47) and was registered on ClinicalTrials.gov before beginning (NCT: 04110665).

*Reprint requests: Philippe Cuvillon, MD, PhD, Department of Anesthesiology and Pain Management, Centre Hospitalo-Universitaire (CHU) Carémeau, Place du Professeur Debré, 30 000 Nîmes, France.
E-mail address: philippe.cuvillon@chu-nimes.fr (P. Cuvillon).

1058-2746/$ - see front matter
https://doi.org/10.1016/j.jse.2020.08.040

Arthroscopic shoulder surgery is one of the most common ambulatory surgical procedures. This functional surgery is often performed on patients with few serious comorbidities.[5,18] Unfortunately, postoperative pain relief is often poorly experienced by patients and is a source of discomfort on the first night or later.[6-8] Thus, more than 20% of patients report maximum pain scores on the first postoperative day, which is a source of readmission.[7,13] For this reason, over the past decade, pain relief with continuous regional analgesia with interscalene nerve block (ISB) has been recommended.[2,7,13,17,22] Because of multiple complications (paresthesia, motor block, catheter misplacement, infection, cost) and the difficulty of managing this technique in an outpatient setting, many anesthesiologists have withdrawn continuous regional analgesia in favor of a single-shot injection.[9,12,16,30] However, the duration of the sensory block is short (6 and 8 hours with motion and at rest, respectively) and there is rebound pain at 24 hours.[1,28,29] In many types of surgery including shoulder surgery, oral opioids are prescribed to avoid an increase in pain after a peripheral nerve block. However, uncontrolled, abusive, and inappropriate long-term use of opioid treatments contributes to what is known as "the opiate crisis."[28,29] Recently, different combinations of drugs using multiple mechanisms to synergistically enhance analgesia have been suggested for opioid sparing at home.[20,25] In practice, the choice of the multimodal analgesic regimes (combination of simple analgesics acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], nefopam) remains a daily challenge for prescribers as the ideal combination must take into account pain scores, side effects (nausea, vomiting, constipation), quality of recovery (QoR), and pain control in opioid naïve patients.[25] Recently, PROSPECT group recommendations stated that opioids should only be used as a rescue therapy.[29]

In order to evaluate the best rescue analgesia after ambulatory shoulder surgery with a multimodal pain management strategy (noninvasive surgery, single ISB, intravenous [iv] dexamethasone, followed at home by oral acetaminophen, and NSAIDs), we conducted an original pilot study evaluating 4 strategies in a sequential analysis method.[19] The first strategy (single ISB, oral acetaminophen, and NSAIDs) used tramadol as rescue and this was our control group. The second group (tramadol + nefopam group) used a similar strategy with the addition of nefopam in the rescue analgesics. The third group used oxycodone, an immediate-release opioid (IR opioid group). For the fourth group (extended-release [ER] opioid group), we combined IR opioid with an ER opioid. The transition between rescue strategies (sequential analysis) was conditioned by the QoR 40 score obtained on the second postoperative day compared with the control group.[14,26] The primary objective of the study was the QoR 40 score evaluated within the first 2 postoperative days compared with the tramadol group.

Methods

Institutional human committee, consent, and setting

The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) recommendations for reporting case series were followed.

Written informed consent was obtained from all participants before inclusion.

Study design and patients

This was a prospective nonrandomized controlled trial using a sequential analysis. Patients older than 18 years (ASA, 1-2) scheduled for ambulatory shoulder surgery (rotator cuff repair in beach-chair position) under general anesthesia with a single-shot ISB were eligible and approached by the surgeon or the investigators. Noninclusion criteria were as follows: ASA status 4 or unstable 3, refusal to participate, age >80 years, weight <50 kg, emergency or bilateral surgery, any contraindication to regional anesthesia, psychiatric disorders (delirium, dementia), pregnancy, patients with alcohol or drug abuse, known deficit in cytochrome P450, uncontrolled epilepsy, patients unlikely to be fully cooperative during the study, and participation in another study within the previous 30 days. Any patients with chronic pain (strong opioid intake >3 months) or reporting any allergy or contraindication to the study drugs, hepatic insufficiency, were not included. Likewise, any patients already taking narcotics, opiate agonists (codeine, dextromoramide, dihydrocodeine, oxycodone PO, morphine-like) or agonist-antagonists (buprenorphine, nalbuphine, pentazocine) before surgery were not included.

Study groups

Study drug administration began on discharge from the outpatients' center and lasted 2 days. Information on analgesia given to the patients was the same for all groups, that is, that study drugs were to be taken if the pain score was >3/10 on a numeric ranking scale (NRS) (0 no pain, 10 worst pain) or during physiotherapy if required. To reduce the risk of misunderstanding after discharge, the investigator reminded all patients at the center just before discharge and a nurse reminded them by phone every day for 2 days. Interventions were as follows:

Tramadol group: 100 mg of tramadol was taken orally every 4-6 hours, with a maximum daily dose of 400 mg.
Tramadol + nefopam group: 120 mg of iv nefopam injected continuously using an elastomeric pump at the patient's home. Injection was started before discharge at the center. As a second-line analgesic (NRS pain score >3/10), these patients on nefopam could also use tramadol, with the same instructions as the tramadol group.
IR group: 10 mg of oxycodone was taken orally every 4-6 hours, with a maximum daily dose of 60 mg.
ER group: 20 mg of ER oxycodone was taken orally in a single dose per day at 8 pm on the night of surgery and stopped on day 2. As a second-line analgesic (NRS pain score >3/10 under oxycodone), these patients also had IR oxycodone with the same prescription as the IR group.

Surgery, anesthesia, and standard postoperative analgesia

Surgery was performed in the morning under general anesthesia and ISB. Before induction, all patients received a single shot of ISB performed under ultrasound guidance. For ISB, injected medication was 15 mL of ropivacaine 5 mg/mL. The efficacy of ISB was evaluated by loss of sensation in the skin around the shoulder area 30 minutes after injection. General anesthesia was then induced with propofol (2-3 mg/kg), sufentanil (0.3 μg/kg), and cisatracurium (0.3-0.5 mg/kg). Airways were maintained with tracheal tubes and the lungs were ventilated with an oxygen-air mixture (50/50). Tidal volume and respiratory rate were set to maintain end-expiratory CO_2 between 4.6 and 5.3 kPa. A 5-cm H_2O positive end-expiratory pressure was set. Anesthesia was maintained with sevoflurane 1%-2% and additional iv sufentanil (5-10 μg) on need. Intravenous fluid administration was ringer lactate 2 mL/kg/h.

All surgeries were performed by experienced surgeons (>5 years of practice, >500 procedures) with an arthroscopic approach and patients in a beach-chair position.

Thirty minutes before the end of the surgery, all patients received 1 g of iv acetaminophen over 15 minutes, 100 mg of iv ketoprofen, and 20 mg of iv nefopam. Postoperative nausea and vomiting prevention was iv dexamethasone 0.1 mg/kg.

At the end of surgery, patients were extubated and transferred to the postanesthetic care unit (PACU). At the PACU, patients experiencing pain with an NRS (0-10) >3 were given an iv manual titration of 3 mg of morphine (2 mg when <60 kg) at 5-minute intervals until an NRS score ≤ 3 was obtained. All groups were then managed similarly and standardized with a rapid rehabilitation approach (early oral intake, walking, and eating as early as possible and before discharge); iv ondansetron (4 mg) was injected in the event of nausea or vomiting. Patients were discharged from the ambulatory unit when their Chung score was 9-10/10.

On discharge from the ambulatory center, all patients received standard information regarding postoperative recovery and care at home (analgesia, dressing change, etc.). They were informed to contact a 24-hour telephone helpline if questions or concerns arose out of office hours. Participants were advised to contact the local hospital's emergency department if in need of acute care.

After discharge, all groups of patients systematically received standard oral analgesic drugs, including acetaminophen (1 g every 6 hours) in combination with ketoprofen (100 mg every 12 hours) for 5 days.

Clinical assessment

Pain intensity at rest and maximum pain felt were recorded using an NRS (0, no pain; 10, worst pain) at the PACU, at discharge, and every day over the study period (7 days). Adverse events (AEs) were assessed. AEs arising from the analgesic protocol were systematically assessed: nausea, vomiting, urinary retention, drowsiness, dizziness, headache, sweating, pruritus, confusion/hallucination, sedation, and sore throat. On days 1, 2, 3, 5, and 7, nurses from the ambulatory outpatient center called the patients and recorded any AEs and quality of sleep, comfort, and anxiety using an NRS (0-10).

Rescue doses of study drugs, additional drugs, or discontinuation of study drugs were also recorded every day.

On day 2, patients self-reported the QoR 40 questionnaire in a file that was sent to the center via e-mail. All medical or surgical complications (including readmission) were recorded throughout the study period.

Endpoints

The primary endpoint was the QoR 40 score on day 2. A score below 159 (95% confidence interval: 145-165) was recognized as poor, and a score above 170 was considered as optimal. A QoR score >170 with any particular rescue strategy was considered as optimal and ended the trial.[14,19]

Secondary endpoints were NRS pain score, AEs (presence/absence of at least one), and dose of rescue drugs.

Sample size calculation, predefined stopping rule, and group order

As this was a sequential analysis, the sample size was not fixed in advance. On the basis of previous studies, Myles et al had estimated that a QoR score below 159 (95% confidence interval: 145-165) was recognized as poor.[14,19] We calculated a need for 30 patients in the first sequence (tramadol group) to set a reference score (2-sided $\alpha = 0.05$ to support the hypothesis). Before starting the study, we planned an intermediate analysis for each group after 20 inclusions. A score below the control group (tramadol) or less than 170 allowed us to stop inclusions in this group and begin the next group. If the final analysis of any sequence reported a score more than 170 and significantly higher than the control group, the trial was ended. An intermediate analysis was performed every 20 patients to avoid futile treatments. Five points on the QoR 40 score above the tramadol group score were required to consider the result significant. Using a 5-point difference, based on a 2-tailed test with $\alpha = 0.05$, a sample size of 20 patients was determined to provide at least 80% power to detect a difference compared with the tramadol group. Before starting the study, the order of strategies was determined as follows: tramadol, tramadol + nefopam, IR, ER.

Statistical analysis

The statistical analysis was conducted using SAS (9.4; SAS Inc., Cary NC, USA). An intention-to-treat analysis was performed with sequential analysis (as interim analysis) every 20 patients. Data were evaluated as they were collected, and further sampling was stopped in accordance with the predefined stopping rule as soon as significant results were not observed after >20 patients.

Statistical results were expressed with mean (standard deviation) or median (25-75 inter quartile [IQ]) according to the distribution. The numbers and associated percentages were given for categorical variables. Comparisons of continuous variables between the groups were performed using a Student's t test or Wilcoxon-Mann-Whitney test according to the distribution. Categorical variables were compared between groups by the χ^2 or Fisher's exact test. A univariate analysis was performed to identify the predictive variables of the QoR 40. For secondary endpoints, parameters were fitted via mixed models with group, time, and

interaction as fixed effects and subjects as a random effect. Effects were further assessed at each time point if the interaction was significant. Comparisons between groups at each time were adjusted for multiple comparisons using the Holm procedure.

Results

Study population

From September 2019 to December 2019, we screened 187 consecutive patients scheduled for arthroscopic shoulder surgery and enrolled 116 patients. Five patients refused to participate after allocation and surgery was canceled for 2. These patients were not included in the analysis (n = 109).

Baseline patient characteristics, preoperative pain relief, surgery, and general anesthesia were similar in all 4 groups (Table I). Total intraoperative sufentanil administration, duration of surgery, and PACU time were also similar between groups. One failed block was observed in the nefopam group.

Primary outcome

QoR 40 scores for each study group are listed in Table II. During the first stage, 35 patients were evaluated in the tramadol group and the QoR 40 score was 168 (161-172). All QoR 40 scores were compared with the tramadol group. After 22 inclusions, the tramadol + nefopam group was stopped because of a lower QoR 40 score, 161 (151-173), $P = .09$. The IR group had a lower QoR 40 score: 164 (153-169), $P = .17$. By contrast, the QoR 40 score was higher for the ER group: 177 (167-186), $P = .03$.

The analysis by component of the QoR 40 scores found worse comfort scores in the tramadol + nefopam group (45 vs. 48; $P = .01$) and the IR group (46 vs. 48; $P = .03$). The autonomy score was decreased in the tramadol + nefopam group (14 vs. 18; $P < .01$) and better for the ER group (21 vs. 18; $P < .05$) and the emotional score was also better for the ER group (42 vs. 40; $P < .05$). In the univariate analysis, the dominant side operated on, age, sex, and preoperative pain score were not correlated with the importance of the QoR 40 score.

Secondary outcomes

All patients included in the analysis left the outpatient center on the day of the surgery, and there were no readmissions within the first 7 days (Table III). One extended hematoma was noted but did not require surgery.

The pain scores at rest and maximum daily pain scores before the procedure and up to day 5 are shown in Figs. 1 and 2, respectively. Regarding AEs (Table III), there were fewer painful awakenings during the first night for the ER group compared with the tramadol group (5 vs. 17; $P < .05$). The main complaints on days 1 and 2 were sore throat due to orotracheal intubation, followed by nausea. In the ER group, 1 case of excessive sedation was reported with no consequences (marked fatigue during interrogation) but resolved spontaneously. No other significant adverse effects were noted.

In the tramadol + nefopam group, 8 patients (36 %) stopped infusions early (before 48 hours) and 6 patients reported difficulties in prolonging the infusion at home.

The number of patients requiring group rescue drugs is noted in Table III. More patients required rescue drugs in the tramadol + nefopam and IR groups than in the tramadol group.

Discussion

This original study demonstrated that the use of tramadol as a rescue drug provided a suboptimal quality of postoperative recovery within the first 48 hours after arthroscopic shoulder surgery. Nefopam and IR opioids did not demonstrate superiority. By contrast, this sequential study showed that the combination of ER opioids over a short period of time (48 hours and only in the evening) significantly improved the QoR 40 and pain relief scores, and limited the painful rebound often observed on the first night.

Pain relief after arthroscopic shoulder surgery remains a clinical challenge, and the PROSPECT group recently provided new recommendations to improve pain relief and reduce AEs.[29] However, QoR was poorly analyzed when rescue analgesia was proposed. To our knowledge, only 1 study has ever assessed the quality of patient recovery in ambulatory shoulder surgery using recovery scores. Elkassabany et al[11] found better recovery quality scores (QoR 9) before and after the introduction of a multimodal analgesia protocol combining acetaminophen, NSAIDs, gabapentin, and IR oxycodone (similar to our IR group) compared with rescue therapy by acetaminophen/oxycodone only (QoR 9 at 24 hours: 13.4 vs. 14.9, $P < .05$). Moreover, with their protocol, Elkassabany et al reported better quality of pain management in the domains of pain intensity, pain interference with activity, and sleep. Using a QoR 40 at 48 hours, our study observed no difference when either tramadol or IR opioids were added to a standard multimodal analgesia protocol.[2] QoR 40 scores, pain relief, and AEs were similar for the tramadol and IR groups, underlining the fact that simply replacing one painkiller by another is not the ideal solution.

The main advantage of optimizing multimodal analgesia after a single-block injection is to limit the incidence of painful postoperative rebound pain, which is still poorly understood and whose origin seems multifactorial.[10,23] Its incidence is high, up to 40%. The clinical risk factors identified are gender (female), age <60 years, presence of severe preoperative pain,[13,15,27] the type of surgery

Table I Characteristics of patients, surgery, and discharge

	Tramadol (n = 35)	Tramadol + nefopam (n = 22)	IR opioid (n = 31)	IR + ER opioid (n = 21)
Patients				
Age (yr)	51 (42-59)	56 (47-67)	48 (35-58)	52 (42-61)
BMI (m/kg^2)	25 (23-28)	26 (25-31)	26 (23-29)	22 (21-26)
Sex (M/F)	20/15	11/11	24/7	12/9
ASA status				
1	19	13	13	14
2	9	7	7	6
3	7	2	2	1
Preoperative assessment				
NRS pain at rest (0-10)	3 (0-5)	2.5 (0-5)	3 (0-6)	2 (1-3)
NRS pain on movement (0-10)	5 (4-8)	5 (3-8)	4 (0-7)	3.5 (3-4)
Duration of pain (mo)	12 (6-42)	10 (6-36)	12 (6-24)	12(9-17)
Preoperative analgesics				
Simple (NSAIDs)	5 (15)	3 (13)	4 (12)	2 (9)
Weak opioid	4 (11)	1 (5)	3 (9)	1 (5)
Strong opioid	0	1 (5)	3 (9)	1 (5)
Apfel score (0-4)	1 (1-2)	2 (0-2)	1 (1-2)	1 (1-2)
Active smoker	16 (45)	4 (18)*	6 (20)*	5 (20)*
Surgery				
Shoulder already operated on, n (%)	8 (22)	1 (5)*	3 (10)	3 (14)
Dominant side operated	25 (71)	18 (81)	16 (51)*	(77)
Type of surgery				
Rotator cuff repair	28 (80)	18 (82)	22 (70)	18 (81)
Other arthroscopy	7 (20)	4 (18)	9 (30)	3 (19)
Duration (min)	55 (45-66)	48 (37-75)	53 (38-69)	50 (36-60)
Regional anesthesia and intraoperative opioid				
Ropivacaine (mg)	56 (55-75)	65 (55-75)	65 (55-75)	60 (56-75)
ISB efficacy, n (%)	35 (100)	22 (100)	31 (100)	21 (100)
Sufentanil (μg)	20 (18-20)	20 (15-20)	20 (20-30)	20 (15-20)
PACU				
PACU time (min)	60 (40-75)	63 (41-76)	61 (40-80)	65 (45-80)
Morphine titration, n (%)	1 (3)	0	1 (3)	2 (9)
AEs in PACU				
PONV	5 (15)	0*	1 (3)*	1 (4)*
Hypoxemia (supplementary nasal O_2)	3 (9)	0	1 (3)	0
Urinary retention	0	0	0	0
Confusion	1 (3)	0	0	0
Bradycardia (HR < 40/min)	1 (3)	0	0	0
At discharge				
Additional paracetamol	2 (6)	1 (5)	0	1 (4)
PONV	1 (3)	1 (5)	1 (3)	0
Tiredness (0-10)	1 (0-5)	0 (0-3)	1.5 (0-3)	1.5 (0-2)
Comfort (0-10)	8 (5-10)	10 (9.25-10)	9.5 (7-10)	9.5 (8-10)

Data are numbers (percentages), medians (25-75).
BMI, body mass index; *ASA*, American Society of Anesthesiology score; *NRS*, numeric ranking scale; *NSAID*, nonsteroidal anti-inflammatory drug; *ISB*, interscalene nerve block; *PACU*, postanesthetic care unit; *AE*, adverse event; *PONV*, postoperative nausea and vomiting; *HR*, heart rate; *IR*, immediate-release; *ER*, extended-release.
* $P < .05$ vs. tramadol.

(pressure and volume in the joint), and lack of post-operative rescue analgesia. Our study clearly demonstrates the interest of ER oxycodone intake before the regional anesthesia wears off to significantly reduce the rebound pain, and may explain the increase in the QoR 40.

Regarding ER forms of opiates, their use has led to abuse and controversy, with recommendations to ban them from the postoperative period.[20,24,25] The originality of our study is to have used them only in the evening for the first 2 nights, without continuing, leading to much

Table II QoR 40 score (primary endpoint)

	Tramadol (n = 35)	Tramadol + nefopam (n = 22)	IR opioid (n = 31)	IR + ER opioid (n = 21)
QoR 40 score: total (/200)	168 (161-172)	161 (151-173)	164 (153-169)	176 (167-181)*
QoR 40 score: domains				
Pain (/35)	30 (27-31)	29 (28-32)	29 (26-31)	31 (30-33)
Comfort (/60)	48 (45-50)	45 (42-47)†	46 (42-47)*	49 (44-51)
Emotions (/45)	40 (38-42)	40 (34-43)	39 (34-41)	42 (37-44)*
Patient support (/35)	35 (32-35)	34 (31-35)	35 (30-35)	35 (34-35)
Physical independence (/25)	18 (14-21)	14 (9-22)†	15 (12-21)	21 (16-23)*

Data are median (25-75).
QoR, quality of recovery; *IR*, immediate-release; *ER*, extended-release.
* $P < .05$ vs. tramadol.
† $P < .01$ vs. tramadol.

Table III Adverse events at home and rescue analgesics

	Tramadol (n = 35)	Tramadol + nefopam (n = 22)	IR opioid (n = 31)	IR + ER opioid (n = 21)
Rescue analgesics				
Patients requiring rescue drugs				
0-24 h	15 (42)	7 (31)	23 (74)*	10 (50)
24-48 h	10 (28)	4 (18)	16 (51)*	6 (30)
48-72 h	6 (17)	7 (31)*	9 (29)*	3 (15)
Number of rescue doses				
0-24 h	1 (0-1)	0 (0-1)	1 (0-1)	1 (0-1)
24-48 h	0 (0-1)	0 (0-0)	1 (0-1)	0 (0-1)
48-72 h	0 (0-1)	0 (0-0)	0 (0-1)	0 (0-1)
Tramadol rescue (day 3-day 7)	6 (17)	7 (31)*	9 (29)*	4 (20)
AEs at home (0-24 h/24-48 h)				
Nausea	3 (6)/2 (6)	4 (18)/1 (4)	3 (9)/1 (3)	2 (10)/2 (10)
Vomiting	0/1 (2)	4 (18)/0 (0)	3 (9)/1(3)	2 (10)/0
Hallucinations	0	0	0	0/1(5)
Sore throat	15 (42)/10 (28)	6 (27)/4 (18)	11 (35)/4 (12)	3 (15)/2 (10)
Sedation	0	0	0	0/1 (5)
Respiratory distress	0	0	0	0
Sleep quality and fatigue				
ISB recovery: painful awakening on the first night	17 (48)	13 (59)	14 (45)	5 (25)*
Painful awakening day 3	8 (22)	7 (31)	2 (6)*	3 (15)*
Painful awakening day 7	1 (3)	0	2 (6)	1 (15)
Complications on day 7				
Surgical complications	0	0	1 (3)	0
Medical complications	0	0	0	1 (5)

AE, adverse event; *ISB*, interscalene nerve block; *IR*, immediate-release; *ER*, extended-release.
Data are in numbers (percentages).
* $P < .05$ vs. tramadol.

better pain and recovery scores. This is a new approach with a reasoned choice for limited use over time.

Similar models for use in surgery have been proposed. For example, after arthroplasty surgery, Kerpsack et al[21] found better pain scores for patients receiving ER oxycodone analgesia than those receiving IR oxycodone + acetaminophen analgesia until 48 hours after surgery. After spinal surgery, Blumenthal et al[4] showed a decrease in morphine consumption at 24 and 48 hours postoperatively, better pain management, and fewer adverse effects by administering ER oxycodone from the day of the procedure up to 48 hours postoperatively. We could have improved our study by including the evaluation of a delayed form of tramadol given under the same conditions as ER opiates. This will be analyzed in another study.

Regarding adverse effects, the risk of respiratory depression may be of concern: patients can have a subclinical

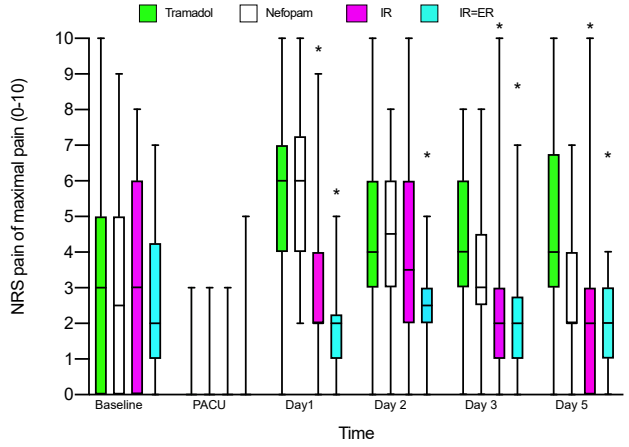

Figure 1 NRS pain (0: no pain, 10 worst pain) at rest over time. *NRS*, numeric ranking scale; *IR*, immediate-release; *ER*, extended-release; *PACU*, postanesthetic care unit.

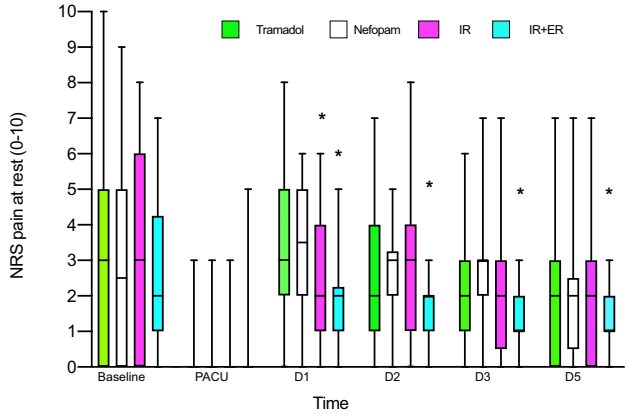

Figure 2 NRS maximal pain (0: no pain, 10 worst pain) over time. *NRS*, numeric ranking scale; *IR*, immediate-release; *ER*, extended-release; *PACU*, postanesthetic care unit.

phrenic nerve palsy that may be worsened by ER opioids, especially in a patients not needing them (according to the results of this study, >50% of the patients slept without pain using only tramadol). The incidence of throat pain related to tracheal intubation was the most important AE (from 15% to 42% on day 1 and from 10% to 28% on day 2). These results are consistent with other studies in which a 40% incidence was found in immediate postoperative care.[3] As throat pain is included in the QoR 40 questionnaire, this result has a negative impact on the score.

Analyzing the NRS shoulder pain score or the overall quality of pain management alone does not reflect the reality experienced by patients on a daily basis. This is the advantage of multifactorial scores. Regarding sleep disorders, 31% of patients complained about the discomfort associated with the position (arm in a sling) and the need to sleep on the back rather than the side (data not initially collected).

Our study had several limitations, the first of which being the sequential analysis. This method is less powerful than a randomized controlled trial, but given the lack of literature on weak opiates, we did not wish to subject the patients to a futile research protocol that may have been stopped earlier because of a sequential analysis (as for the tramadol + nefopam group). Another limitation was the absence of a blinding: as the investigators were not blind to the groups, they may have inadvertently directed some questions. Another well-known bias is related to changes in practice over time that may affect sequential studies. In our study, this bias was limited because of identical surgical techniques and identical basic analgesia. Another possible bias is related to therapeutic information and education whose impact on pain management was not evaluated in our study and will need to be assessed. Indeed, further studies on the subject seem to be necessary to confirm our results. The design of our study would be optimized by randomization of patients rather than consecutive inclusion, blind investigators to improve the objectivity of results, a large number of patients, evaluation of the preoperative QoR 40 score, and a group of patients with an interscalene catheter.

Conclusion

Immediate analgesia with short-term use of ER oxycodone (<48 hours) was associated with better recovery and pain control at home after ambulatory shoulder surgery and no increase in AEs. A randomized study with a weak opioid in a larger population should be conducted to further our observations.

Disclaimer

The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

References

1. Abdallah FW, Halpern SH, Aoyama K, Brull R. Will the real benefits of single-shot interscalene block please stand up? A systematic review and meta-analysis. Anesth Analg 2015;120:1114-29. https://doi.org/10.1213/ANE.0000000000000688
2. Aubrun F, Nouette-Gaulain K, Fletcher D, Belbachir A, Beloeil H, Carles M, et al. Revision of expert panel's guidelines on postoperative pain management. Anaesth Crit Care Pain Med 2019;38:405-11. https://doi.org/10.1016/j.accpm.2019.02.011
3. Biro P, Seifert B, Pasch T. Complaints of sore throat after tracheal intubation: a prospective evaluation. Eur J Anaesthesiol 2005;22:307-11. https://doi.org/10.1017/s0265021505000529
4. Blumenthal S, Min K, Marquardt M, Borgeat A. Postoperative intravenous morphine consumption, pain scores, and side effects with

perioperative oral controlled-release oxycodone after lumbar discectomy. Anesth Analg 2007;105:233-7. https://doi.org/10.1213/01.ane.0000266451.77524.0d
5. Boissard M, Crenn V, Noailles T, Campard S, Lespagnol F. Recovery after shoulder arthroscopy: inpatient versus outpatient management. Orthop Traumatol Surg Res 2018;104:39-43. https://doi.org/10.1016/j.otsr.2017.10.010
6. Borgeat A, Schäppi B, Biasca N, Gerber C. Patient-controlled analgesia after major shoulder surgery: patient-controlled interscalene analgesia versus patient-controlled analgesia. Anesthesiology 1997;87:1343-7.
7. Capdevila X, Dadure C, Bringuier S, Bernard N, Biboulet P, Gaertner E, et al. Effect of patient-controlled perineural analgesia on rehabilitation and pain after ambulatory orthopedic surgery: a multicenter randomized trial. Anesthesiology 2006;105:566-73. https://doi.org/10.1097/00000542-200609000-00022
8. Cho CH, Song KS, Min BW, Lee KJ, Ha E, Lee YC, et al. Multimodal approach to postoperative pain control in patients undergoing rotator cuff repair. Knee Surg Sports Traumatol Arthrosc 2011;19:1744-8. https://doi.org/10.1007/s00167-010-1294-y
9. Cuvillon P, Le Sache F, Demattei C, Lidzborski L, Zoric L, Riou B, et al. Continuous interscalene brachial plexus nerve block prolongs unilateral diaphragmatic dysfunction. Anaesth Crit Care Pain Med 2016;35:383-90. https://doi.org/10.1016/j.accpm.2016.01.009
10. Dada O, Gonzalez Zacarias A, Ongaigui C, Echeverria-Villalobos M, Kushelev M, Bergese SD. Does rebound pain after peripheral nerve block for orthopedic surgery impact postoperative analgesia and opioid consumption? A narrative review. Int J Environ Res Public Health 2019;16:3257. https://doi.org/10.3390/ijerph16183257
11. Elkassabany NM, Wang A, Ochroch J, Mattera M, Liu J, Kuntz A. Improved quality of recovery from ambulatory shoulder surgery after implementation of a multimodal perioperative pain management protocol. Pain Med 2019;20:1012-9. https://doi.org/10.1093/pm/pny152
12. Fredrickson MJ, Leightley P, Wong A, Chaddock M, Abeysekera A, Frampton C. An analysis of 1505 consecutive patients receiving continuous interscalene analgesia at home: a multicentre prospective safety study. Anaesthesia 2016;71:373-9. https://doi.org/10.1111/anae.13385
13. Gerbershagen HJ, Aduckathil S, van Wijck AJM, Peelen LM, Kalkman CJ, Meissner W. Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. Anesthesiology 2013;118:934-44. https://doi.org/10.1097/ALN.0b013e31828866b3
14. Gornall BF, Myles PS, Smith CL, Burke JA, Leslie K, Pereira MJ, et al. Measurement of quality of recovery using the QoR-40: a quantitative systematic review. Br J Anaesth 2013;111:161-9. https://doi.org/10.1093/bja/aet014
15. Gramke H-F, de Rijke JM, van Kleef M, Kessels AGH, Peters ML, Sommer M, et al. Predictive factors of postoperative pain after day-case surgery. Clin J Pain 2009;25:455-60. https://doi.org/10.1097/AJP.0b013e31819a6e34
16. Ilfeld BM. Continuous peripheral nerve blocks: an update of the published evidence and comparison with novel, alternative analgesic modalities. Anesth Analg 2017;124:308-35. https://doi.org/10.1213/ANE.0000000000001581
17. Ilfeld BM, Morey TE, Wright TW, Chidgey LK, Enneking FK. Continuous interscalene brachial plexus block for postoperative pain control at home: a randomized, double-blinded, placebo-controlled study. Anesth Analg 2003;96:1089-95. https://doi.org/10.1016/j.rapm.2003.08.016
18. Jain NB, Peterson E, Ayers GD, Song A, Kuhn JE. US geographical variation in rates of shoulder and knee arthroscopy and association with orthopedist density. JAMA Netw Open 2019;2. https://doi.org/10.1001/jamanetworkopen.2019.17315. e1917315.
19. Jennison C, Turnbull BW. Group sequential methods with applications to clinical trials. Boca Raton, FL: Chapman & Hall; 2000.
20. Jo CH, Shin JS, Huh J. Multimodal analgesia for arthroscopic rotator cuff repair: a randomized, placebo-controlled, double-blind trial. Eur J Orthop Surg Traumatol 2014;24:315-22. https://doi.org/10.1007/s00590-013-1208-z
21. Kerpsack JM, Fankhauser RA. The use of controlled-release versus scheduled oxycodone in the immediate postoperative period following total joint arthroplasty. Orthopedics 2005;28:491-4.
22. Krone S, Chan VW, Regan J, Peng P, Poate EM, McCartney C, et al. Analgesic effects of low-dose ropivacaine for interscalene brachial plexus block for outpatient shoulder surgery—a dose-finding study. Reg Anesth Pain med 2001;26:439-43.
23. Lavand'homme P. Rebound pain after regional anesthesia in the ambulatory patient. Curr Opin Anaesthesiol 2018;31:679-84. https://doi.org/10.1097/ACO.0000000000000651
24. Levy N, Mills P. Controlled-release opioids cause harm and should be avoided in management of postoperative pain in opioid naïve patients. Br J Anaesth 2019;12:e86-90. https://doi.org/10.1016/j.bja.2018.09.005
25. Levy N, Mills P, Rockett M. Post-surgical pain management: time for a paradigm shift. Br J Anaesth 2019;123:e182-6. https://doi.org/10.1016/j.bja.2019.05.031
26. Myles PS, Weitkamp B, Jones K, Melick J, Hensen S. Validity and reliability of a postoperative quality of recovery score: the QoR-40. Br J Anaesth 2000;84:11-5.
27. Sort R, Brorson S, Gögenur I, Nielsen JK, Møller AM. Rebound pain following peripheral nerve block anaesthesia in acute ankle fracture surgery: an exploratory pilot study. Acta Anaesthesiol Scand 2019;63:396-402. https://doi.org/10.1111/aas.13290
28. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. JAMA Intern Med 2016;176:1286-93. https://doi.org/10.1001/jamainternmed.2016.3298
29. Toma O, Persoons B, Pogatzki-Zahn E, Van de Velde M, Joshi GP. on behalf of the PROSPECT Working Group collaborators. PROSPECT guideline for rotator cuff repair surgery: systematic review and procedure-specific postoperative pain management recommendations. Anaesthesia 2019;74:1320-31. https://doi.org/10.1111/anae.14796
30. Vorobeichik L, Brull R, Bowry R, Laffey JG, Abdallah FW. Should continuous rather than single-injection interscalene block be routinely offered for major shoulder surgery? A meta-analysis of the analgesic and side-effects profiles. Br J Anaesth 2018;120:679-92. https://doi.org/10.1016/j.bja.2017.11.104