Ann Anesth Crit Care . 2018 October; 3(2):e81667. doi: 10.5812/aacc.81667.

Published online 2019 April 14. **Research Article**

Postoperative Pain Treatment in Day Surgery: A Quality Improvement Study Examining the Needs of Opioid and Effects of Oxycodone and Morphine

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Received 2018 July 03; **Revised** 2019 February 27; **Accepted** 2019 March 16.

Abstract

Background: There is sparse literature providing evidence for postoperative pain treatment in day surgery and for differences between morphine and oxycodone.

Objectives: The objectives of this study were to examine the need for opioids and the effects of morphine versus oxycodone for pain relief and side effects at home after day surgery.

Methods: This study was a prospective observational study with a quasi-randomized approach. Data consisted of self-reported three-day registration of use and the effects of the opioids, their side effects, and patient satisfaction with regards to pain treatment in a Danish day surgery conducting orthopedic and abdominal surgery. The outcomes, including the use of opioids, self-reported pain relief, and related side effects (nausea, fatigue, dizziness, and skin itchiness) were measured by a numeric rating scale and patient satisfaction with regards to pain treatment.

Results: Out of the 199 included day surgery patients, 162 (81%) returned self-reported postoperative data. A total of 73% of the patients had used opioids an average of 4 times (range 1 - 16). Median levels of nausea, dizziness, and skin itching were 0 (IQR 0 - 3) whereas the median level of fatigue was 3 (IQR 0 - 6). More than 90% of the patients were satisfied or very satisfied with their postoperative pain treatment. No statistically significant differences were found between oxycodone and morphine in regard to onset time, level, duration of pain treatment, and the experienced side effects.

Conclusions: Three-quarters of the patients used opioids after day surgery with a substantially varied number of doses. Few patients experienced substantial side effects, and the patients were generally satisfied with their pain treatment. No significant difference was found between oxycodone and morphine. The need for opioids after day surgery varies substantially and further investigations on individuals and follow-up are needed.

Keywords: Quality Improvement, Pain Treatment, Patient Satisfaction, Patient-Centered Care, Surgery

1. Background

During the last three decades, ambulatory surgery has increasingly become popular due to the development of surgical and anesthetic techniques (1, 2). However, one of the challenges of ambulatory surgery is the need for a sufficient and safe postoperative pain treatment protocol. Local anesthetics have been widely used, and in recent years, ultrasound-guided techniques have improved the quality of perioperative blockades (3, 4). Supplements, pain treatment with paracetamol, and nonsteroidal anti-inflammatory drugs (NSAID) constitute the base of postoperative pain treatment (5, 6). In spite of these conventional treatments, some patients still need supplemental opioids, and oral pain treatment is most safely and easily administered out of a hospital. Oxycodone immediate-release capsules (oxycodone IR) have become increasingly popular as oral opioid therapy for postoperative pain (7). Pharmacokinetic data indicate that oxycodone has a more rapid uptake and longer duration than morphine (8, 9). In some studies, the use of slow release oxycodone compared to slow release morphine seem to show fewer side effects, such as nausea and vomiting (10-12). Postoperative nausea and vomiting are major problems in postoperative care (13). A Cochrane review from 2009 suggested a single dose of oxycodone IR for acute postoperative pain and concluded that it is an effective analgesic for acute postoperative pain (14).

2. Objectives

Planned postoperative pain treatment is based on a general expected need, but more knowledge is needed to clarify which specific postoperative day surgery requires opioid treatment and which opioid provides the best pain management and the fewest side effects.

Therefore, the objectives of the current study were to examine the need for opioids and the effects of morphine and oxycodone IR for pain relief and the related side effects at home after day surgery.

3. Methods

3.1. Design

The study was a prospective observational study using a quasi-randomized approach conducted at a Danish day surgery. The inclusion criteria were patients with surgical procedures, which were expected to need oral treatment with opioids within the first 3 days after surgery. The patients had to be over 17 years old. In addition, they had to understand and speak Danish. The exclusion criteria were patients with chronic pain, which was treated with opioids (all types) and/or secondary analgesics as anticonvulsants or antidepressants.

During the study period, pre- and per-operative pain treatment was identical for all patients. Preoperatively, all patients were treated with paracetamol 1 g orally. Some of the orthopedic patients were not allowed NSAID due to the risk of reduced bone-healing. This meant that no orthopedic patient received NSAID on arrival, but they received it later as intravenous administered ketorolac if accepted by the surgeon. Patients in general surgery with a weight $>$ 50 kg received ibuprofen 600 mg orally before surgery. The dosage was reduced to ibuprofen 400 mg in the case of weight $<$ 50 kg. By the age $>$ 65 years, omeprazole 20 mg orally was added, as long as NSAID was administered.

In the recovery room, pain management was based on frequent assessments of the patients' pain using the numerical rating scale (NRS) 0 - 10. If NRS was below 4, no extra medication was offered. At NRS 4 - 6, NSAID was used if not already given, otherwise oral opioid was administered. At NRS 7 - 10, IV opioid and oral opioid was administered. All patients had to have an NRS $<$ 4 at the time of discharge from the recovery room.

Postoperatively, all patients were recommended the use of paracetamol 1 g $\times$ 4 and NSAID (a dose associated to weight as described above) $\times$ 3 (unless it was decided by the orthopedic surgeon) as baseline pain medication for the first three days. Additionally, based on former patient surveys of pain issues at home, specific operations were identified as expected to require opioids. All patients received necessary pieces of advice at arrival at the unit and again before discharge on the use of pain scales and on when and how to use the drugs.

3.2. Study Groups

The included patients were initially divided into three groups in blocks of two weeks. In group A, patients received pain treatment with opioids in accordance with the current practice. This consisted of intravenous fentanyl, intravenous morphine, and capsule oxycodone IR in the recovery room. Patients who were expected to need opioids at home for the first 3 days were offered a package of oxycodone 5 mg IR capsules to take home. The number of capsules was based on the current practice in accordance with the surgical procedure, with some patients being offered doses for 1.5 days and others for 3 days. With the recommended daily dose administered at a frequency of 4 capsules a day, this corresponds to either 6 or 12 capsules.

In group B, treatment in the recovery room was identical with group A, but oxycodone IR was replaced with tablet morphine 10 mg for opioid use at home. The patients were offered the same amount at home with respect to 1.5 or 3 days. Tablet morphine has to be administered with a frequency of 6 per day to ensure a full daily dose. This meant that the patients received either a total of 9 or 18 morphine tablets of 10 mg to take home. In group C, patient treatment in the recovery room consisted of intravenous fentanyl, intravenous morphine, and tablet morphine. Treatment at home was identical to group B.

Using oral administration, it is impossible to achieve the same equipotent doses of oxycodone and morphine, as capsule oxycodone IR is available as 5 mg capsules and tablet morphine as 10 mg tablets. The usual equipotent dose is that a 5 mg oxycodone capsule taken orally is equal to a 7.5 mg morphine tablet (15). As both oxycodone IR 5 mg and morphine 10 mg are commonly used in Danish day surgery departments, the difference of 2.5 mg morphine between equal dose morphine with oxycodone and the available tablets was accepted.

The patients were placed in the groups in two-week blocks. For the first two weeks, all the included patients were placed in group A. For the following two weeks, the included patients were placed in group B and then in group C for two weeks after that. This continued until at least 50 patients were included in each group to ensure a substantial participant population for analyses.

3.3. Data Registration

Patient's data, surgery-related data, and the use of analgesics were obtained from the anesthesia records. Data

from the first 3 postoperative days were registered by the patients using a registration form which covered each day. The registration form was developed by the study group and pilot tested on 6 patients. The form was returned by mail in a pre-paid envelope. If the registration form was not returned, a person not involved in patient treatment made a reminder by telephone.

On the registration form for each day, the patients were asked to register the use of the opioid with the addition of an NRS-score before, 0.5 hour after and then 1 hour after its administration. The patients were also asked to evaluate the duration of the effect of the opioid, the use of other pain-treating drugs, and their general satisfaction with the treatment of their pain on a five-point Likert scale, and their need to consult their own doctor or the emergency department. The most common side effects of opioids possible for self-reporting (nausea, fatigue, dizziness, and itching) were also evaluated daily using the NRS, with 0 indicating no side effects and 10 indicating the worst possible.

3.4. Statistics

The base sample size was calculated based on the hypothesis that there would be an NRS difference 0.5 hour after opioid intake of 2 (NRS 4 for oxycodone and 6 for morphine) and a joint SD of 3.5. With an α of 0.05 and a β of 0.80, 48 patient had to be included in each group.

Categorical data were analyzed using the chi-square test or the Fischer's exact and the Kruskal Wallis test for non-parametric continuous data. To adjust for the clustered structure of the data, a mixed model with linear regression and random effects was used to compare the effects and durability of the pain treatment, and a collapse command using maximum the NRS values was used to compare the side effects. A P value < 0.05 was considered statistically significant.

4. Results

In the study period (April to September 2016), 288 patients were screened for possible participation. Here, 80 patients were excluded due to the project criteria, nine patients declined participation, and 199 patients agreed to take part in the study. All patients were discharged on the day of the surgery. A total of 162 patients (81%) returned the postoperative registration forms, and 29 (18%) returned it after a phone reminder. The 162 patients were from group A: 55 patients, group B: 51 patients and group C: 56 patients. Groups B and C were merged in the analyses between oxycodone and morphine because only two out of the 56 patients in group C received treatment with tablet morphine in the recovery room, and therefore, treatment in the recovery room would have had only a minimal influence on the postoperative use of the opioids and the side effects.

Table 1 presents the characteristics of the participants. The majority of the patients were orthopedic. Prolonged block refers to extending the blockade by adding dexamethasone and or clonidine to the nerve block. There were no significant differences between the groups, except plan for posti-operative pain medication

The majority of the patients within each group were assessed to need 1.5 day of opioid post-surgically. A total of 38 patients (13, 11, and 14) had received IV opioid in the recovery room (data not shown). Table 2 shows that 73% of the participants used opioids after day surgery, with a range of between 50% (laparoscopic cholecystectomies) to 91% (hand/arm surgery). The median number of doses taken was 3.5 - 4 for all groups, but this covered a wide range between 1 and 16 doses. Orthopedic shoulder patients had the widest range (1 - 16) and laparoscopic cholecystectomies had the smallest one (2-8).

A total of 23 patients (15%) had contact with a doctor from the emergency services (six from the oxycodone group and 17 from the morphine group) with a total of 28 contacts. No statistically significant differences were found in pain relief between oxycodone IR and tablet morphine. The two groups had a reduction in the NRS of 1.9 and 1.6, respectively after 30 minutes (P = 0.30), and of 2.9 and 2.8 after one hour (P = 0.93). This corresponds to a measurable clinical effect (Table 3). The median levels of side effects of the opioids were zero, except for fatigue, which had a median level of three. The 75% percentile was between zero and six, but the full range for all four common side effects was 0 - 10. No significant difference was found between morphine and oxycodone (Table 4).

More than 90% of the patients were either satisfied or very satisfied with the pain treatment and no significant differences were found between orthopedic or abdominal surgery patients or between the oxycodone and morphine groups (Table 5). Phone calls to remind the participants to return the registration form revealed different postoperative scenarios. An elderly lady had not had any pain, but had taken the opioid every night because she then slept very well. A few patients had serious pain issues after the first three days of post-operation and had found it difficult to get help from the emergency services or their general practitioner. Even though the medians for nausea and dizziness were 0 and the IQR ranged from 0 to 2 - 3 (Table 4), a few patients (both from the oxycodone and morphine groups) had experienced serious side effects such as fainting when standing up quickly after taking the opioid. These patients would rather be in pain than risk a repetition of those particular side effects.

Table 1. Patient Characteristics[a]

Variables	Total	Oxycodone (N = 55)	Morphine (N = 107)	P Value[b]
Women	108 (67)	34 (62)	74 (69)	0.35
Age median (IQR)	49 (36 - 57)	51 (36-59)	48 (35 - 57)	0.42
BMI	27 (23 - 30)	27 (23 - 30)	26 (23 - 29)	0.15
ASA classification				
ASA 1	61 (38)	15 (27)	46 (43)	0.09
ASA 2	92 (57)	35 (63)	57 (53)	
ASA 3	9 (6)	5 (9)	4 (4)	
NRS arrival median (IQR)	2 (0 - 4)	2 (0 - 5)	1 (0 - 3)	0.39
Operation				
Laparoscopic cholecystectomy	20 (12)	5 (9)	15 (14)	0.66
Other abdominal surgeries	11 (7)	4 (7)	7 (7)	
Orthopedic	131 (81)	46 (84)	85 (79)	
Shoulder	53 (40)	19 (41)	34 (40)	0.88
Foot	51 (39)	17 (37)	34 (40)	
Knee	16 (12)	5 (11)	11 (13)	
Hand/arm	11 (8)	5 (11)	6 (7)	
Block before knife time	100 (81)	34 (77)	66 (83)	0.48
Type of nerve block				
Femoral block	11 (9)	3 (7)	8 (10)	0.79
Interscalene block	53 (44)	19 (44)	34 (44)	
Axillary block	7 (6)	4 (9)	3 (4)	
Toe or ankle block	46 (38)	16 (37)	30 (38)	
Femoral + obturator	4 (3)	1 (2)	3 (4)	
Prolonged block	(19)	8 (18)	15 (19)	0.89
Duration of operation median (IQR)	40 (27 - 60)	40 (27 - 65)	45 (28 - 59)	0.58
NRS max, recovery median (IQR)	0 (0 - 5)	0 (0 - 5)	1 (0 - 5)	0.21
Nausea, recovery	13 (8)	4 (7)	9 (8)	0.55
Vomiting, recovery	2 (1)	1 (2)	1 (1)	0.56
Plan for pain medication				
1.5 day with opioid pn[c]	143 (88)	47 (86)	96 (90)	0.03
3 days with opioid pn[c]	6 (4)	5 (9)	1 (1)	
Prescribed opioid (knee)	13 (8)	3 (5)	10 (9)	

Abbreviations: ASA, American Society of Anesthesiologists Classification; BMI, body mass index; IQR, interquartile range; NRS, numeric rating scale.
[a] Values are expressed as No. (%) or No. (range).
[b] Chi-square test or Fischer's exact test for categorical data and Mann-Whitney U-test for not normally distributed continuous data.
[c] pn: pro necessitate (as needed).

5. Discussion

Three-quarters of the patients used opioids after day surgery with a substantially varied number of doses. Few patients experienced substantial side effects, and the patients were generally satisfied with their pain treatment. No significant difference was found between oxycodone and morphine groups.

Although all studied participants were assumed to need opioids as supplementary pain medication after day surgery, a quarter did not use any opioid and the rest (within all types of surgery) took a wide range of doses

Table 2. The Number of the Patients Using Opioid and Doses

Variables	Total, N	Used Opioid, No. (%)	Number of Doses, Median (Min - Max)
Laparoscopic cholecystectomy	20	10 (50)	4 (2 - 8)
Other abdominal surgeries	11	9 (82)	4 (1 - 11)
Orthopedic	131	100 (76)	4 (1 - 16)
Shoulder	53	43 (81)	4 (1 - 16)
Foot	51	35 (69)	4 (1 - 14)
Knee	16	12 (75)	3.5 (2 - 10)
Hand/arm	11	10 (91)	4 (1 - 10)
Total	162	119 (73)	4 (1 - 16)

regardless the type of operation. A recent review has examined post-discharge opioid consumption with the conclusion that surgical patients used substantially less opioid than prescribed, The range of prescribed opioid consumed varied from 11% to 90% (16).

As the patients were asked only to register levels of the pain in relation to their opioid intake, the present study does not provide a comprehensive overview of the levels of the pain after day surgery. Therefore, the study cannot prove whether the lack of the need to use opioids was due to the absence of the pain, a mistrust of opioid, or an acceptance of certain levels of the pain. Studies have shown that pain management is important for patients (17) and there is a relationship between pain severity and patient satisfaction (18). Furthermore, just being aware that you have an option if the pain gets too strong may decrease use of opioids.

Although more than 90% of the patients in this study were satisfied or very satisfied with the pain treatment that was offered, a small group remained to whom the treatment was still not sufficient. A non-planned advantage of the reminder phone calls was the collection of detailed information about the varied experiences of the patients regarding the pain and the side effects after day surgery. If the pain prevailed, some of the patients did not have sufficient options to manage their pain. Therefore, providing a high-quality postoperative pain treatment after day surgery for all patients is comprised of clear (and usable) options for what to do and whom to contact if standard treatment is not sufficient.

Based on the pharmacokinetics (8, 9), the hypothesis was that oxycodone would reduce NRS faster than morphine. However, this study revealed no differences in the clinical use of capsule oxycodone IR 5 mg and tablet morphine 10 mg when comparing the effects and common side-effects in a mixed population of day surgery patients. This is in accordance with a study of pancreatic cancer pain, which no significant differences were found in pain and symptom intensity between oral morphine and oral oxycodone (19). A study comparing IV morphine with IV oxycodone after percutaneous kidney stone surgery could not confirm their hypothesis that oxycodone would be superior in the treatment of visceral pain (20).

The study was conducted with the clinically available amount of the drugs. The national recommendations in Denmark (15) prescribe that the equipotent oral doses are 5 mg oxycodone IR equal to 7.5 mg morphine. Several studies have evaluated the equipotent oral doses (21-23). The ratio reported between oral oxycodone and oral morphine varies from 1:1 to 1:2. With this variation in the estimated potency, it can be argued that equipotent doses were given. The onset time of oxycodone IR is supposed to be faster than morphine when administered orally (8, 9), but this was not found in this study when looking at the 30- and 60-minute time points after intake. However, giving a larger equipotent dose, in this case, morphine tablet will accelerate the onset time and could explain the same clinical onset time. This could potentially induce a higher incidence of side effects, but this was not found in the current study. Oxycodone IR has become popular in postoperative settings (7). Studies have shown that the duration of oxycodone IR is slightly longer than tablet morphine (8, 9, 15, 24), which could suggest why it has become the drug of choice. However, a longer duration of oxycodone IR was not shown in this study. The studies testing the controlled released oxycodone and morphine also seem to show a difference in the side effects (10-12). This finding was not supported by the current study.

The strengths of the study include the high response rate, the quasi-randomized approach, and the participation of a mixed population of day surgery patients, which increases the generalizability of the results. However, the mixed population with different surgeries and the use of various medications and blocks during surgery are also limitations to this study and the comparison between groups should be considered with caution. The main limitations are the only quasi-randomized and the non-blinded study design, which may induce bias with respect to the use of regional anesthesia blocks and other aspects of patient handling. However, all surgery and anesthetic procedures were carried out based on current practice and were most likely not influenced by the study. A bias may also be found in the non-systematic use of NSAIDs in orthopedic patients. Whether a patient was allowed to use an NSAID or not, it would cause a potential difference between oxycodone and morphine. However, with the quasi-randomized design, it is assessed that the using or not-

Table 3. Effect and Duration of Pain Medication

	Total	Oxycodone	Morphine	P Value[a]
NRS before intake				
Mean ± SD	5.9 ± 2.4	5.9 ± 2.1	5.9 ± 2.1	
Regression coefficient (CI)		0	-0.2 (-1.0; 0.6)	0.62
NRS difference 0.5 hour				
Mean ± SD	-1.7 ± 1.6	-1.9 ± 1.8	-1.6 ± 1.5	
Regression coefficient (CI)		0	0.3 (-0.3; 0.8)	0.30
NRS difference 1 hour				
Mean ± SD	-2.8 ± 2.0	-2.9 ± 2.0	-2.8 ± 2.0	
Regression coefficient (CI)		0	0.03 (-0.6; 0.7)	0.93
Duration				
Mean ± SD	4.5 ± 2.3	4.6 ± 1.9	4.5 ± 2.5	
Regression coefficient (CI)		0	0.004 (-0.8; 0.8)	0.99

Abbreviations: CI, confidence interval; NRS, numeric rating scale; SD, standard deviation.
[a] A mixed model with linear regression and random effects.

Table 4. Side Effects

Variables	Total		Oxycodone		Morphine		P Value[b]
	N	Median (IQR)[a]	N	Median (IQR)[a]	N	Median (IQR)[a]	
Nausea	139	0 (0 - 2)	45	0 (0 - 2)	94	0 (0 - 3)	0.26
Fatigue	138	3 (0 - 6)	45	2 (0 - 5)	93	3 (0 - 6)	0.53
Dizziness	136	0 (0 - 3)	45	0 (0 - 3)	91	0 (0 - 3)	0.50
Skin itching	136	0 (0 - 0)	44	0 (0 - 0)	92	0 (0 - 0)	0.81

[a] Interquartile range.
[b] Mann-Whitney U-test based on collapse command using median NRS values.

Table 5. Satisfaction with Pain Treatment[a,b]

Variable	Total (N = 153)	Orthopedic (N = 125)	Abdominal Surgery (N = 28)	P Value	Oxycodone (N = 54)	Morphine (N = 99)	P Value
Very satisfied	84 (55)	71 (57)	14 (50)	0.73	32 (59)	53 (53)	0.76
Satisfied	56 (37)	45 (36)	11 (39)		18 (33)	38 (38)	
Other	12 (8)	9 (7)	3 (11)		4 (7)	8 (8)	

[a] Chi-square test based on collapse command using median values.
[b] Values are expressed as No. (%).

using NSAID individuals were equally divided between the groups. Likewise, the non-equipotent doses of morphine and oxycodone may induce bias in comparing. Although a significant difference was found between the groups regarding the plan for opioid treatment at home, the vast majority of subjects in all groups were assumed to need opioid pn necessitate for 1.5 day. Therefore, this difference most likely did not influence the results. Information is missing on whether the patients adhered to the recommendations of taking paracetamol and NSAID. However, it is unlikely that there would be a difference between the oxycodone and the morphine groups. Other side effects such as constipation and sleepiness need more clarification in further studies.

Although this is a prospective observational study with a quasi-randomized approach, the study does not provide solid evidence for differences between morphine and oxycodone. As neither the patients nor the researchers were blinded, the risk of bias exists. Other limitations include a lack of knowledge of reasons for either using or not using opioid, having NRS scores only for patients taking opioids, and the self-reported data, which could induce the risk of

information biases. Reasons for using or not using opioids would be interesting to pursue in future research. More detailed knowledge about pain issues and pain levels after day surgery for specific operations would be helpful in offering optimal pain treatment for postoperative after day surgery. However, the results from this study suggest that there is no model that fits all, so more precise individual assessment and follow-up are needed. A randomized double-blinded controlled study still needs to be carried in order to recommend the use either oxycodone or morphine.

5.1. Conclusions

Three-quarters of the patients used opioids after day surgery with a substantially varied number of doses. Few patients experienced substantial side effects, and the patients were generally satisfied with their pain treatment. No significant difference was found between oxycodone and morphine. The need for opioids after day surgery varies substantially and individual assessments and follow-up are needed.

Acknowledgments

The authors thank all patients for willingness to participate in the study.

Footnotes

Authors' Contribution: All authors took part in designing the study and management of the studied participants. Hanne Irene Jensen had the main responsibility for data analyses, Kurt Wesenberg Christiansen and Hanne Irene Jensen drafted the manuscript. All authors took part in the critical revision of the manuscript and approved the final version.

Conflict of Interests: The authors declare they have no conflict of interest.

Ethical Considerations: The Regional Committee on Health Research Ethics for Southern Denmark was asked for approval prior to the commencement of this study. The Committee assessed the study as a patient quality improvement project which according to Danish law does not require (and cannot achieve) Institutional Review Board approval (IRB). The study was registered with the Danish Data Protection Agency. All participants provided written informed consent, which was obtained on arrival at the Day Surgery clinic.

Funding/Support: The authors declare there is no Funding/support in this study.

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