

COMPARISON OF POST-OPERATIVE ANALGESIA WITH FENTANYL AND SUFENTANIL VIA EPIDURAL ROUTE IN THORACIC AND UPPER ABDOMINAL SURGERIES

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ABSTRACT

Background: Post-operative analgesia has been considered very important for patient in terms of early mobilization and prevention of complications. Opioid analgesics have long been recognized as among the most effective treatments for pain. Opioids like fentanyl and sufentanil have been successfully used for post-operative analgesia by epidural route.

Aims & Objective: To evaluate the efficacy of Sufentanil and Fentanyl for post-operative analgesia following thoracic and upper abdominal surgeries through epidural route.

Materials and Methods: This was a prospective randomized parallel group study of 60 patients. They were divided into two groups randomly, F and SF. They were given fentanyl and sufentanil by epidural route for post-operative pain relief following upper abdominal and Thoracic surgery. Pain was assessed through Visual analogue scale. Pain Relief assessment, Pulse rate, BP, Respiratory rate, SPO₂, Sedation Score and complication if any were assessed after administration of drug at 0,2,5,10,30,60,120, 240 and 300 minutes. Result obtained were statistically analysed using students unpaired t test after calculating mean and standard deviation.

Results: Patients in both group were comparable in terms of demography with male predominance, ASA grade and type of surgery performed. Onset of pain relief was 7.22 ± 1.82 minutes with fentanyl while 3.40 ± 0.90 with sufentanil. Peak analgesic effect was achieved at 20.36 ± 3.44 minutes with fentanyl while it was quicker with sufentanil (9.3 ± 2.4). Duration of analgesia was higher in sufentanil group (254.1 ± 53.80) in comparison to fentanyl (185.2 ± 43.33).

Conclusion: Sufentanil via epidural route provides early onset, peak effect and longer duration of effective analgesia in comparison to Fentanyl. Use of either drug via epidural route provide safety and better stabilization as far as the hemodynamic and respiratory parameters were concerned. But, Patients with sufentanil remained sedated for longer duration than fentanyl.

Key Words: Fentanyl; Sufentanil; Epidural Analgesia; Post-Operative Pain

Introduction

Post-operative analgesia has been considered very important for patient in terms of early mobilization and prevention of complications. It should provide enough analgesia during rest as well as in movement in post-operative period. Post-operative analgesia can be achieved by various pharmacological measures including systemic opioids, NSAIDs and regional analgesia techniques like epidural analgesia.^[1]

Opioid analgesics have long been recognized as among the most effective treatments for pain. Opioids like fentanyl and sufentanil have been successfully used for post-operative analgesia by epidural route.^[2-5] Advantages includes avoidance of systemic toxicity, easy supplementation by catheter, early mobilization and low failure rate. Opioids since their first use in the epidural and subarachnoid space, have become the mainstay of post-operative pain relief. With the availability of newer agents like fentanyl and sufentanil these drugs have gained widespread use as post-operative analgesic via the

epidural route.

Fentanyl has been considered as potent analgesic action with rapid onset, but of short duration of action with good cardiovascular stability. Sufentanil is proven to be more potent than fentanyl with less sedation.^[5] Potency ratio of sufentanil/fentanyl has been reported to be 5-7:1 for intravenous administration, but we cannot extrapolate this data in case of epidural route. As lipid solubility of sufentanil is higher in case of intravenous route this will result into higher penetration of BBB resulting into higher ratio, while in case of epidural route, higher lipid solubility results into larger uptake of it into epidural fat, which ultimately results into decreased potency ratio in comparison to intravenous route.^[6]

Various studies have compared fentanyl and sufentanil in major abdominal surgeries, caesarean section for post-operative analgesia by epidural route.^[4-7] So keeping these aspects in mind, we decided to compare and contrast sufentanil with the time tested and widely used opioid fentanyl for the relief of pain after thoracic and upper

abdominal surgeries via epidural route.

Aims of study: Considering the importance of post-operative pain relief in thoracic and upper abdominal surgeries we conducted current study to evaluate the efficacy of Sufentanil and Fentanyl for post-operative analgesia following thoracic and upper abdominal surgeries through epidural route with the following parameters. Our co primary end points were time required for onset of action, peak effect and duration of analgesia. Secondary end points were changes in hemodynamic and respiratory parameters and depth of sedation.

Materials and Methods

This was a prospective randomized study carried out at SSG Hospital Vadodara during 2006 to 2008. Total 60 patients were enrolled for this study. Patients scheduled for planned thoracic and upper abdominal surgery, with ASA grade I, II and III were selected. Patients from 20-60 year age irrespective of gender were enrolled. Patients with history of allergy to drugs used in study were excluded. Other exclusion criteria includes local infection around spine, bleeding disorders, spinal deformities, convulsions and alcoholic patients. Patient suffering from psychiatric disorders and pregnant and lactating patients were excluded. Patient who refused to participate in the study were excluded. Written informed consent was obtained from patients.

All patients underwent thorough pre anaesthetic check-up, including detailed history, general examination and systemic examination. All routine investigation i.e. Hemoglobin, Random blood sugar, blood urea, serum creatinine, urine routine and microscopic examination, bleeding time and clotting time were carried out. Anaesthetic plan was explained in detail to all patients who were about to enter the study. The visual analogue score for pain was explained.

All the patients were kept Nil by Mouth overnight. Tab. Ranitidine 150 mg and tab Diazepam 10 mg were given at 10 o'clock night. All the patients were premedicated with inj. Glycopyrrolate 10 µg/kg IM, Inj. Ranitidine 50 mg IV, inj. Ondansetron 4mg iv and inj Midazolam 0.3 mg/kg IV. Pre-operative pulse, Blood pressure, respiratory rate and oxygen saturation were recorded. All patients were given Bupivacaine (25%, 8 ml) followed by Thiopentone Sodium for induction of general anesthesia with Succinyl choline. General anaesthesia was maintained with Isoflurane, N₂O and O₂ with Vecuronium.

They were randomly divided into 2 groups by random sequence into Group F and Group SF. They were given either inj. Fentanyl 1 µg/kg diluted up to 10 ml with normal saline or inj Sufentanil 0.5 µg/kg diluted up to 10 ml with normal saline.

Pain was analyzed by visual analogue scale in which score ranges from 0 for No pain to 9-10 for unbearable pain. Pain Relief assessment, Pulse rate, BP, Respiratory rate, SPO₂, Sedation Score and complication if any were assessed after administration of drug at 0,2,5,10,30,60,,120, 240 and 300 minutes. After single shot of the above mentioned drug and rescue analgesia was given to the patient when VAS>5 in form inj.Tramadol 1mg/kg intravenous.

Result obtained were statistically analysed using students unpaired t test after calculating mean and standard deviation.

Results

In our randomized comparative clinical study of 60 patients from ASA physical status, I, II and III scheduled for thoracic and upper abdominal surgeries of age group 20-60 years of either sex were undertaken at the medical college and SSG Hospital, Vadodara in the year 2006 to 2008. Patients were randomly divided in to two groups for post-operative analgesia via epidural route after thoracic and upper abdominal surgeries.

- Group F: inj fentanyl (1 µg/kg) diluted in 10 ml Normal saline
- Group SF: inj Sufentanil (0.5 µg/kg) diluted in 10 ml Normal saline

Mean duration of surgery was 2.46± 0.82 hour in fentanyl group while it was 2.38 ± 1.02 hour in Sufentanil group. Pulse rate, Systolic blood pressure, Diastolic blood pressure and O₂ saturation remain statistically insignificant during entire study in both group. There was no statistically significant sedation score at baseline. Sedation score started to increase in SF group from mean value of 0 to 0.6±0.13 while in group f there was no change in mean value. This change was statistically significant in group SF as compared to group F and continued as significant in group SF up to 120 min. with mean value 0.30±0.38 as compared to 0 sedation score in group f.

Incidence of Nausea /vomiting was same in both the groups.(n=2), while Pruritus occurred in 1 case in SF group, while 2 patients in group f failed to relieve pain following surgery due to technical reason in epidural catheter insertion.

Table-1: Demographic data

Parameters		Group F	Group SF
Age in years (mean ± SD)		36.83 ± 10.89	39.27 ± 12.17
Weight in kg (mean ± SD)		46.33±6.46	46.83±6.25
Sex	M	21 (70%)	18 (60%)
	F	9 (30%)	12 (40%)
ASA grade	I	12 (40%)	16 (53.33%)
	II	8 (26.67%)	8 (26.67%)
	III	10 (33.33%)	6 (20%)

Table-2: Type of Surgery

Surgery	Group F		Group SF	
	N	%	N	%
Pyelolithotomy	15	50	15	50
CMV	3	9.99	3	9.99
MRM	2	6.67	2	6.67
Pericardiectomy	1	3.33	1	3.33
Pneumonectomy	1	3.33	-	-
Decortication	-	-	1	3.33
Thoracotomy	2	6.67	1	3.33
Pancreas surgery	3	9.99	4	13.32
Cholecystectomy	3	9.99	3	9.99

Table-3: Onset of action, Peak effect and Duration of effective analgesia

Parameter	Group F (mean ± SD)	Group SF (mean ± SD)	P value
Onset of action (min)	7.22 ± 1.82	3.40 ± 0.90	< 0.001
Peak effect (min)	20.36 ± 3.44	9.3 ± 2.4	<0.001
Duration of analgesia(min)	185.2 ± 43.33	254.1 ± 53.80	<0.05

Table-4: Visual Analogue Score

Time (Minute)	Group F (mean ± SD)	Group SF (mean ± SD)	P value
0	5.9 ± 0.88	5.63 ± 1.27	>0.05
2	5.1 ± 1.27	4.03 ± 1.67	<0.05
5	4.43 ± 1.48	3.0 ± 1.88	<0.001
10	3.88 ± 1.51	0.83 ± 1.02	<0.001
30	1.48 ± 1.38	0.97 ± 1.16	<0.05
60	1.63 ± 1.52	1.37 ± 1.50	<0.005
120	3.52 ± 1.67	3.0 ± 1.88	<0.005
240	5.26 ± 0.65	4.2 ± 1.58	<0.001
300	-	5.38 ± 0.87	-

Table-5: Sedation Score

Time (Minute)	Group F (mean ± SD)	Group SF (mean ± SD)	P value
0	0	0	-
2	0	0.6 ± 0.13	<0.05
5	0.40 ± 0.46	1.0 ± 0.51	<0.05
10	0.37 ± 0.49	1.0 ± 0.51	<0.05
30	0.80 ± 0.81	1.0 ± 0.51	<0.05
60	0.10 ± 0.31	0.3 ± 0.47	<0.05
120	0	0.3 ± 0.38	<0.05
240	0	0	-
300	-	0	-

Discussion

Surgical procedure in thoracic and upper abdominal region cause severe post-operative pain and if treated adequately or appropriately results in less incidence of post-operative complication and morbidity.

It has now been established that post-operative epidural analgesia after surgery in addition to providing patients comfort, can facilitate accelerated recovery an approach labelled as "post-operative rehabilitation".^[8] An ideal

analgesic should provide relief of pain without change in consciousness, early return of normal function, localized effect and be devoid of systemic side effects. Post-operative pain is most marked after operation in the thorax and upper abdomen.^[9]

In search of other opioids with good analgesic potency and fewer incidence of side effects mainly respiratory depression, a phenyl piperidine derivative fentanyl and thienyl analogue of fentanyl- Sufentanil and many more were discovered and studied. Fentanyl is primarily a μ receptor agonist of phenyl piperidine which is lipid soluble. Sufentanil is a thienyl analogue of fentanyl and μ receptor agonist. The analgesic potency of Sufentanil is 5 to 10 times that of fentanyl and having greater affinity for opioid receptors compared with that of fentanyl.

In this study 60 patients aged between 20 to 60 years of either sex were selected. Demographically groups were comparable with unintentional male predominance. The mean weight and ASA physical status were also comparable in both groups.

Patients undergoing thoracic and upper abdominal surgeries were selected. E. Geller et al compared epidural fentanyl and sufentanil for abdominal surgeries while in a similar study these two drugs were compared for efficacy in intra and post-operative pain management.^[2,5] These opioids were also compared in case of caesarean section.^[3,4]

Patients were randomly divided in two groups and pain relief was provided via epidural catheter at the end of surgery after reversal as in previous studies.^[2,5] Opioids have been used for the relief of severe pain. Main routes of administration are intravascular, intramuscular, oral and epidural. Segmental extradural analgesia is considered to be superior to any other method of managing post-operative pain. Ram Kumar and Prasad suggested that fentanyl and sufentanil being lipophilic, has less cephalad spread and therefore needed administration close to the segmental level where analgesia is required.^[10] We have used inj. Fentanyl 1 μ g/kg and inj Sufentanil 0.5 μ g/kg. At these doses analgesic effects seen predominantly with minimum side effects. Our study dose is comparable with other studies.^[2]

The visual analogue score was used for assessment of pain. As shown in table 6 Mean onset of algesia (VAS<5/10 after administration of the drug via epidural route). Mean onset of analgesia was faster with sufentanil. This can be explained by the greater lipid solubility of sufentanil.^[6] Our

study results are comparable with similar study in which mean onset of action was 5 minutes with sufentanil while it was 10 minutes with fentanyl.^[2] We can also conclude that Mean Peak analgesic effect (VAS < 3/10 after administration of drug via epidural route) was highly significant in group SF in compared to group F. Mean peak effect develops earlier in SF group. The mean duration of effective analgesia was statistically significantly higher in SF group.

Other vital parameters like pulse rate, systolic blood pressure and diastolic blood pressure were comparable in both groups. This findings correlates with findings of other studies.^[2,5] Mean sedation was statistically significant at 120 minutes in SF group. Same findings are observed in other studies.^[2,3]

Conclusion

Sufentanil via epidural route provides early onset, peak effect and longer duration of effective analgesia in comparison to Fentanyl. Use of either drug via epidural route provide safety and better stabilization as far as the hemodynamic and respiratory parameters were concerned. But, Patients with sufentanil remained sedated for longer duration than fentanyl.

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