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EVALUATION OF TRANSDERMAL FENTANYL PATCH FOR THE CONTROL OF POST OPERATIVE ANALGESIA

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ABSTRACT

Aim is to compare the quality and duration of post-operative analgesia 40 patients were randomly allocated into 2 group. Group F: Transdermal fentanyl patch releasing 25microgram/hr of fentanyl Group P: Placebo patch of same size. Patches were applied 4-6 hours before surgery. Heart Rate, Blood Pressure and Oxygen Saturation was recorded during surgery. At approximately 30 minutes before the end of the surgery, Inj Diclofenac 2mg/kg IV given to the patients. Rescue analgesic (Inj. Diclofenac 2mg/kg IV) was given to patients if they complain of pain or if VAS score greater than 4 postoperatively. Duration of analgesia was longest with group f (fentanyl) without any significant side effect. Conclusion is Low dose transdermal fentanyl patch releasing 25µg/hr fentanyl is safe and effective alternative for postoperative analgesia results in significant reduction in postoperative pain score and significantly decrease in requirement of supplementary analgesic postoperatively without any clinically evident respiratory depression. Stastical Analysis Used: Student T test.

Key words: Fentanyl Patch, Post-Operative Analgesia.

INTRODUCTION

Pain relief is one of the important functions of an anaesthesiologist. It must be safe, effective and feasible [1]. The traditional approach of repeated intramuscular administration of opioid analgesics is well known to suffer from such disadvantages as the requirement of patients to convince staff of their need for additional analgesic medication, of possible misinterpretations of doctor's orders, and of inevitable delays before the analgesic agents is actually administered [2-5]. Appreciation of these problems has led to inventions of alternative methods of opioids administration. The control of postoperative pain has led to the development of increasingly invasive techniques. The use of Opioids by epidural, spinal, intravenous and intramuscular analgesia are different invasive modalities mainly used for the relief of postoperative pain. These techniques have inherent risks (bleeding, infections, and pneumothorax) as well as risks related to systemic effects of drugs (pruritus, nausea, respiratory depression and local anesthetic toxicity). Transdermal drug administration results in consistent, stable concentrations of this drug in plasma [6-9]. Transdermal drug administration has got some advantages like direct absorption into the systemic circulation so gastrointestinal destruction and hepatic first pass metabolism are avoided, predictable and extended duration of activity, minimizing undesirable side effects, greater patient compliance due to elimination of multiple dosing profiles and provide suitability for self-administration.

The purpose of this study is to determine the efficacy and safety of a new transdermal fentanyl patch for the control of postoperative pain and to compare it with placebo patch in respect to supplementary analgesic requirement and level of pain relief.

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MATERIALS AND METHODS

We have selected 40 patients withASA grade I and II risk undergoing laparoscopic cholecystectomy and appendicectomy. The patients were electively kept NBM (Nil by Mouth) for 6 hrs before surgery and randomly allocated into 2 groups.

Group F (n =20): Transdermal fentanyl patch

Group P (n =20): Placebo patch

After arrival in operating room, standard monitors like ECG, pulse oximeter and NIBPwere applied. The patient was given premedication of Injection Glycopyrrolate (4µg/kg), Injection Ondansetron (150µg/kg) and Injection Fentanyl (1 µg/kg) intravenously. Then patient was pre-oxygenated through a face mask for 5min. The induction was done with Injection Thiopentone Sodium (2.5%) 5-7 mg/kg and Injection Succinylscoline 2mg/kg intravenously. The patient was intubated with a suitable size portex cuffed endotracheal tube. Throughout the procedure controlled ventilation was maintained with 50%O_2, 50%N_2O (Nitrous Oxide) and sevoflurane and muscle relaxant Injection Vecuronium Intravenously. Heart Rate, Blood Pressure and Oxygen Saturation were recorded during surgery. At approximately 30 minutes before the end of the surgery, Inj Diclofenac 2mg/kg IV given to the patients. After completion of surgery, residual neuromuscular block was reversed with Inj. Neostigmine 0.05 mg/kg and Inj. Glycopyrrolate 0.08 mg/kg. The patients were then extubated after thorough oral and ET suction.

After completion of surgery all patients were observed for 2hrs in recovery room before returning to ward. HR, BP, RR were monitored continuously. Postoperatively VAS (Visual Analogue Scale) Score were recorded at every 2 hourly for 36 hrs. Rescue analgesic (Inj. Diclofenac 2mg/kg IV) was given to patients if they complain of pain or if VAS score greater than 4 postoperatively. Total dose of Inj Diclofenac up to 36 hrs postoperatively were recorded. The incidences of adverse effects such as nausea, vomiting, sedation, pruritus or respiratory depression were evaluated. Respiratory depression was defined by respiratory rate <10 breaths/min.

All the data were filled up in proforma and were statistically analyzed by applying student's t-test for analysis in between two groups for various parameters. The results were considered significant if P value is <0.05.

RESULTS

Table 1. Pulse rate changes in both groups at different intervals.

Time	Group F (Mean±SD)	Group P (Mean±SD)	p value
0min	87.8 ± 6.18	87.5 ± 6.15	0.87
2 hr	88.1 ± 6.17	87.7 ± 6.09	0.83
4 hr	88.9 ± 5.74	88.5 ± 6.18	0.83
6 hr	89.4 ± 6.22	89.1 ± 6.37	0.88
8 hr	89.8 ± 5.26	89.3 ± 5.08	0.76
12 hr	89.1 ± 4.61	89.2 ± 4.42	0.94
16 hr	81 ± 3.008	89 ± 4.83	0.0001
20 hr	76.9 ± 2.93	89.7 ± 5.07	0.0001
24 hr	87.2 ± 5.08	87.6 ± 5.52	0.81
30 hr	87.3 ± 4.55	86.6 ± 4.81	0.63
36 hr	87.9 ± 3.80	87.6 ± 3.76	0.803

Table 2. Systolic blood pressure changes in both groups at different intervals.

Time	Group F (Mean±SD)	Group P (Mean±SD)	p value
0min	131.4±11.48	130.9±10.55	0.88
2 hr	129.8±8.72	127.9±9.025	0.50
4 hr	131.3±8.13	132±8.207	0.787
6 hr	129.3±8.99	129.4±8.33	0.971
8 hr	131.2±7.26	131.5±7.59	0.899
12 hr	130.5±7.30	130.3±7.20	0.93
16 hr	129.5±6.67	128.9±6.30	0.77
20 hr	129±7.66	129.1±7.003	0.96
24 hr	127.9±8.29	127.3±8.21	0.819
30 hr	127.9±7.32	128.2±7.16	0.896
36 hr	128±6.29	127.8±6.18	0.919

Table 3. Diastolic blood pressure changes in both groups at different intervals.

Time	Group F (Mean±SD)	Group P (Mean±SD)	p value
0min	76.9±8.88	76.6±8.00	0.911
2 hr	76.3±7.92	75.4±7.97	0.722
4 hr	77.4±7.62	76.5±7.75	0.695
6 hr	76.9±8.88	76.8±8.69	0.97
8 hr	77.9±8.37	77.6±8.09	0.90
12 hr	78.3±8.76	78±7.89	0.910
16 hr	75.7±8.85	75.2±8.59	0.85
20 hr	76±9.26	75.7±8.71	0.91
24 hr	77.5±8.40	78.1±8.59	0.824
30 hr	77.8±8.65	78±7.89	0.939
36 hr	76.6±8.97	76.1±8.49	0.857

Table 4. Respiratory rate changes in both groups at different intervals.

Time	Group F (Mean±SD)	Group P (Mean±SD)	p value
0min	13.85±1.46	13.1±1.33	0.098
2 hr	13.2±0.767	12.95±0.82	0.327
4 hr	12.95±0.82	12.9±0.85	0.85
6 hr	13.85±1.46	13.55±1.37	0.499
8 hr	13±0.91	13.05±0.825	0.857
12 hr	13.55±2.64	12.85±0.93	0.271
16 hr	12.8±0.833	12.75±0.85	0.852
20 hr	12.85±0.875	12.75±0.85	0.716
24 hr	12.7±0.73	12.35±0.489	0.083
30 hr	12.7±0.80	12.75±0.78	0.843
36 hr	12.25±0.444	12.5±0.512	0.107

Table 5. Supplementary analgesic requirement (average no. of doses)

Time after patch application	Group F (Mean±SD)	Group P (Mean±SD)	p value
0-12 hr	3.2±0.4103	3.5±0.5129	0.048
12-24 hr	1.65±0.4893	2.65±0.4893	0.0001
24-36 hr	0.95±0.6048	2.15±0.6708	0.0001

Table 6. Supplementary analgesic requirement (no. of patients)

Total no. of Doses	Group F (%)	Group P (%)
6	45%	10%
9	0%	40%

Table 7. Side Effects

Side Effects	Group F	Group P
Sedation	0	0
Pruritus	4	0
Bradycardia	0	0
Hypoxia	0	0
Nausea & vomiting	4	2
Respiratory depression	0	0
Allergic reaction	0	0

DISCUSSION

Fentanyl patches are designed to deliver fentanyl at four constant rates: 25, 50, 75, and 100 µg/hr for a period of 72 h. After initial application, a depot of fentanyl forms in the upper skin layers and serum fentanyl Concentrations increase gradually, generally levelling off between 12 and 24 h. The steady state serum concentration is reached after 24 h and maintained as long as the patch is removed. The gradual increase in plasma concentration

when a fentanyl patch is first applied means that some other analgesic is likely to be necessary in the first 12 h.

We studied Transdermal fentanyl patch releasing 25µg/hr of fentanyl and compared with control group (placebo patch) for control of postoperative pain. Our study has demonstrated that Transdermal fentanyl patch is safe and effective for the control of postoperative pain. There was no statistically significant difference in systolic blood pressure, diastolic blood pressure and respiratory rate between two groups since the time of application of transdermal patch. There was a statistically significant difference in pulse rate changes at 16th and 20th hr after patch application in fentanyl group as compared to placebo group. The mean VAS score was 3.0812±1.6355 in fentanyl group and 4.05±0.3419 in control group which was not statistically significant. There was no statistically significant difference in postoperative VAS score at 6 and 8 hr after application of patch in both groups, but there was statistically significant ($P<0.05$) difference seen in fentanyl group as compared to control group in reducing postoperative VAS score 12hr-36hr after application of transdermal patch.

There was no statistically significant difference in supplementary analgesic requirement at 6-12 hrs after patch placement but difference in supplementary analgesic requirement at 12-24 hrs and 24-36 hrs after patch application were statistically significant between two groups($P<0.05$). There were no any major side effects like Bradycardia, Respiratory depression or Hypoxia occurred in both groups.

Pulse rate, blood pressure and Respiratory rate changes

In our study, there was no statistically significant difference in systolic blood pressure, diastolic blood pressure and respiratory rate between two groups since the time of application of transdermal patch. There was a statistically significant difference in pulse rate changes at 16thand 20th hr after patch application in fentanyl group as compared to placebo group. There was significant decrease in heart rate in fentanyl patch group during 8th, 16th, 36th hr observations. This pulse rate changes after fentanyl patch application is consistent with known effects of Opioids on heart rate during effective analgesia.

Supplementary Analgesic Requirement (Average No. of Doses)

We have observed that there was no significant difference in supplementary analgesic requirement at 6-12 hrs after patch placement but difference in supplementary analgesic requirement at 12-24 hr and 24-36 hr after patch application were statistically significant between two groups ($P<0.05$).

Postoperative Side Effects

In our study there were no any major side effects like Bradycardia, Respiratory depression or Hypoxia occurred in both groups. In fentanyl group 4 patients developed pruritus as compared to none in control group ($p<0.05$). Incidence of nausea and vomiting occurred in 4 patients in fentanyl group as compared to 2 patients in control group.

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