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COMPARATIVE EVALUATION OF SEDATION AND ANALGESIA OF FENTANYL AND BUTORPHANOL WHEN USED WITH PROPOFOL IN INTRA CAVITATORY RADIATION THERAPY.

Anesthesiology

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ABSTRACT

Background and Aim: Opioids have been used since long as a component of balanced anaesthesia for day care procedures thus reducing the anaesthetic requirement and faster recovery. In cancer patients short procedures like intracavitatory radiation therapy, chemo port insertion, picc line placement require sedation and analgesia. Combination of propofol and opiods provide excellent analgesia with sedation for such procedures. The present study aimed at comparing the sedation and analgesia as postoperative recovery characteristics of fentanyl and butorphanol in patients undergoing intra cavitatory radiation therapy (ICRT).

Materials and Methods: The present study configured 160 adults patients of American Society of Anaesthesiologists (ASA) grade 1 or 2 female scheduled to undergo ICRT and were randomly assigned to receive fentanyl (group A; $n = 80$) or butorphanol (group B; $n = 80$). Both group were premedicated with ondensetron 0.08 mg/kg intravenously followed by injection
fentanyl 2 mcg/kg or butorphanol 20 mcg/kg. Standard induction was done with propofol 0.8 mg/kg followed by 0.4 mg/kg in incremental doses. Oxygen was given via mask at 4 L /min. Intraoperative hemodynamic parameters were observed and recorded. Postoperatively analgesia, sedation, respiratory depression and recovery score were observed.

Results: The recovery time was less in group A ($P > 0.05$) while post operative analgesia ($P < 0.001$) and sedation ($P > 0.05$) was more in group B.

Conclusion: It is concluded that at low cost and hassle free availability butorphanol decreases propofol consumption intraoperatively and provided better analgesia in postoperative period.

KEYWORDS

Butorphanol, Fentanyl, Propofol, Sedation, Analgesia, Icrt.

Introduction:

Procedural sedation has become more popular with day care procedures along with emergence of newer drugs. It enables clinicians to perform diagnostic tests and clinical procedures that are sometimes painful or highly anxiety provoking in a manner that prevents or minimizes patient discomfort (1). Many oncologic procedures are day care procedures which includes chemoport insertion, high- dose –rate (HDR) intracavitory radiotherapy (ICRT), biopsy etc. HDR – ICRT is a well known modality for treatment of cancer cervix. Successful treatment requires a combination of external beam X-Ray and brachytherapy. There are various anaesthetic techniques described for high- dose –rate (HDR) intracavitory radiotherapy (ICRT) for carcinoma cervix i.e. conscious sedation, local infiltration, regional anaesthesia ,general anaesthesia etc. (2) American Society of Anesthesiologists (ASA) has recommended that all patients receiving conscious sedation be monitored by a designated individual who is primarily responsible for administering sedative and analgesic drugs and monitoring the patient's vital sign (1) . HDR – ICRT involves the insertion of brachytherapy applicators into the uterus and vagina under anaesthesia or analgesia. Applicators have hollow tubes which are inserted and connected later to the radioactive source. Vaginal packing done so that the applicator stays in situ. The number of insertion varies from 2-6.

In the present study we compared the two different anaesthetic techniques for HDR- ICRT (i.e.- propofol with fentanyl and propofol with butorphanol induced sedation.)

Materials and method:

After the approval of hospital's ethical committee and written informed consent from the patients, a prospective, randomized, double blind study was carried out among 160 American Society of Anaesthesiologists (ASA) grade 1 and 2 adult patients undergoing HDR – ICRT.

Inclusion criteria: patients with Cancer cervix with age group between 40 yrs to 70 yrs.

Patients with history of hypertension, coronary artery disease, hepatic, renal and endocrine disorders and patients on psychoactive drugs or with history of narcotic abuse and allergy were excluded from the study. In the operation theatre standard monitors including Electrocardiogram (ECG), non-invasive blood pressure (NIBP) and pulse oximetry were applied and baseline parameters recorded. After securing intravenous access a slow drip of ringer lactate was started. The study drugs were prepared by an anaesthesia-technician either as 25 mcg/ml of fentanyl or 500 mcg/ml of butorphanol. Injection ondensetron 0.8 mg/kg was given as IV premedication followed by the study drug i.e., either 2 mcg/kg of fentanyl or 40 mcg/kg of butorphanol (3). Induction of anaesthesia was achieved with propofol 0.8 mg/kg over 10 seconds and then 0.4ml/kg intermittently. Hemodynamic parameters were recorded at various intervals. Intraoperatively, any untoward incident requiring emergency intervention was recorded and treated symptomatically. Patients were then shifted to linac room only after patient is awake and obeys command. Postprocedure , pulse rate and blood pressure and oxygen saturation was noted. Patients were observed for respiratory depression (respiratory rate < 8 breath/minute) or hypoxemia (SPO2 < 92%), PONV, shivering, sedation in addition to postoperative pain. Post operative analgesia was measured by visual analogue scale (VAS) at fifteen minutes interval from arrival in linac room till the end of the procedure. Injection diclofenac sodium 75 mg iv was given as rescue analgesic if the patient had VAS > 3.. Postoperative sedation was assessed by Ramsay sedation score,(4) till the patient attained a score of 2.

Statistical analysis was done with SPSS software and student T test was applied.

Results:

A total of 160 female patients were randomly assigned to two groups. The two groups were comparable with respect to demographic characterstics like age, weight, and duration of procedure.[table1] Pre-operative, pre-induction and maintenance hemodynamic parameters were also comparable in both the groups. During the intraoperative period, propofol consumption was lower in group B as compared to group A as is also evident clinically from the intraoperative hypertension and tachycardia that occurred in 44% patients in group A. Mean propofol consumption in group A was slightly higher (150.7 ± 16.36 mg) as compared to 130.5 ± 20.54 mg in group B. The difference however was

statistically not significant (P > 0.05).[table 3] Recovery time to orientation (on asking name of the patient etc.,) which was measured after the end of the procedure from the repositioning to supine position, was less in group A. Mean recovery time was lower (4 ± 1.2 min) in group A as compared to group B (6.5 ± 2 min). 12 patients in the group B and 3 patient in group A showed delayed recovery. Significant pain was experienced by 66% of patients in group A while only 10% patients in group B required rescue analgesic on shifting to recovery room. This difference is highly significant (P < 0.001). 55 patients in group A required rescue analgesic within 30 minutes of shifting to linac room while in group B 63 patients were pain free after 30 minutes of stay in linac room. The mean respiratory rate was lower in group B as compared to the group A upto 1 hour postoperatively. However, there was no incidence of respiratory depression in any patient from either group (respiratory rate < 8 breaths/minute). Postoperatively, hypoxemia (SPO2 < 92% on room air) occurred in 10% patients in group B while no such episode occurred in fentanyl group.[table 2] Postoperative sedation as assessed by Ramsay sedation score was higher in group B. 4 patients had Ramsay grade -1 sedation and 1 patient had grade -2 sedation, 1 patient in group F had grade -1 sedation 10 minutes after the procedure.

Discussion

Intracavitary brachytherapy is a well-known treatment modality for cervical cancer despite this many patients suffer from severe vaginal pain and discomfort during treatment without anesthesia. It is reported that general, spinal (5) and epidural anesthesia, and conscious sedation with fentanyl and midazolam (6,7) are sufficient for pain relief during HDR intracavitary brachytherapy. As a day care procedure faster recovery and adequate analgesia is of greater importance for anaesthesiologist.

Opioids with propofol has been widely studied for procedural sedation. Along with sedation and analgesia the combination also tends to cause nausea, vomiting and shivering in recovery room.

Our study compared the efficacy of fentanyl and butorphanol when given in combination with propofol for HDR- ICRT.

Opioids bind to specific receptors located throughout central nervous system and other tissues. The pharmacodynamic properties of a particular opioid depends on the type of receptor to which it is bound, its binding affinity and whether the receptor is activated. The main difference between fentanyl and butorphanol lies in their binding receptors. Butorphanol is a agonist-antagonist opioid of phenanthren group. It is a kappa receptor agonist as well as mu receptor antagonist, while fentanylis primarily a mu receptor agonist. Butorphanol is extensively metabolized in liver, mainly by hydroxylation. Equipotent doses of butorphanol, morphine, pethidine and pentazocine produces same duration of analgesia (8). Fentanyl a pure agonist and is extensively metabolized in the liver producing norfentanyl. Fentanyl in different doses can be used to provide analgesia, as component of balanced anaesthesia or surgical anaesthesia in very high doses. We used equipotent doses of both drugs as has been used earlier. In the present study, 2 hrs after the procedure complaint of pain was significantly less in group B as compared to group A.

In our study, in the intraoperative period, propofol consumption was lower in group B as compared to group A as is also evident clinically from the intraoperative hypertension and tachycardia that occurred in 44% patients in group A. Mean propofol consumption in group A was slightly higher (150.7 ± 16.36 mg) as compared to 130.5 ± 20.54 mg in group B. Recovery time to orientation (on asking name of the patient etc.,) which was measured after the end of the procedure from the repositioning to supine position, was less in group A. 12 patients in the group B and 3 patient in group A showed delayed recovery . Significant pain was experienced by 66% of patients in group A while only 10% patients in group B required rescue analgesic on shifting to recovery room. This difference is highly significant (P < 0.001). 55 patients in group A required rescue analgesic within 30 minutes of shifting to linac room while in group B only 63 patients were pain free after 30 minutes of stay in linac room. The mean respiratory rate was lower in group B as compared to the group A upto 1 hour postoperatively. However, there was no incidence of respiratory depression in any patient from either group (respiratory rate < 8 breaths/minute). Postoperatively, hypoxemia (SPO2 < 92% on room air) occurred in 10% patients in group B while no such episode occurred in fentanyl group. All 8 cases of hypoxemia in our study occurred in elderly females. Butorphanol clearance is decreased in geriatric patients resulting in prolonged elimination-half life and this could be the reason for postoperative hypoxemia. The incidence of sedation was much less in our study than that reported earlier.(3) Propofol was used in the present study for induction. Based on observations made in the present study it can be concluded that use of butorphanol is associated with less anaesthetic (propofol) consumption, better post operative analgesia and discomfort. (1,8)

Butorphanol for procedural sedation is superior to fentanyl at equipotent doses with only major drawback of hypoxemia and sedation specially in geriatric patients.

Table 1: Demographic profile and duration of anaesthesia

Parameter	Group A (Mean±SD)	Group B (Mean±SD)
Age (yrs)	46.23±6.62	48.20±3.82
Weight (kg)	54.20±9.4	51.33±7.12
Anaesthesia time (min)	13.10±3.10	12.30±3.56

Table 2: Hemodynamic parameters

Parameter Group	Pulse rate (beats/min)		Mean BP (mmHg)		n saturation (SpO2 %)		Oxyge	
	Group A		Group B		Group A	Group B	Group A	Group B
Preoperative	87.24±7.74		85.61±3.95		84.6±14.12	92.12±8.66	98±1.2	99±0.7
Induction	85.68±8.16		83.40±5.35		80.68±7.01	78.52±7.51	97±1	95±1.2
Post procedure (15 min)	88.45±12.10		76.12±3.65		84.78±12.52	76.34±8.28	98±1	96±1
Post procedure (120 min)	96.34±14.20		88.56±32		90.11±12.22	86.52±10.18	99±1	98±1

Table 3: Perioperative profile

	Group A	Group B	P Value
Propofol dose (mg)	150.7 ± 16.36	130.5 ± 20.54	>0.05
Recovery time (min)	4 ± 1.2 min	6.5 ± 2 min	<0.05
Rescue analgesic	52	8	<0.001

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