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Comparison of Oxycodone vs Morphine Administered by Intravenous PatientControlled Analgesia for Postoperative Pain at A Tertiary Care Center in Saudi Arabia

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Abstract:
Objectives: Intravenous Morphine is widely used for postoperative analgesia by the Patient-Controlled Analgesia (PCA). Oxycodone is becoming commonly used for postoperative analgesia due to its potent analgesic effects, high safety profile. We compared the efficacy and safety of both drugs when administered intravenously through PCA at King Fahad Medical City, Riyadh, Saudi Arabia.

Methods: We conducted a prospective observational study at King Fahad Medical City (KFMC), Riyadh, Kingdom of Saudi Arabia for six months. Patients enrolled in the study were >18 years of age, underwent general, plastic or orthopedic surgeries and were candidates for postoperative PCA. The primary outcome was pain score at 6h, 12h, and 24h after commencing the PCA infusion. The secondary results were total consumption of both drugs in 24 hours and the incidence of nausea and vomiting, itching, and urinary retention.

Results: We included 85 patients in this study. Patients randomly allocated to receive Morphine or Oxycodone by PCA following abdominal, gynecological, or orthopedic surgeries. There was no significant difference between morphine and oxycodone groups in pain score post 6 hours of administration (mean 1.762 ± 0.983 vs. 1.837 ± 0.871 (p = 0.710), respectively, however, the morphine group showed a lower mean pain score post 12 hours and 24 hours compared to the oxycodone group

(Post 12 hours: 1.571 ± 0.991 vs. 2.023 ± 0.963 (p = 0.036), respectively), (Post 24 hours: 1.071 ± 0.973 vs. 1.674 ± 1.085 (P = 0.008), respectively). The safety profile was similar between both groups.

Conclusion: PCA Morphine utilization in postoperative pain management gave a noticeable pain relief after 12h and 24h of administration compared to PCA Oxycodone. The study has shown a similar incidence of side effects.

Keywords:
Morphine, Opioids, Oxycodone, Patient-Controlled Analgesia (PCA), Surgery

Introduction:

Adequate postoperative pain control following surgery is an essential consideration in perioperative care.[1] [2] [3] Inflammation or direct damage commonly cause postoperative pain.[4] adequate postoperative pain control encourages early mobilization and participation in functional rehabilitation, increases patient satisfaction, reduce the risk of cardiac complications and reduce healthcare costs.[5] [6]

Assessing pain severity by using assessment tools is an essential approach during pain management. The primary target during postoperative pain management is to reach pain relief with fewer adverse effects.[7] [8] [9]

Opioids are effective analgesic drugs with a high capability to relieve Pain when administrated parenterally[10] [11]. However, Opioids are well known to increase the risk of histamine release (flushing, hypotension, pruritus, and bronchospasm), respiratory depression, constipation, sedation, and bradycardia.[12] [13] [14] [15]

Patient-controlled analgesia (PCA) is one of the most common methods used to provide continuous opioid infusion in the postoperative period.[16]

This method allows patients to control their Pain by utilizing a programmed pump.

The main advantage of this method is the reduction in the risk of opioid overdose by using a fixed amount with a lockout interval.

Different opioid analgesics have been used widely by PCA. Many factors should be considered during PCA-analgesic selection (drug efficacy, safety, duration, and patient factors.[17] [18] Morphine is the standard opioid used in PCA.[19] Oxycodone is a potent semi-synthetic opioid commonly used in the management of acute and chronic Pain.[20] It has been shown to have the same potency as Morphine, but slightly longer acting and does not induce histamine release.[21] [22] [23]

This study aims to assess the efficacy and safety outcomes of intravenous Oxycodone vs. Morphine administered by the PCA pump in postoperative patients.

Materials & Methods:

We conducted a prospective observational study at King Fahad Medical City (KFMC), a tertiary care center in Riyadh, Kingdom of Saudi Arabia for six months.

85 participants enrolled in this study were randomized to receive either IV Oxycodone (42 subjects), or Morphine (43 subjects).

We included in our study adult surgical patients undergoing General Surgical, Plastic or Orthopedic procedures at King Fahad Medical City. Patients were randomly selected to receive either Morphine 1mg PCA dose and Oxycodone 0.5 mg PCA dose with a lockout time set at 8 minutes. Both drugs were prepared by the pharmacy, and both the person administering the PCA and the data collector were blinded on which subject received which drug.

Since our study population considered to be opioid naïve; therefore, the researchers have decided to compare 1 mg Morphine to 0.5 mg Oxycodone through PCA. Furthermore, Oxycodone recently introduced into the drugs formulary at KFMC; the researchers are not familiar with the previous use of this drug in this setting.

Exclusion criteria included hypersensitivity to either Morphine or Oxycodone, unstable systemic diseases (sickle cell disease and cancer), and a history of opioid dependence. Patients' demographic data, type of surgery, and adverse events obtained from the patient's medical records. Pain intensity assessed using the Visual Analogue Score (VAS).

The primary outcome of our study was to record the VAS of the participants at 6, 12, 24 hours respectively after the commencement of IV PCA infusions of Oxycodone vs Morphine. The secondary outcome was to compare total consumption of each drug at 24 hours, and the incidence of adverse effects.

Statistical Analysis:

All Categorical variables such as gender, BMI group, medication, etc. presented as numbers and percentages.

Whereas continuous variables such as age, weight, height, BMI and Pain scores expressed as Mean ± SD. Pearson's Chi-square / Fisher's exact test applied according to whether the cell expected frequency is smaller than 5, and it used to determine the significant relationship between categorical variables. An independent sample t-test was applied to determine the mean significant difference between study characteristics and drugs. P–values less than 0.05 considered statistically significant. All data entered and analyzed through Statistical Package for the Social Sciences (SPSS) 22 (SPSS Inc., Chicago, IL, USA).

Data Collection Methods:

We identified patients in the study through two methods: the operating room admission sheet, or through pharmacy PCA morphine and oxycodone order lists. Any patient started on PCA morphine, or Oxycodone evaluated. The patients' demographic data, type of surgery, interventions, efficacy, and adverse events extracted from a patient's medical record and patient interview to ensure blindness of the results. During the study, we evaluated pain intensity by using the VAS as a pain assessment tool. In addition to patient satisfaction, Morphine and Oxycodone consumption, length of hospital stays, and adverse drug reactions assessed.

Ethical Considerations:

Ethical approval obtained from the KFMC ethical committee. Before interviewing patients, the researchers explained the purpose to all respondents, and written consent obtained from all the participants. The participants had the right not to participate in the study or to withdraw from the study before completion. Patient confidentiality was wholly protected. The study data was collected anonymously **Results:**

Out of the 85 subjects enrolled in the study, 53 (62.4%) were male, and 32 (37.6%) subjects were female. Participants were randomly allocated to receive either Morphine (42 participants) (49.4%) or Oxycodone (43 participants (50.6%). The persons interviewing the patients postoperatively were blinded of which patient received either drug.

Table 1 describes participant's characteristics in terms of gender, BMI, comorbidities, allergies, and adverse effects of the drugs (nausea & vomiting, itching and urinary retention).

Table – 1: Basic and clinical characteristics of all participants (N= 85 100%)

Characteristics	Descriptions	N (n%)
Gender	Male	53 (62.4%)
	Female	32 (37.6%)
BMI	Underweight ≤ 18.5	41 (48.2%)
	Normal weight = 18.5–24.9	16 (18.8%)
	Overweight = 25–29.9	27 (31.8%)
	Obesity ≥ 30	1 (1.2%)
Comorbid disease	None	47 (55.3%)
	Hypertension	6 (7.1%)
	Diabetes	6 (7.1%)
	Asthma	4 (4.7%)
	Hodgkin lymphoma	2 (2.4%)
	Polycystic ovary	1 (1.2%)
	Ischemic heart disease	1 (1.2%)
	Multiple Comorbid Disease	18 (21.2%)
Allergy	No	81 (95.3%)
	Egg	2 (2.4%)
	Egg, Fish, Fruit Candy	1 (1.2%)
	Egg, Banana, Tuna	1 (1.2%)
Nausea/ Vomiting	No	77 (90.6%)
	Yes	8 (9.4%)
Pruritus/ Itch	No	84 (98.8%)
	Yes	1 (1.2%)
Urinary Retention	No	83 (97.6%)
	Yes	2 (2.4%)

Table 2 describes the mean age of our participants (45.35 ± 14.44 years) range14-81 years, and mean BMI (29.93 ± 7.23). Mean Pain Score before PCA was 2.41 ± 1.37 which decreased after 6 hours to a mean pain score of 1.8 ± 0.92 while after next 12 hours and 24 hours the mean pain score reached 1.8 ± 1 and 1.38 ± 1.07, respectively. The minimum time for onset of pain relief after administration of the drugs was 5 minutes, and the maximum time was 18 hours and 6 minutes. The mean cumulative dose of Morphine and Oxycodone were 18.81 ± 12.95 ml and 20.74 ± 13.4 ml, respectively.

Table – 2: Descriptive analysis of study characteristics (n = 85)

Study Characteristics	N	Minimum	Maximum	Median	Mean ± SD
Age (Years)	85	14	81	46.0	45.35 ± 14.44
Weight (Kg)	85	33	113	77.0	77.21 ± 18.26
Height (cm)	85	128	178	160.0	160.85 ± 9.56
BMI (Kg/m^2)	85	14.69	50.90	29.070	29.93 ± 7.23
Pain Score Before PCA	85	0.0	8.0	2.0	2.41 ± 1.37
Time Pain relief (hours: minutes)	85	0:05	18:06	0:23	1:27 ± 2:55
Pain Score Post 6 hours	85	0	4	2	1.8 ± 0.92
Pain Score Post 12 hours	85	0	4	2	1.8 ± 1
Pain Score Post 24 hours	85	0	4	2	1.38 ± 1.07
Total Demand (ml)	85	2	280	20	29.85 ± 36.59
Good Demand (ml)	85	2	48	16	19.79 ± 13.14
Cumulative Morphine (ml)	42	3	47	14.5	18.81 ± 12.95
Cumulative Oxycodone (ml)	43	2	48	18	20.74 ± 13.4

Table 3 describes the association between the studied drugs and the study characteristics. In the Morphine group, there were 33 males (78.6%) and 9 females (21.4%), while in the Oxycodone group, there were 20 males (46.5%) and 23 females (53.5%) (p=0.02)

Table – 3: Impact and association between drugs and study characteristics N = 85

Characteristics	Descriptions	Morphine (N=42)	Oxycodone (N=43)	P Value
Gender	Male	33 (78.6%)	20 (46.5%)	0.002
	Female	9 (21.4%)	23 (53.5%)	
Comorbid Disease	None	21 (50.0%)	26 (60.5%)	0.518
	Hypertension	2 (4.8%)	4 (9.3%)	
	Diabetes	3 (7.1%)	3 (7.0%)	
	Asthma	3 (7.1%)	1 (2.3%)	
	Hodgkin's Lymphoma	2 (4.8%)	0 (0.0%)	
	Polycystic Ovary	1 (2.4%)	0 (0.0%)	
	Ischemic Heart Disease	1 (2.4%)	0 (0.0%)	
	Multiple Comorbid Diseases	9 (21.4%)	9 (20.9%)	

Table 4 describes the mean time for onset of pain relief for morphine and oxycodone was 0:56 ± 1:18 minutes and 1:57 ± 3:51 minutes respectively, which was not significantly different (p=0.103). However, at 12- and 24-hours post starting of PCA, the morphine group showed a lower mean pain score than the oxycodone group. (1.571 ± 0.991 at 12 hours and 1.071 ± 0.973 at 24 hours for Morphine), and 2.023 ± 0.963 at 12 hours and 1.674 ± 1.085 at 24 hours for Oxycodone).

Table - 4 Standard deviation

Characteristics	Mean ± SD	Morphine (N=42)	Oxycodone (N=43)	P Value
Age (Years)	(Mean ± SD)	45.405 ± 11.474	45.302 ± 16.98	0.974
Weight (Kg)	(Mean ± SD)	78.576 ± 17.207	75.884 ± 19.334	0.499
Height (cm)	(Mean ± SD)	159.214 ± 8.612	162.442 ± 10.248	0.120
BMI (Kg/m^2)	(Mean ± SD)	31.165 ± 7.246	28.723 ± 7.09	0.120
Pain Score Before PCA	(Mean ± SD)	2.429 ± 1.172	2.395 ± 1.545	0.911
Time pain relief (hours: minutes)	(Mean ± SD)	0:56 ± 1:18	1:57 ± 3:51	0.103
Pain Score Post 6 hours	(Mean ± SD)	1.762 ± 0.983	1.837 ± 0.871	0.710
Pain Score Post 12 hour	(Mean ± SD)	1.571 ± 0.991	2.023 ± 0.963	*0.036
Pain Score Post 24 hour	(Mean ± SD)	1.071 ± 0.973	1.674 ± 1.085	*0.008
Total Demand (ml)	(Mean ± SD)	35.357 ± 49.093	24.465 ± 16.285	0.178
Good Demand (ml)	(Mean ± SD)	18.81 ± 12.954	20.744 ± 13.404	0.500

Table 5 reveals adverse effects of morphine (N=42) and Oxycodone (N=43) which were not significant. Nausea and vomiting were addressed in 3 patients in morphine group (7.1%) and 5 patient in Oxycodone group (11.6%) and regarding itching was only one patient in oxycodone group (2.3%).

Table – 5: Adverse Effect addressed in morphine and oxycodone Groups (n = 85)

Adverse Effect	Descriptions	Morphine (N=42)	Oxycodone (N=43)	P Value
Nausea / Vomiting	No	39 (92.9%)	38 (88.4%)	0.479
	Yes	3 (7.1%)	5 (11.6%)	
Pruritus/ Itch	No	42 (100.0%)	42 (97.7%)	0.32
	Yes	0 (0.0%)	1 (2.3%)	

Discussion:

This study compares the efficacy of intravenous PCA Oxycodone and Morphine by comparing the total consumption dose of both drugs in 24 hours, time of pain relief after dose administration, and Pain scores pre and post administration of both drugs. The safety of both drugs evaluated by comparing the adverse effects occurring from the administration of both drugs.

IV Oxycodone is used widely for the treatment of acute postoperative Pain. The pharmacological effects of Oxycodone closely resemble those of Morphine, but it has some distinct differences.[24] There were a variety of trials that have shown a good efficacy of Oxycodone in controlling postoperative pain.[25] [26] [27]

The 12 and 24 post-administration pain scores differed between the two drugs significantly. (P=0.036 and 0.008). Morphine achieved a lower mean pain score than Oxycodone (P=1.571 ± 0.091 and 1.071± 0.973) 12 and 24 hours postoperatively. Mean pain score only recoded 2.023 ± 0.963 and 1.674 ± 1.085 in post 12 hours and 24 hours. Our results nearly resemble a study conducted in Germany, where the sum of the pain intensity differences from baseline to 65 minutes during the dose-titration phase was 1.8 for Morphine alone versus 2.7 for morphine/oxycodone (P = 0.12).[28] In a study by Ginsberg et al., higher pain relief scores achieved with oral doses of controlled-release Oxycodone (based on individual conversion factors from IV Morphine). Oral Controlled Release (CR) Oxycodone achieved a significant reduction in pain intensity (score < or =4) within 6 hours of the initial dose. Their results may contribute to the fact that the conversion factors of IV to oral Oxycodone in postoperative patients may play a significant role.[29]

The observed results revealed that there was no significant difference between the mean onset time for pain relief of Morphine and Oxycodone (0:56 ± 1:18 minutes and 1:57 ± 3:51 minutes, P=0.103). Kalso et al., in their study, used Intravenous Morphine and Oxycodone for Pain following abdominal surgery and found that the "first state of pain relief" was achieved faster with Oxycodone (28 min) than Morphine (46 min), and the duration of pain relief was longer with Oxycodone (39 min) than with morphine (27 min).[30]

Opioids often cause adverse effects (AEs) and lead to an economic burden; hence we studied the safety outcomes of intravenous Oxycodone vs. morphine [36]. Our results showed that there was no significant difference between Morphine and Oxycodone regarding allergy, nausea or vomiting, pruritus or itch, and urinary retention. Many studies showed that minimal adverse events occurred with opioids when used postoperatively. [31] [32] [33] [34] [35]

Conclusion:

PCA Morphine utilization in postoperative pain management gave a better pain relief after 12h and 24h of administration compared to PCA Oxycodone. The study showed a similar incidence of adverse effects in both drugs. Further studies are needed to confirm these findings, probably by utilizing higher doses of Oxycodone.

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