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Observation on Clinical Effects of Postoperative Analgesia with Sufentanil After Upper and Lower Abdominal Surgery: A Prospective Study

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Abstract: Post-operative analgesia is crucial to facilitate early ambulation, prevent complications, increase patient satisfaction while ensuring a faster recovery pace. Opioid analgesics have been recognized as the mainstay for treatment of acute pain in a majority of postoperative care units. Intravenous patient-controlled analgesia (IVPCA) with the opioids drugs sufentanil and fentanyl has proven to be effective when used in the immediate postoperative period. The aim of the study was to determine the efficacy and safety of sufentanil for postoperative analgesia based on the same principle, and, fentanyl citrate was chosen as a control drug for upper and lower abdominal operations under general anesthesia. Methodology; It was a prospective clinical study carried out at Union hospital, from December 2014 to March 2015. 240 patients were scheduled for upper and lower abdominal surgery requiring general anesthesia. They were divided into four groups: test group (A) and control group (B); (C) and (D), and are given fentanyl and sufentanil by IVPCA for postoperative analgesia relief following surgery. Pain was assessed by the visual analogue Scale. The determined pain relief; pulse rate, BP, ECG, sedation score, SPO2, pruritus score, nausea score and vomiting score were all recorded for each patient. Results The pressing times values show that fentanyl (A) and high dose sufentanil (C, D) both provided a satisfactory level of analgesia. Moreover, VAS scores of the patients on high dose sufentanil (C, D) were lower, implying superior analgesic effects at these doses. However, low dose sufentanil (B) may only provide limited and inadequate analgesia. The degree of pruritus was less marked in patients on sufentanil than those on fentanyl as demonstrated by the lower Pruritus scores in sufentanil groups (B, C, D). Low dose sufentanil and fentanyl have shown to have similar extent of side effects overall. Conclusion It was found that sufentanil had superior analgesic effect to that of fentanyl in patients who had undergone open abdominal surgery. The extent of the

occurrence of adverse reactions to light in the low-dose sufentanil group (B) is less than that in the high-dose groups (C, D), the concentration of persistent postoperative analgesia sufentanil should reach 0.02μg / (kg ml), and the flow rate maintained at 2ml / h.

Keywords: Sufentanil, Pain, Analgesia Postoperative, IVPCA, General Anesthesia, Upper Surgery, Low Surgery, Wuhan Union Hospital

1. Introduction

Management of acute pain in the intensive care requires emphasis to be laid on achieving satisfactory analgesia with drugs which can suppress pain which is otherwise resistant to conventional analgesics and nonsteroidal anti inflammatory drugs. Morphine is the most commonly used analgesic for providing immediate postoperative pain relief owing to its rapid transport to target tissues after intravenous injection, and, it also exhibits hydrophobic properties thus allowing it to provide analgesia for longer period. However, sufentanil may be preferred over morphine because of its even faster onset of action and shorter duration of action, without exhibiting the side effects of the longer-acting morphine on the system. [1, 2].

In 1979, the International Association for the study of pain (IASP) published the definition of pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". [2, 3]

Acute pain is often due to nociceptive stimuli such as injury, organ dysfunction or disease; the surgery can be assimilated to an injury. [4, 7]

Pain acts as an alarm system to help locate the site of injury and sometimes the cause of an aggression (burning, cramping, and cut). There are 2 types of nociceptive pain visceral pain and somatic pain.

Clinically the consequences of pain on mortality and morbidity are high particularly due to severe pain and the neuroendocrine stress response that follows. Surgical stress can cause tachycardia, increased resistance to systemic circulation and tension. This implies an increase in cardiac work and its need for oxygen therefore being troublesome for patients suffering from coronary heart disease or pericardial disease.

Furthermore, respiratory system will have to increase its activity in order to meet the demand of oxygen. However, this function may be compromised if pulmonary disease is present. Hormonal response induced by pain causes an increase of catecholamine, glucagon and cortical, and a decrease of insulin and testosterone. The increased glucagon and insulin decreased in some patients who undergo a major stress explains the decompensated diabetic mellitus. The cortical stimulate the renin- angiotensin-aldosterone system (RAAS) causing water and salt retention. Increased platelet adhesion and leukocytosis combined with lymphopenia are responsible for the production of a hypercoagulable state due to hematological stress [8, 9, 10].

Our framework is based on the sympathetic hyperactivity in abdominal surgery and also the impacts on the smooth muscles. Urine retention and ileus reflux characterized by nausea and vomiting are noted along with stress gastritis increased gastric acid secretion. Eventually, pain can be a major threat to the patient's mental state resulting in depression, anxiousness and aggression [9, 11].

Thence, the management of postoperative analgesia pain is paramount. The management of postoperative pain depends on the patient's antecedents, surgery, anesthesia and socio-cultural factors. [11, 12]. Post-operative pain management involves the use of analgesics such as sufentanil.

The assessment of postoperative pain is challenging, particularly to know the pain intensity. The mostly used measurement is the visual analogue scale (VAS) which evaluate the pain intensity on the scale of 0 (no pain) to 10 or 100 (severe and intense pain). [10, 13]

2. Methods

2.1. Type and Period of Study

This study was a prospective clinical study carried out at Union hospital from January 2014 to May 2015. 240 patients who were scheduled for upper and lower abdominal surgery and requiring general anesthesia. The patients' (both male and female) age ranged from 18 to 65 years old with ASA I-II (American Society of Anesthesiology). Surgery duration was estimated to be between 1.5 to 4 hours. Patients were informed to sign an agreement in order to conduct the study.

2.2. Inclusion Criteria

Patient aged more than 30 years or older-programmed for upper or lower abdominal surgery and do not have any history of chronic respiratory, renal or hepatic insufficiency.

2.3. Exclusion Criteria

Exclusion criteria consisted of: Patients with ASA grade ≥III and who participated in other clinical trials 4 weeks prior to the start of the study, patients with a history of poorly-controlled hypertension, pregnancy or lactating female, patients with neurological and psychiatric disorders, severe alcoholism, history of prolonged high doses of sedatives, patients not aged between 18 to 30 years old, patients with known allergy to non-steroidal anti-inflammatory (NSAIDs) and patients with existing heart disease.

2.4. Anesthesia Assessment

Consent forms were collected from patients before proceeding with anesthesia. All patients received the pre-anesthetists check-up including a detailed systemic examination and general examination. Preoperative blood pressure, pulse, respiratory rate and oxygen saturation were recorded.

Anesthesia Induction

Induction of anesthesia was done intravenously by administration of an opiate (fentanyl) at a dose of 2-4 µg / kg, a barbiturate (propofol) of 1.5-2mg / kg, a neuromuscular Blocker (rocuronium) 0.6 mg / kg or (vecuronium) 0.1mg / kg and a benzodiazepine (midazolam) of 1-2mg and finally a rapid intubation was given. All routine investigation like hemoglobin, random blood sugar, serum creatinine, urine routine, blood urea and microscopy examination, clotting time and bleeding time were carried out during the time of induction. All the patients needed pure oxygen. Supplemental Remifentanil and propofol were pumped intravenously by 1% to 3% and sufentanil were given by 0.25µg/kg.

The general anesthesia was maintained with sevoflurane inhalation which is an agent whose minimum alveolar concentration (MAC) is 2, and rocurium or vecuronium bolus for muscle relaxation.

Furthermore, the patients were randomly allocated into 4 groups for postoperative analgesic treatment. Fentanyl (2.5µg/kg) was administered intravenously in control group A (n=60) just 1 hour before the end of the surgery and was maintained with 0.2 µg/ (kg.ml) postoperatively. In group B (n=60), C (n=60) and D (n=60), sufentanil was administered 1 hour before the surgery ends with a dose of 0.25 and was maintained postoperatively with 0.0175 µg/ (kg.ml), 0.02 µg/ (kg.ml), .0225 µg/ (kg.ml) respectively.

2.5. Postoperative Analgesia Assessment

At thirty minutes post-surgery, the patients were connected to an analgesia pump of 120ml total capacity, with a flow rate 2 ml/h, bolus 0.5ml, interval of 15mins and PCA of 48 hours. General information was recorded such as, sex, age, weight, height, physical examination, medical history, drug allergies, co-morbidities and medication history. Effectiveness outcome measures observed indicators, each with a score, at every follow-up point; PCA: patient effective, ineffective press time, dose; VAS Score and the vital signs: SPO2, respiratory rate, pulse rate, BP, pruritus score, sedation score (RAMSAY) and complication if any were assessed after administration of drug.

Table 1. *Sedation score (RAMSAY).*

SCORE	RESPONSE
1	Patient awake and anxious, agitated or restless
2	patient awake and cooperative, oriented, tranquil
3	Patient asleep, responsive to commands
4	Patient asleep with brisk to stimulus (light and noise)
5	Patient asleep with response to pain only

Table 2. *Vomiting score.*

SCORE	RESPONSE
0	No vomiting
1	Mild vomiting, 1-2times /24h
2	Moderate vomiting, 3-5times /24h
3	Severe vomiting > 5times /24h

Table 3. *Pruritus score.*

SCORE	RESPONSE
0	No itching
1	Mild itching
2	Severe itching

2.6. Statiscal Analysis

All statistical analyzes were performed using (SAS) statistical analytic software to complete professional. Parametric statistical test were used wherever possible methods or models. The test, the control group and the test group. $P \leq 0.05$ considered the establishment of superiorly. Other statistical tests all indicators are used two-sided test, $P \leq 0.05$ differences will be considered statistically significant test.

3. Results

Patients (n=240) both female and male with a ASA grade I-II were admitted for lower and upper abdominal surgery with their age ranging from 18 to 65 years old in Union Hospital in the year 2014-2015. The patients were divided postoperatively into 4 groups namely A, B, C, D, A being the control group receiving injection fentanyl and B, C, D group receiving injection sufentanil.

Out of 240 cases, only 184 completed the test. The number of cases in each group was as follows; group A; 42, group B; 41, group C; 51, and group D; 50.

Evaluation

Compared with group A, there was no statistical difference in the group B, group C and D, as the point in the time at each visit pressing times.

Table 4. *Nausea Score.*

Follow-up Point	A with B	A with C	A with D	A with D	A with C	A with B
1h	0.7347	0.2438	0.1211	0.3415	0.1795	0.6621
2h	0.0116	0.0082	0.0264	0.9361	0.7308	0.6649
4h	0.0935	0.0002	0.0263	0.0557	0.6085	0.1537
8h	0.0095	0.0003	0.0011	0.2414	0.4268	0.6978
12h	0.0034	<0.0001	0.0012	0.1676	0.7396	0.2902
24h	0.0010	0.0006	0.0002	0.9570	0.7433	0.7793
48h	0.0001	<0.0001	<0.0001	0.7136	0.7426	0.9837

In each follop-up point there was no statistically significance difference for Ramsay sedation score among all the four groups (Table 5).

The nausea scores groups B, C and D after 2h, 8h, 12h, 24h and 48h were less compared to group A except after 4h.

Evaluation

Table 5. *Pruritus Score.*

Follow-up Point	A with B	A with C	A with D	B with C	B With D	C with D
1h	0.5564	0.2345	0.3874	0.4879	0.7528	0.7028
2h	0.2931	0.4611	0.0479	0.7807	0.2596	0.2081
4h	0.1101	0.0642	0.0344	0.7666	0.5350	0.7443
8h	0.0609	0.0619	0.1215	0.9958	0.7275	0.7316
12h	0.0152	0.0332	0.1136	0.7011	0.3089	0.5196
24h	0.0506	0.0750	0.0215	0.7905	0.7916	0.5682
48h	0.0175	0.0179	0.0088	0.9953	0.7485	0.7443

Table 6. *Distribution of patients according to the pressing times.*

Parameter/time	A and B	A and C	A and D	B and C	B and D	C and D
1 (1h)						
95% CI	0.01 (-0.13, 0.15)	0.06 (-0.08, 0.21)	0.08 (0.06, 0.23)	0.05 (-0.09, 0.20	0.07 (-0.07, 0.22)	0.02 (-0.12, 0.16)
P	1.000	1.0000	0.7196	1.0000	1.0000	1.0000
2 (2H)						
95% CI	-0.05 (-0.28, 0.180	0.17 (-0.06, 0.05)	0.18 (-0.05, 0.41)	0.22 (-0.00, 0.45)	0.23 (0.00, 0.46)	0.01 (-0.22, 0.24)
P	1.0000	0.7909	0.2575	0.0588	0.0459	1.0000
3 (4H)						
95% CI	-0.25 (-0.59, 0.009)	0.21 (-0.12, 0.55)	0.15 (-0.18, 0.49)	0.46 (0.13, 0.80)	0.40 (0.07, 0.74)	-0.06 (-0.40, 0.77)
P	0.2975	0.5612	1.0000	0.0017	0.009	1.0000
4 (8h)						
95% CI	-0.47 (-0.98, 0.04)	0.25 (-0.26, 0.76)	0.27 (-0.26, 0.78)	0.72 (0.22, 1.23)	0.74 (0.23, 1.25)	0.02 (0.40, 0.52)
P	0.0877	1.0000	1.0000	0.0011	0.0008	1.0000
5 (12H)						
95% CI	-0.55 (1.24, 0.14)	0.34 (-0.35, 1.03)	0.40 (-0.29, 1.09)	0.89 (0.21, 1.58	0.96 (0.27, 1.64)	0.06 (-0.62, 0.75)
P	0.2045	1.0000	0.7363	0.0034	0.0014	1.0000
6 (24h)						
95%CI	-0.08 (-2.79, 0.33)	-0.22 (-1.53, 1.10)	0.21 (-1.11, 1.53)	0.77 (-1.54, 2.07)	1.19 (0.11, 2.50)	0.43 (-0.88, 1.73)
P	0.1529	1.0000	1.0000	0.7672	0.0966	
7 (48)						
95%CI	-0.00 (-1.00, 0.40)	0.20 (-0.81, 1.20)	0.52 (-0.49, 1.53)	0.79 (-0.20, 1.79)	1.1790.12, 2.12)	0.32 (-0.68, 1.32)
P	0.6911	1.0000	1.0000	0.2321	0.0187	1.0000

1 The pruritus scores at 12h for groups A and C were equivalent to the scores of group B and D at 48h.

4. Discussion

Postoperative pain is most marked after operation in the upper and lower abdomen and, if treated appropriately or adequately, it may result in low incidence of post-operative complication and morbidity. [10]

This study has shown that there was no significant difference in analgesia among the four groups. The study was designed to compare the efficacy of fentanyl and sufentanil as a postoperative analgesic drug. It has now been established that postoperative analgesia, besides providing relief and comfort to patients, can also facilitate accelerated recovery, an approach labelled as “postoperative rehabilitation”. An ideal analgesicis sought to provide relief of pain without change in consciousness, early return of normal function, having localized effect and be devoid of systemic side effects.

Fentanyl is a μreceptor agonist which belongs to the phenylpiperidine group and exhibits lipophilic properties. Sufentanil is a newer thienyl analogue of fentanyl, and also acts a μreceptor agonist. Sufentanil displays a higher opioid receptor affinity, thus, explaining its analgesic potency of 5 to 10times greater than that of fentanyl. [12, 13]

Demographical groups were comparable with predominance.

In this study, 240 patients aged 18 to 65 years old, of both genders were selected, and their ASA grade, height, physical status, weight and age were arranged in comparable groups. Itching episodes, Ramsay sedation score, the score vomiting, VAS score and score nausea were found to be similar in the four groups.

Pressing times of group B after 2h, 4h, 8h, 12h and 24h respectively compared with the values in group D showed a significant decrease in group D at 4h, 8h and 12h. Group C also showed a significant decrease postoperatively. (table 6)

Fentanyl and sufentanil can achieve good analgesic effect, and, high-dose sufentanil is superior to low dose for providing pain relief.

The results of the 4 groups are presented in table 5. The VAS scores in Group C were considerably lower after 1h and 2 h, while in group D, the scores at 2h, 4 h and 8h were lower than that of group A. When compared with group B, VAS

scores of group D at 4h and 8h were also found to be lower.

Patients in the high-dose sufentanil group (C, D) have reported higher analgesic effects than patients on fentanyl (A), while the lower-dose sufentanil (B), has shown to be less effective to control the pain than high-dose group D. [14, 15, 16, 17]

The VAS activity score after 1h and 2h for Group C, and the VAS score for Group D at 2h post-op displayed lesser values when both were compared with group A. These scores helped to validate the superior analgesic properties at high dosages of sufentanil (C, D) when compared with fentanyl (A).

There were also significant differences (P=0, 05) in the occurrence of pruritus:

Comparison of the pruritus scores in the 4 groups revealed that after 12h, group C had a lower score than group B, C and D were all significantly decreased. This observation showed that the occurrence of pruritus at the 3 doses of sufentanil was less frequent than in the fentanyl patients of Group A.

5. Conclusion

From the results of our study, we can appraise the crucial role of opioids in the management of acute moderate to severe pain. Patient-controlled analgesic administration resulted in a higher degree of satisfaction than nurse-managed approaches. Sufentanil use for analgesia in surgical patients was shown to have superior effect to fentanyl, with lesser extent of adverse reactions to light. Based on the finding that low-dose sufentanil (B) yields less adequate analgesia compared to high dosages (C, D), the concentration of persistent postoperative analgesia sufentanil should reach 0.02μg / (kg ml), the flow rate of 2ml / h.

Conflict of Interest

The authors declare that there is no conflict of interest with any financial organization or corporation or individual that can inappropriately influence this work.

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