EFFECTIVE COMPARISON OF INTRAVENOUS PATIENT CONTROLLED ANALGESIA WITH THE NEFOPAM - FENTANYL MIXTURE AND FENTANYL AFTER BURN NECROSIS EXCISION AND SKIN-GRAFT SURGERY

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ABSTRACT

Objectives: *Compare the analgesic and adverse effects between intravenous patient-controlled analgesia with Nefopam - Fentanyl mixture and single Fentanyl after burn necrosis excision and skin-graft surgery.*

Patients and methods: *A prospective study was conducted on 60 patients in the Intensive care unit (ICU) and the Adult Burn Department of Le Huu Trac National Burn Hospital from 11/2019 to 8/202, divided into 2 groups: Group 1 using single Fentanyl; Group 2 using the Nefopam - Fentanyl mixture via intravenous patient-controlled after burn debridement and grafting surgery. Patients were from 16 to 60 years old with an indication surgery, with area ≥ 5% total body area; without contraindications to Nefopam and Fentanyl; without mechanical ventilation or maintaining mechanical ventilation after surgery.*

Results: *The difference in VAS at rest and movement was not statistically significant. The Fentanyl consumption in group 2 was lower than that in group 1. Although the bolus times were lower, the amount of Fentanyl bolus of patients in group 1 was higher than that in group 2. The "very satisfied" and "satisfied" rates were high in both groups. There were no patients with serious respiratory and circulatory disorders. The rate of nausea and vomiting of patients in group 1 was higher than that in group 2.*

Conclusion: *Intravenous patient-controlled analgesia with Nefopam - Fentanyl mixture and single Fentanyl had a good analgesic effect after burn necrosis excision and skin graft surgery but the rate of nausea and vomiting of patients in a group using the mixture was lower than that in the other group.*

Keywords: *Nefopam, Fentanyl, intravenous patient-controlled analgesia, after burn necrosis excision and skin graft surgery.*

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1. INTRODUCTION

In burn treatment, necrosis excision and skin-graft surgery are common and often repeated, leading to badly continuous postoperative pain. Suppose pain after burn surgery is inadequately managed, it will adversely affect the recovery such as causing bleeding at the necrosis removal and skin donor sites, hematoma under grafted skin where skin pieces start to peel, cardiovascular, respiratory, endocrine and immune system disorders and leading to negative psychophysiological effects on patients. In burn pain treatment, using opioids such as Morphine and Fentanyl is common and considered the gold standard [1].

Fentanyl is a synthetic opioid with a rapid onset of action that is 100 times stronger than morphine. However, it may have some adverse effects such as nausea and vomiting, sedation, respiratory inhibition, urinary retention, pruritus and vertigo [2], [3].

Nefopam (Acupan) is a non-opioid analgesic that has been in clinical application since 1980 in Europe and used for postoperative analgesia in Vietnam.

Currently, in Vietnam, there has not been any research using intravenous PCA with the combination of nefopam and fentanyl for analgesia after this type of surgery.

2. MATERIALS AND METHOD

2.1. Materials

2.1.1. Patients

Patients with the indication of burn necrosis debridement and grafting surgery in Le Huu Trac National Burn Hospital from 2019 November to 2020 August.

2.1.2. Inclusion criteria

- Patients and their relatives agreed to participate in the study.

- Patients aged from 16 to 60 years, who were suggested surgical treatments with areas ≥ 5% total body surface area.

- Patients with ASA (American Society of Anaesthesiologists) I, II.

- Without contraindication to Nefopam, Fentanyl and Kevindol.

2.1.3. Exclusion criteria

- Patients with an endotracheal tube, tracheostomy and mechanical ventilation or maintenance of mechanical ventilation after surgery.

- Patients were addicted to opioids and alcohol.

2.1.4. Elimination criteria

- Patients with surgical or anesthetic accidents and complications.

- Did not collect enough parameters.

2.2. Method

2.2.1. Study design

A clinical, prospective, descriptive study with comparisons.

2.2.2. Procedure

- ***Preoperative preparation for patients at the ward***

- Paranaesthesia evaluation, compared with the inclusion criteria.

- Guided patients to use the VAS ruler.

- Guided patients and their relatives to use PCA electric injection pump.

- ***At the operating room***

- Carried out anaesthesia following the procedure:

+ Premedication: Midazolam 0.05mg/kg; Atropine 5mcg/kg; Fentanyl 2mcg/kg, injected 5 minutes before general anaesthesia.

+ Induction: Ketamine 1 - 2mg/kg; Propofol 2 - 3mg/kg (slow in 60 seconds); when patients had enough anaesthesia, applied laryngeal mask.

+ Maintenance: Propofol 5 - 10mg/kg/h via an electric injection pump, supplied 1mcg/kg/dose of Fentanyl based on the PRST score.

- Monitored the vital signs every 5 minutes until the end of surgery.

- Collected the parameter following the study medical record.

- Prepared analgesics and set up the PCA electric injection pump:

+ Group F: Mixed 2 Fentanyl 500mcg/10ml ampoules with distilled water to 40ml of Fentanyl solution with a concentration of 25mcg/ml. Patient-controlled analgesia (PCA) settings: 1ml/h (25 mcg/h) basal dose, 1ml (25mcg) bolus dose, 10 min lockout interval, 15ml/4 hours dose limit. If VAS was ≥ 4 after three consecutive bolus presses, a pain rescue intravenous injection with 30 mg of Kevindol was needed. 5 minutes after the first pain rescue injection, if VAS ≥ 4, used the second dose of intravenous Kevindol 30mg.

+ Group NF: Mixed 1 Fentanyl 500mcg/10ml and 4 Nefopam 20mg/1ml ampoules with distilled water to 40ml of solution mixture (Fentanyl 12.5mcg/ml and Nefopam 2mg/ml). PCA settings: 1ml/h (12.5mcg Fentanyl + 2mg Nefopam/h) basal dose, 1ml (12.5mcg Fentanyl + 2mg Nefopam) bolus dose, 10 min lockout interval, 15ml/4 hours dose limit. If VAS was ≥ 4 after three consecutive bolus presses, a pain rescue intravenous injection with 30 mg of Kevindol was needed. 5 minutes after the first pain rescue injection, if VAS ≥ 4, used the second dose of intravenous Kevindol 30mg.

- ***At the post-anesthesia care unit (PACU):***

- Removed the laryngeal mask when patients meet the criteria of consciousness, body temperature, hemodynamics and respiration. Started the PCA procedure.

- Patients were transferred to the postoperative care unit when Aldrete score ≥ 9.

2.2.3. Parameters

- General parameters: Age, gender, height, BMI, total burn size, deep burn area, and the surgical area, operation duration, anesthesia duration

- Postoperative analgesia assessment: VAS score, PCA duration, the total amount of Fentanyl and Nefopam consumed for PCA, Number of bolus doses, amount of Fentanyl bolus, A/D index.

- Adverse effects: Respiratory depression, nausea and vomiting, dry mouth, palpitation, sweating…

2.2.4. Timeline

Data were collected at the following times:

H_0: start of PCA (the patient awoke and removed the laryngeal mask)

H_1: 1 hour after the start of PCA

H_2: 2 hours after the start of PCA

H_3: 3 hours after the start of PCA

H_6: 6 hours after the start of PCA

H_9: 9hours after the start of PCA

H_{12}: 12 hours after the start of PCA

H_{kt}: end of PCA (before dressings change on the next day).

2.3. Data processing

Data were collected and processed according to the medical statistical method with the software SPSS 22.0. Results were displayed as mean ± standard deviation ($\overline{X} \pm SD$), percentage (%), compared mean values by T-student and χ^2 test; statistical significance with p-value < 0.05.

3. RESULTS

Table 3.1. General parameters

Parameter	Group F (n = 30) $\overline{X} \pm SD$ (Min-Max)	Group NF (n = 30) $\overline{X} \pm SD$ (Min - Max)	p
Age (year)	33.50 ± 10.31 (17 - 52)	34.80 ± 9.46 (20 - 51)	> 0.05
Weight (kg)	61.43 ± 5.86 (50 - 70)	59.47 ± 7.46 (40 - 75)	> 0.05
Height (cm)	165.17 ± 5.03 (155 - 173)	162.53 ± 6.08 (149 - 175)	> 0.05
BMI	22.48 ± 1.34 (19.10 - 25.10)	22.46 ± 2.08 (16.73 - 26.57)	> 0.05
Total burn area (%)	34.40 ± 20.87 (5 - 82)	35.87 ± 17.68 (11 - 74)	> 0.05
Deep burn area (%)	16.57 ± 11.58 (5 - 52)	14.73 ± 875 (5 - 40)	> 0.05
Burn necrosis excision area (%)	8.73 ± 3.55 (5 - 20)	9.40 ± 4.18 (0 - 20)	> 0.05
Skin-graft area (%)	7.07 ± 5.11 (0 - 20)	7.20 ± 4.97 (0 - 20)	> 0.05
Operation duration (minute)	79.17 ± 15.21 (60 - 120)	78.67 ± 17.27 (55 - 115)	> 0.05
Anesthesia duration (minute)	84.17 ± 15.21 (65 - 125)	83.67 ± 17.27 (60 - 120)	> 0.05

Table 3.2. Gender and ASA

Parameter	Group F (n = 30)		Group NF (n = 30)		p
	Number	%	Number	%	
Male	23	76.67	20	66.67	> 0.05
Female	7	23.33	10	33.33	
ASA I	25	83.33	26	86.67	> 0.05
ASA II	5	16.67	4	13.33	

Table 3.3. VAS at rest

Timeline	Group F (n=30) $\bar{X}$±SD (Min-Max)	Group NF (n = 30) $\bar{X}$±SD (Min-Max)	p
H_0	2.13 ± 0.35 (2 - 3)	2.17 ± 0.38 (2 - 3)	> 0.05
H_1	2.30 ± 0.47 (2 - 3)	2.33 ± 0.48 (2 - 3)	> 0.05
H_2	2.27 ± 0.45 (2 - 3)	2.27 ± 0.52 (2 - 4)	> 0.05
H_3	2.23 ± 0.50 (2 - 4)	2.27 ± 0.58 (2 - 4)	> 0.05
H_6	2.23 ± 0.57 (2 - 4)	2.23 ± 0.63 (2 - 4)	> 0.05
H_9	2.17 ± 0.46 (2 - 4)	2.20 ± 0.55 (2 - 4)	> 0.05
H_{12}	2.13 ± 0.43 (2 - 4)	2.23 ± 0.50 (2 - 4)	> 0.05
H_{kt}	2.10 ± 0.31 (2 - 3)	2.13 ± 0.35 (2 - 3)	> 0.05

$^*p < 0.05$ when comparing with the value at H_0.

Table 3.4. VAS on movement

Timepoint	Group F (n = 30) $\bar{X}$±SD (Min-Max)	Group NF (n = 30) $\bar{X}$±SD (Min-Max)	p
H_0	2.27 ± 0.45 (2 - 3)	2.30 ± 0.47 (2 - 3)	> 0.05
H_1	2.97 ± 0.41* (2 - 4)	3.00 ± 0.59* (2 - 4)	> 0.05
H_2	3.20 ± 0.61* (2 - 5)	3.27 ± 0.64* (2 - 5)	> 0.05
H_3	3.57 ± 0.77* (3 - 5)	3.63 ± 0.77* (2 - 5)	> 0.05
H_6	3.50 ± 0.57* (3 - 5)	3.60 ± 0.62* (2 - 5)	> 0.05
H_9	3.47 ± 0.51* (3 - 4)	3.53 ± 0.51* (3 - 4)	> 0.05
H_{12}	3.30 ± 0.47* (3 - 4)	3.37 ± 0.56* (2 - 4)	> 0.05
H_{kt}	3.00 ± 0.46* (2 - 4)	3.03 ± 0.32* (2 - 4)	> 0.05

$^*p < 0.05$ when comparing with the value at H_0.

Table 3.5. PCA duration and amount of fentanyl and nefopam used for postoperative analgesia, Number of a bolus, amount of fentanyl bolus and A/D index

Parameter	Group F (n = 30) $\bar{X}$±SD (Min-Max)	Group NF (n = 30) $\bar{X}$±SD (Min-Max)	p
PCA duration (hour)	20.47 ± 0.57 (20 - 22)	20.63 ± 0.85 (19 - 22)	> 0.05
Fentanyl (mcg)	562.50 ± 17.06 (525 - 600)	295.42 ± 17.52 (262,5 - 350)	< 0.05
Nefopam (mg)	0	47.27 ± 2.80 (42 - 56)	
Number of bolus (time)	2.03 ± 0.67 (1 - 3)	3.00 ± 1.05 (1 - 6)	< 0.05
Amount of Fentanyl bolus (mcg)	50.83 ± 16.72 (25 - 75)	37.50 ± 13.13 (12.5 - 75)	< 0.05
A/D index (%)	97.50 ± 7.63 (75 - 100)	96.58 ± 9.25 (62,5 - 100)	> 0.05

Table 3.6. Patient satisfaction

Satisfaction scale	Group F (n = 30)		Group NF (n = 30)		p
	Number	%	Number	%	
Very satisfied	5	16.67	3	10	> 0.05
Satisfied	22	73.33	26	86.67	> 0.05
Not satisfied	3	10	1	3.33	> 0.05

Table 3.7. Adverse effects

Adverse effects	Group F (n = 30)		Group NF (n = 30)		p
	Number	%	Number	%	
Nausea and vomiting	8	26.67	2	6.67	< 0.05
Itching	4	13.33	2	6.67	> 0.05
Dizziness	3	10	1	3.33	> 0.05
Dry mouth	2	6.67	4	13.33	> 0.05

4. DISCUSSION

4.1. General parameters

The results in the Table 3.1 showed that the mean age of patients in the group F was 33.50 ± 10.31 years (ranged from 17 to 52 years old) and in the group NF, the figure was 34.80 ± 9.46 years (ranged from 20 to 51 years old). The difference in age between the two groups was not statistically significant (p > 0.05).

In the study, we selected patients aged 16 and over because, at this age range, the patients were able to answer questions accurately, feel and describe the postoperative pain based on the VAS ruler. We did not choose patients over 60 years old due to co-morbidities and contraindications to the drugs used in the study.

According to the results from Table 3.1, the mean weight of patients in group F was 61.43 ± 5.86kg, and in group NF was 59.47 ± 7.46kg. The difference was not statistically significant (p > 0.05). The mean height of the patients was 165.17 ± 5.03 cm in the group F and 162.53 ± 6.08cm in the group NF (p > 0.05), which was appropriate to the height of Vietnamese. The difference was not statistically significant (p > 0.05). The BMI index in the two groups was 22.48 ± 1.34 and 22.46 ± 2.08 (p > 0.05) respectively. Hence, most patients in our study were in moderate physical status.

The total burn size was 34.40 ± 20.87% and 35.87 ± 17.68%, the deep burn area was 16.57 ± 11.58% and 14.73 ± 8.75%, the burn necrosis excision area was 8.73 ± 3.55% and 9.40 ± 4.18%, the skin-graft area was 7.07 ± 5.11% and 7.20 ± 4.97%, respectively. The difference was not statistically significant (p > 0.05). Our results were lower than those of Nguyen Ngoc Thach (2020) when using Fentanyl via PCA after burn necrosis excision and skin-graft surgery, the total burn size and deep burn were 41.6 ± 15% and 16.9 ± 11.9%, respectively [4]. It was probably because the patients in his study were in the ICU with a major burn and depth.

In contrast, in our study, the patients were in both ICU and Adult Burn Department with less burn size and depth. However, with over 30% of burn size, most of our burn patients were severe and required a large surgical area that helps to assess the analgesic effect more accurately.

All the patients in our study were given intravenous general anaesthesia and the airway was controlled with the laryngeal mask. The results in Table 3.5 showed that in group F and NF, the operation duration was 79.17 ± 15.21 minutes and 78.67 ± 17.27 minutes, the anaesthesia duration was 84.17 ± 15.21 minutes and 83.67 ± 17.27 minutes, respectively (p > 0.05).

Table 3.2 described a higher proportion of males in both groups (76.7% in group F and 66.7% in group NF). The difference in gender between the two groups was not statistically significant with p > 0.05. Overall, in both groups, the rate of males was 43/60 (71.67%) and the rate of females was 17/60 (28.33%). The gender distribution in our study was similar to Le Hai Trung (2016) when he studied postoperative analgesia with continuous intravenous infusion of morphine in 7 female patients (21.87 %) and 25 male patients (78.13 %) after burn debridement and grafting surgery.

In our study, most patients had ASA I with 25 patients (83.33%) in group F and 26 patients (86.67%). The difference was not statistically significant with p > 0.05 (Table 3.2). We did not choose the patients with ASA III because the severity of comorbidities might lead to complications due to the side-effects of analgesics.

4.2. Evaluation of the analgesic effect

4.2.1. The VAS at rest and on movement after surgery

In the study, we evaluated the postoperative pain level based on the VAS at rest (VASr) and on movement (VASm). Table 3.3 showed that the mean VASr was < 3 (mild pain) during the analgesia process. The VASr increased at H_1 comparing to H0, then dropped gradually until Hkt. It could be explained by the persistent effect of analgesics and anaesthetics at H_0 (mild pain). This effect decreased at H_1 and the patients were more painful (VASr increased). From H_2, under the effect of PCA, the VASr went down gradually until H_{kt}. It also proved that our technique brought real postoperative analgesia. At most time points, the VASr in group NF was higher than that in group F. However, the difference was not statistically significant with p > 0.05 and the VASr was < 3 (mild pain) in group NF. It meant that the analgesic effect was good adequately for patients. In the study by Nguyen Ngoc Thach (2020) [4], the VASr fluctuated from 2.03 ± 0.17 to 5.03 ± 0.17.

So, the VASr in our study fluctuated less than those in these authors', which showed that our technique had a more stable analgesic effect. Hyun Seung Jin (2016) [5] evaluated the pain severity based on the NRS scale and found that IV PCA with Nefopam - Fentanyl reduced NRS at rest (NRSV) and the NRSr was in 2 - 4 range (mild pain) at 24 hours postoperatively. Thus, our results were appropriate with these authors. Jee Youn Moon et al. (2016) [6] using the IV PCA for patients with laparoscopic total hysterectomy found that at 24 hours postoperatively, the NRS score of the single fentanyl group was 2.9 ± 2.4 and the two nefopam-fentanyl groups were 2.9 ± 1.8 and 3.1 ± 1.7 correspondings to mild pain.

Regarding VASm, the results in Table 3.4 showed that the mean VASm was < 4 (mild pain) during the analgesia process. In both groups, the VASm increased and was highest at H3, then dropped gradually. At the time points from H1 to Hkt, the VASm was higher than that at H0 with a statistical significance (p < 0.05).

However, the VASm always maintained < 4 (mild pain) throughout the analgesia process. The VASm in group NF was higher than that in group F at any time points, but the difference was not statistically significant with p > 0.05. In the study by Hyun Seung Jin (2016) [5], the NRSm of patients in group Nefopam - Fentanyl decreased and was always lower than that in group fentanyl. At 24 hours after surgery, the NRSm was in the 4 - 6 range, which meant moderate pain.

4.2.2. The PCA duration, cumulative consumption of Fentanyl and Nefopam during the PCA process, the number of bolus times, the amount of Fentanyl bolus, the A/D index and pain rescue issue

According to the results in Table 3.5, the mean PCA duration was 20.47 ± 0.57 hours in group F and 20.63 ± 0.85 hours in group NF (p > 0.05). In the study, we

ended the PCA before dressings change on the next day because the patients would be given opioids or general anaesthesia during this procedure. Our PCA duration in our study was similar to that in the study by Nguyen Ngoc Thach (2020) [4] with 20.9 ± 0.87 hours.

The cumulative consumption of Fentanyl was 562.50 ± 17.06mcg in group F, which was more than that in group NF with 295.42 ± 17.52mcg. The difference was statistically significant with $p < 0.05$. The total amount of Nefopam in group NF was 47.27 ± 2.80mg. The amount of Fentanyl in group F was corresponded to that in the study by Nguyen Ngoc Thach (2020) [4] with 568.2 ± 85.9mcg.

In the study by Jee Youn Moon et al. (2016) [6], the cumulative consumption of Fentanyl over 48 hours was 236.1 ± 128.1mcg in the group Fentanyl and 107.5 ± 74mcg in the group Nefopam - Fentanyl, which was much lower than our figures. It could be explained that we used the basal dose and a higher concentration of fentanyl (25mcg/ml and 12.5mcg/mg comparing with 10mcg/ml and 5mcg/ml). That was because apart from surgical pain, burn patients often underwent the basal pain caused by burn damage. On the other hand, most patients were given opioids for dressings change every day; therefore, it needed a larger dose of drugs to reach the desired analgesic effect.

Table 3.5 indicated that the number of bolus times was 2.3 ± 0.67 times in group F), which was lower significantly than that in group NF with 3.00 ± 1.05 times ($p < 0.05$). However, the amount of Fentanyl bolus in group F was 50.83 ± 16.72 mcg, which was higher than that in group NF with 37.50 ± 13.13 ($p < 0.05$). Thus, IV PCA with Nefopam - Fentanyl mixture reduced the Fentanyl consumption significantly and ensured a good analgesic effect. The A/D index at the end of the PCA process was quite similar and high in both groups with 97.50 ± 7.63 % in group F and 96.58 ± 9.25% in group NF ($p > 0.05$). It meant that the IV PCA met the patients' demand for analgesia quite well. Therefore, no patient needed the "pain rescue" with Kevindol 30mg in our study.

In the study by Jee Youn Moon et al. (2016) [6], at 48 hours postoperatively, the number of bolus times was 30.3 ± 21.8 in group F, and 27.6 ± 24.4 in group NF, which were much higher than our figures and the patients in group fentanyl needed 1.1 ± 1.4 while the group Nefopam - Fentanyl needed 0.9 ± 1.1 pain rescue injection with Ketorolac 30mg. The A/D index in our study was higher than that in the study by Nguyen Ngoc Thach (2020) [4] with 90.4 ± 10.2% and the pain rescue with Kevindol rate in his study was 5.7%. Therefore, the IV PCA with the basal dose and drug concentration as in our study met the requirement of analgesia better than these authors.

4.2.3. Patient satisfaction

The results in Table 3.6 showed that in group F and NF, the proportion of "very satisfied" accounted for 16.7% and 10%, "satisfied" accounted for 73.33% and 86.67% and "not satisfied" accounted for 10 % and 3.33%. The difference was not statistically significant with $p > 0.05$. Thus, most patients were very satisfied and

satisfied with the postoperative PCA process (90% in group F and 96.67% in group NF).

In the study by Jee Youn Moon et al. (2016) [6], the rate of “very satisfied” and “satisfied patients” in the three groups was 77.7%, 71.4 % and 80.8%. These figures were lower than ours.

In the study by Hyun Seung Jin (2016) [5], the rate of “very satisfied” and “satisfied” patients in group NF was > 90%. Nguyen Ngoc Thach (2020) [4] when using Fentanyl via IV-PCA for pain control after burn debridement and grafting surgery reported that the proportion of “very satisfied”, “satisfied” and “not satisfied” patients were 5.7%, 88.6% and 5.7 % respectively. The “very satisfied” and “satisfied” patients were a majority that demonstrated effective pain control after burn debridement and grafting surgery.

4.3. Side-effects

In our study, the only adverse effects were vomiting and nausea, itching, dizziness and dry mouth. Other undesirable effects such as respiratory depression, shivering, sweating and tachycardia did not appear in the study group of patients.

According to the results in Table 3.7, the proportion of patients with vomiting and nausea in group F was significantly higher than the figure in group NF (26.67% and 6.67. Hyun Seung Jin et al. (2016) when using PCA Nefopam - Fentanyl after laparotomy [5] also showed a 25% prevalence of nausea and vomiting.

Jee Youn Moon et al. (2016) [6] also reported a rate of 59.3 % nausea and vomiting when using PCA Fentanyl after a laparoscopic total hysterectomy. Thus, when combining Nefopam and Fentanyl for the IV PCA, the rate of vomiting and nausea in our study was much lower than IV PCA with single Fentanyl in the above studies. In addition, in our study, the patients underwent skin surgery under total intravenous anaesthesia (TIVA) with Propofol and Fentanyl and most of them were given opioids repeatedly. It probably contributed to making the rate of postoperative nausea and vomiting lower than in the above studies.

Other adverse effects observed in the study were pruritus, dizziness and dry mouth. The difference was not statistically significant between the two groups.

The above adverse effects were only transient and caused discomfort for the patients at a few postoperative time points without any medication or procedure treatment.

5. CONCLUSION

Through a study on 60 patients undergoing postoperative analgesia after burn debridement and grafting surgery with the Nefopam - Fentanyl mixture and single Fentanyl via IV PCA, we drew the following conclusions:

- Both methods gave a good analgesic effect: The mean VAS at rest < 3 and VAS on movement < 4 during analgesia process, the A/D index was high (> 90%) and most patients were very satisfied and satisfied with the procedure. No patient needed the “pain rescue” dose. The cumulative consumption of Fentanyl was

more than that in group NF ($p < 0.05$). Although the bolus times were lower, the amount of fentanyl bolus of patients in group F was higher than that in group NF ($p < 0.05$).

- The adverse effects included nausea and vomiting, itching, dizziness and dry mouth. The rate of nausea and vomiting was lower than that in PCA with single Fentanyl ($p < 0.05$).

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