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ASSESSMENT OF EFFICACY OF PRE-OPERATIVE TRANSDERMAL FENTANYL PATCH IN POST -OPERATIVE ANALGESIA IN PATIENTS UNDERGOING ABDOMINAL SURGERIES UNDER GENERAL ANAESTHESIA – A PROSPECTIVE RANDOMISED CONTROLLED STUDY

Anaesthesiology

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ABSTRACT

Abdominal surgeries done under general anaesthesia is associated with severe pain in the post-operative period. There are many drugs that can be administered to alleviate post-operative pain. Opioids are an essential to the mitigation of visceral pain associated with abdominal surgeries. Apart from needles and epidural catheters which are invasive, transdermal drug delivery systems are novel, non-invasive, and is associated with increased patient comfort. Among drugs that can be delivered by transdermal route fentanyl is an effective opioid analgesic that has a high potency and high lipid solubility making it suitable for transdermal delivery1. This study attempts at the evaluation of the analgesic efficacy of fentanyl patch applied pre-operatively in alleviation of post-operative pain in patients undergoing abdominal surgeries under general anaesthesia.

KEYWORDS

INTRODUCTION

The incidence and severity of post-operative pain in major abdominal surgeries is well known. To mitigate the pain severity several drugs ranging from NSAID's to Sedative hypnotics have been used. However, opioids are very efficacious and widely practiced mode of analgesia. The maintenance of continuous steady concentration of opioids in the plasma can lead to superior pain relief. Apart from Intravenous infusion, transdermal patch is also a novel drug delivery system that can maintain a steady concentration of plasma opioid levels of drugs such as fentanyl and buprenorphine owing to their lipid solubility properties. Unlike an infusion that requires manual assistance, transdermal patches once affixed can elute a steady drug concentration up to 72hours. They were also associated with minimal side effects as opposed to intravenous bolus doses and had a less incidence of respiratory depression.

AIMS AND OBJECTIVES

This study aims at assessing the efficacy of pre-operatively applied Transdermal fentanyl in alleviation of post-operative pain in patients undergoing abdominal surgeries such as Cholecystectomy, colostomy, oophorectomy, total abdominal hysterectomy, and total vaginal hysterectomy, etc. performed under general anaesthesia.

Primary Outcome: Numeric pain Scale(NRS) in immediate post-op period and at 2 hours, 6 hours, 8 hours, 12 hours, 24 hours, 36 hours and 48 hours.

Secondary outcome : Comparison of Ramsey sedation scale, incidence of adeverse effects and the total doses of rescue analgesics needed

MATERIALS AND METHODS

The investigation was carried out on 60 ASA I and II, 18- to 69-year-old patients scheduled for abdominal surgery, including cholecystectomy, colostomy, oophorectomy, total abdominal hysterectomy, and total vaginal hysterectomy. Patients signed informed consent forms to participate in the study, which was approved by our internal review board. Prior to surgery, medical history was obtained and a physical examination was performed on all patients, as well as routine hematologic and clinicopathologic tests. All the patients were examined in the pre-anaesthetic clinic and deemed fit to undergo surgery under general anaesthesia under ASA Grade I and II.

A total of 60 patients were enrolled in the study of Age 18-75 years and of moderate build. The exclusion criteria was 1) Patients who are allergic to opioids, 2)Patients who have obstructive sleep apnea, 3)Patients above age of 70 years (geriatric patients), 4)Patients undergoing oral and laryngopharyngeal surgery, 5)Patients who have constipation, IBD, other pre-existing abdominal conditions for which they are not being operated upon, 6)High risk for aspiration and BMI is more than 35kg/m2. The 60 patients were using simple random sampling and assigned to two Group A – designated to receive a Placebo in the form of a micropore cut to the same dimension of the Duragesic fentanyl patch (25mcg/hr), The other Group B was the test group which received The Duragesic fentanyl patch (25mcg/hr).

On the day of the surgery, Premedication consisted of 0.2 mg glycopyrrolate and 2 mg midazolam administered intramuscularly about 40 - 60 minutes before induction of anaesthesia. At the same time, the patch was applied on the left anterior chest wall in the mid-clavicular line and shifted to the operative area. General anaesthesia induction and maintenance was standardised between both the groups. The patients NBM (Nil by Mouth) status of 8 hours was confirmed and 18G I/V cannula was secured and Ringer's Lactate solution was started. After attaching all the monitors, baseline readings of Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Oxygen Saturation (SpO2) and Electrocardiogram (ECG) were noted. Patients were induced with inj. fentanyl 2 mcg / Kg, induced with inj. Propofol 1 – 2 mg / Kg, endotracheal intubation was facilitated with intubating dose of inj. vecuronium 0.1 mg / Kg and maintained by 1 - 2 % sevoflurane with 50 % oxygen and 50 % nitrous oxide. Inj. Neostigmine 0.05 mg / Kg and glycopyrrolate 0.02 mg / Kg given at the end of surgery was used for reversal of neuromuscular blockade. Vitals like ECG, SPO2, SBP, DBP, ETCO2 were monitored intraoperatively throughout the surgery and in the recovery room for 2 hours Post-operatively, after which the patients were shifted from the recovery room to Post-operative ward. The patients were monitored for vitals, pain by 10 point numeric scale, sedation by Ramsay Sedation Score (RSS) and adverse effects i.e., nausea, vomiting, pruritis, respiratory depression, at the interval of 4 hours for 48 hours from the time of arrival to Post-operative recovery Room (PACU).

A medical officer (who was blinded to the study) was assigned to follow up the patients in both the groups and assessed for Post-operative pain according to the Numeric Pain Score (NRS)[3] and Ramsey sedation score (RSS)[2] along with post operative vitals and the need and number if rescue analgesic doses if any given at 2 hrs, 6hrs, 8 hrs, 12 hrs, 24 hrs, 36 hrs and 48 h post placement of the patch. The

Patients in Group A was administered routine post-operative analgesia in the ward consisting of Inj Paracetamol 1g iv Q8H and inj Tamadol 100mg iv Q12hrly. Those on fentanyl Patch received Inj paracetamol 1g iv Q8Hrly and inj Saline 2ml IV Q12 hrly. The need for rescue analgesia was defined among both groups as NRS>4 and was administered Inj Tramadol 100mg IV Sos. The maximum dose of Tramadol was Limited to 400mg iv. Patients requiring more than the maximum dose were excluded from the Study.

The designated medical officer also followed up on the adverse effects of the transdermal fentanyl patch related complications (i.e., PONV, Drowsiness and sedation) at 2 hrs, 6hrs, 8 hrs, 12 hrs, 24 hrs, 36 hrs and 48 h post placement of fentanyl patch and the assessment carried out by interviewing the patients.

Statistical Analysis

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0.(Armonk, NY: IBM Corp).To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the Unpaired sample t-test and the Mann-Whitney U test was used. To find the significance in categorical data Chi-Square test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. In all the above statistical tools the probability value .05 is considered as significant level

RESULTS

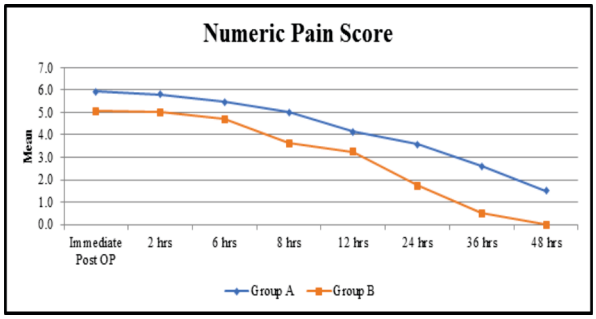
The Age distribution were 21-30 years is 13.3%, 31-40 years is 21.7%, 41-50 years is 28.3%, 51-60 years is 23.3%, >60 years is 13.3%. The Gender distribution were Female is 56.7%, Male is 43.3%. The Age between Groups by Pearson's Chi-Square test were 2=0.921, p=0.921>0.05 which shows no statistical significance between Age and Groups.

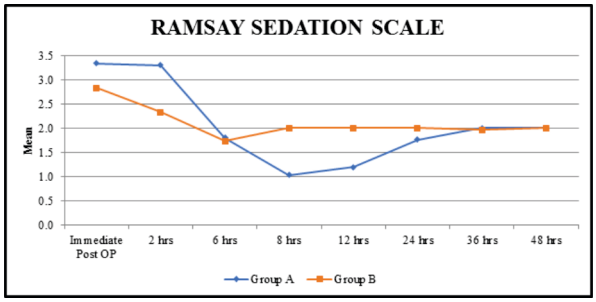
The Gender between Groups by Pearson's Chi-Square test were 2=2.443, p=0.118>0.05 which shows no statistical significance between Gender and Groups. The Weight between Groups by Unpaired t-test were t-value=1.194, p-value=0.238>0.05 which shows no statistical significance difference at p > 0.05 level. The BMI between Groups by Unpaired t-test were t-value=1.701, p-value=0.094>0.05 which shows no statistical significance difference at p > 0.05 level. The Duration of Surgery between Groups by Unpaired t-test were t-value=1.881, p-value=0.065>0.05 which shows no statistical significance difference at p > 0.05 level.

The Numeric Pain Score between the Groups by using Mann-Whitney U test, were all time durations shows highly statistical significance difference at p <0.01 level. The RAMSAY between the Groups by using Mann-Whitney U test, were Immediate Post OP, 6 hrs, 36 hrs, 48 hrs shows no statistical significance difference at p >0.05 level, whereas in 2 hrs shows statistical significance difference at p <0.05 level and similarly in 8 hrs, 12 hrs, 24 hrs shows highly statistical significance difference at p <0.01 level respectively.

The Analgesics Used between Groups by Fisher's exact test were 2=26.447, p=0.000<0.01 which shows highly statistical significance between Analgesics Used and Groups. The Adverse Effects between Groups by Fisher's exact test were 2=5.455, p=0.039<0.05 which shows statistical significance between Adverse Effects and Groups.

There were no adverse effects such as PONV, excess sedation, constipation or any other adverse effects among the study population of both the groups.





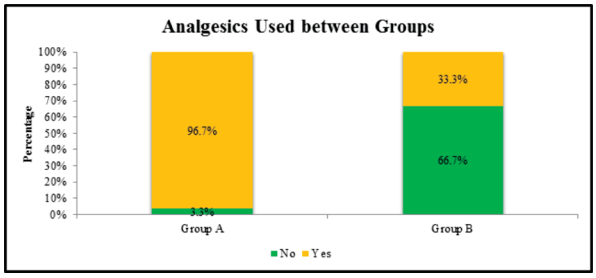


Table 1: Comparison Of Age And Gender Between Groups

			Groups		Total	2 - value	p-value
			Group A	Group B			
Gender	Female	Count	14	20	34	2.443	0.118 #
		%	46.7%	66.7%	56.7%		
	Male	Count	16	10	26		
		%	53.3%	33.3%	43.3%		
Total		Count	30	30	60		
		%	100.0%	100.0%	100.0%		
# No Statistical Significance at p > 0.05 level							
			Groups		Total	2 - value	p-value
			Group A	Group B			
Age	21 - 30 yrs	Count	4	4	8	0.921	0.921 #
		%	13.3%	13.3%	13.3%		
	31 - 40 yrs	Count	6	7	13		
		%	20.0%	23.3%	21.7%		
	41 - 50 yrs	Count	9	8	17		
		%	30.0%	26.7%	28.3%		
	51 - 60 yrs	Count	6	8	14		
		%	20.0%	26.7%	23.3%		
	Above 60 yrs	Count	5	3	8		
		%	16.7%	10.0%	13.3%		
Total		Count	30	30	60		
		%	100.0%	100.0%	100.0%		
# No Statistical Significance at p > 0.05 level							

Table 2 : Comparison Of Weight, Bmi And Duration Of Surgery

Variable	Groups	N	Mean	SD	t-value	p-value
Weight	Group A	30	57.67	8.19	1.194	0.238 #
	Group B	30	60.13	7.81		
# No Statistical Significance at p > 0.05 level						
BMI	Group A	30	22.67	2.12	1.701	0.094 #
	Group B	30	23.60	2.13		
# No Statistical Significance at p > 0.05 level						
Duration of Surgery	Group A	30	3.50	0.91	1.881	0.065 #
	Group B	30	3.04	0.98		
# No Statistical Significance at p > 0.05 level						

CONCLUSION

Pre-operative placement of transdermal fentanyl patch 60 minutes before surgery is associated with significantly less post-operative pain without overt sedation along with minimal adverse effects.

DISCUSSION

Optimal perioperative pain control is an important factor for a good postoperative outcome. Despite significant side effects, opioids are usually the main pharmacotherapy for postoperative analgesia, especially for moderate to severe pain[4].

TFP is considered unseemly for administration in acute pain due to its moderate onset time[5]. To realize a opportune impact, TFP ought to be

connected 1.5 hours some time recently the conclusion of surgery. Its usefulness in chronic pain of nonmalignant origin remains to be confirmed in controlled trials.[5] The adequacy of TFP on postoperative analgesia has been detailed. TFP can weaken the concentrated of postoperative torment and decrease the utilize of protect analgesics securely by fastening the TFP at the ideal time some time recently surgery, by considering onset time and optimizing the dosage.

The worst pain reported by the patients in both treatment groups was immediately after surgery, as expected, after which the pain gradually diminished. The overall consumption of rescue oxycodone can also be considered moderate in both treatment groups. Fentanyl patches have been authorized and are marketed for the treatment of chronic and cancer pain.[8] Furthermore, they have been used off-label for postoperative pain. The delayed onset and a large interindividual variability in pharmacokinetics aredisadvantages of transdermal fentanyl.[9]

According to previous studies, the observed delay for the minimal effective serum concentration to be reached has been up to a mean of 12.7 and 16.7 hours. 5,17 Because the onset of the action is delayed, pain relief in the immediate postoperative period may be inadequate, necessitating other forms of pain medication to be used in the meantime.[10]The most serious and feared adverse effect of opioids is respiratory depression, also during the use of transdermal fentanyl. 16,18 The dose of fentanyl used in these studies has often been higher than that used in our study. In a placebo-controlled study evaluating the safety and efficacy of transdermal fentanyl after major shoulder surgery, there was a small but significant decrease in respiratory rate during fentanyl treatment.[11] Another significant difference was observed in the increased incidence of vomiting in fentanyl-treated patients. Still, the patch used in that study delivered fentanyl at a rate of 75 mg/h, whereas the rate of our patch was only 12 mg/h. We used a low-dose fentanyl patch to avoid respiratory depression and nausea.

In a study by Sandler AN, et al.,[12] the pre-operative placement of Fentanyl patch 2 hours before surgery was associated with moderate reduction in post-operative pain and discomfort. However, the dosage of the fentanyl patch was 50mcg/hr to 75mcg/hr. at such dosages the study population experienced significant Nausea and vomiting along with respiratory depression. However, our study only utilised 25mcg/hr patches and did not witness any such side effects.

In another similar study conducted by Sevarino et al.,[13] in patients undergoing gynaecological procedures, the application of TFP(Trasdermal Fentanyl Patch) was associated with significant morphine sparing effect in post-operative period. This result is also in tandem with our study where there was reduced requirement for Tramadol as rescue analgesia. The combined use of paracetamol has probably facilitated the comparable pain scores achieved in this study while using a 25mcg/hr eluting patch in contrast to the 50mcg/hr patch used in the aforementioned trial.[13]

Thus TFP can be a reliable incorporation into the multimodal analgesic regimen following any major surgery for reliable pain relief that improves patient quality of life and comfort. TFP can be combined with nonsteroidal anti-inflammatory drugs (NSAIDs) or cyclooxygenase (COX)-2-specific inhibitors, and regional analgesia techniques.[14] Multimodal analgesia techniques, including regional analgesia, acetaminophen, nonspecific NSAIDs or COX-2-specific inhibitors, and opioids, have become standard practice. Oral nonopioid analgesics (eg, acetaminophen and nonspecific NSAIDs or COX-2-specific inhibitors) should be administered as "round-the-clock" scheduled dosing, assuming there are no contraindications. Opioids and other systemic analgesics have to be timed to offer adequate analgesia right from the time of emergence from General anaesthesia.

Limitations

- Single centre trial
- Lack of a large sample population
- No quantitative or objective pain measurement parameter
- The difference in pain threshold of every individual has not been taken into account.
- Although we standardised the duration of Surgery, the population consists of individuals undergoing various surgical procedures by different surgeons.

Conflict Of Interest: The authors declare no conflict of interest in this study

Sponsorship: NONE

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