Role Of ß Blockade In Anaesthesia And Postoperative Pain Management After Major Lower Abdominal Surgery

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Abstract

Sixty adult patients of either sex, of ASA status I or II, undergoing major lower abdominal surgeries under general anaesthesia were studied in this randomized double blinded study protocol. Patients were randomly divided into one of the two groups (esmolol or control) .The aim of this study is to evaluate the influence of perioperative esmolol administration upon anaesthesia and postoperative pain management. It was concluded that esmolol decreases the postoperative morphine requirement for pain relief. There was low incidence of post operative side effects of opioids as nausea and vomiting, sedation, respiratory depression, pruritus ($p<0.05$). Postoperative morphine used was 4.65 ±0.91 mg in the esmolol group and 5.95±1.38 mg in the control group ($p<0.05$). Intraoperative variations in MAP and HR were significant in control group as compared to esmolol group ($p <0.05$).Comparing both the groups, intraoperative fentanyl consumption was higher in the control group ($p <0.05$).

INTRODUCTION

Successful outcome is the most desirable end point of any surgical procedure. Therefore anaesthetic and analgesic technique should aim not only to provide optimal conditions for surgery, but also to prevent peri-operative complications & to lower postoperative morbidity and mortality.[1] Recent evidences suggest that peri-operative stress response results in disturbances in the body homeostasis.[2,3]

In the intra-operative period, esmolol was shown to attenuate stress response and reduction of use of opioids. Whereas in the postoperative period, use of morphine through PCA was found to be decreased and it also decreased the incidence of sedation level, postoperative nausea vomiting, respiratory depression, pruritus; allow early ambulation and hasten recovery. [4,5]

The present study was designed to determine the use of perioperative -blocker in postoperative pain relief after major lower abdominal surgery under general anaesthesia.

METHODS

After approval of the Hospital Ethics Committee, 60 adult patients of either sex, of ASA status I or II, undergoing major lower abdominal surgeries under general anaesthesia were studied in this randomized double blinded study protocol. The anticipated duration of surgery was up to two hours. Patients were randomly divided into one of the two groups (esmolol or control).

Exclusion Criteria-

Patients with history of:

- Ischemic heart disease
- Heart block
- Pulmonary diseases
- Hepatic disease
- History of allergy to Opioids
- History of analgesic consumption (NSAIDS< opioids or paracetamol) regularly for three days before the operation.

All the above patients were excluded from the study. After obtaining written and informed consent, patients were randomly allocated into one of the two groups.

Group I (Esmolol Group)

15 minutes before the induction of anaesthesia patients in the esmolol group received a loading dose of esmolol (0.5 mg/kg in 30 ml normal saline) over a period of 5 minutes

followed by an I.V. infusion of esmolol (0.05mg/kg/min) until the end of surgery.

Group 2 (Control Group)

Patients in control group received the same volume of normal saline for loading and continuous infusion.

PREOPERATIVE ANAESTHESIA CHECKUP

A thorough preoperative evaluation of each patient was done. All routine biochemical, hematological and radiological investigations were done.

Anaesthesia was reversed with inj. Neostigmine (0.04 mg/kg) and inj. Glycopyrrolate (0.01 mg/kg). In the esmolol group, esmolol was discontinued at the end of surgery.

Intraoperative hypotension and bradycardia, defined as Mean Arterial Pressure <50mg Hg and Heart rate <40 beats/min. was treated with intermittent inj. Ephedrine 5 mg I.V or inj. Atropine 0.6 mg I.V respectively.

The following parameters were monitored and recorded intraoperatively

MAP and HR: Baseline values and than every 5 min for 1st half hour then every 15 min. till end of surgery. Values at tracheal intubation, skin incision and tracheal extubation were recorded.

Intraoperative fentanyl requirement.

Intraoperative use of Inj. Ephedrine or inj. Atropine.

After surgery of all patients received 3mg. IV morphine bolus and then received IV morphine through a PCA system (VYGON FREEDOM-5) for postoperative analgesia. Morphine 0.5 mg/0.5ml bolus for postoperative analgesia upon patient demand with a 4 hour limit of 24 mg morphine. The lock out time was 5 min. Pain intensity was evaluated using a visual analogue scale for movement (VASM) and at rest (VASR), on a daily basis for 3 days after the operation. A pain score of less than or equal to 3 represented satisfactory pain relief.

The sedation level was recorded to a four point scale:

0= awake

1= mildly sedated, easily aroused

2= moderately sedated but aroused by talking

3= deeply sedated, difficult to arouse.

Associated side effects of morphine consumption such as nausea, emesis, pruritus, respiratory depression were also recorded (Respiratory depression defined as a RR < 8 breaths / min). Both patients and observed were blinded with respect to treatment groups.

Postoperatively following parameters were recorded for three days after the operation at hourly for first 6 hour then at 6,12,24 hour intervals

Pain intensity at rest (VASR)

Pin intensity at movement (VASM)

Total morphine consumption (mg) at indicated time intervals.

Sedation score

Side effects

Each patient was asked to grade satisfaction (Yes/no) at the end of PCA use.

STATISTICS

All data were presented as mean (SD). Patient characteristics and the cumulative morphine consumption was analyzed using one way analysis of variance (Independent t-test). Classification of operations, the incidence of side effects and patient satisfaction were analyzed using x^2 test of Fishers exact test as appropriate. Pain scores and sedation scores were analyzed using the Mann- Whitney U Test. A value of $p<0.05$ was considered to represent statistical significance.

RESULTS

The study was conducted over a period of 30 months. Initially 60 patients were recruited in the study (30 patients in each group).

Demographic data of the two groups were similar (Table-1).

Figure 1

TABLE No. 1-Demographic Data

Groups (n=30)	Group I	Group II
Mean age	44.10	43.13
SD	11.769	10.398
Male	14	16
Female	16	14
ASA I	23	24
ASA II	7	6

The patients underwent surgical procedure under five categories: - donor in renal transplant surgery (8 patients), major surgery for ovarian or uterine malignancy (14 patients), urological surgery (4 patients), abdomino-perineal surgery (10 patients) and exploratory laparotomy (24 patients).

At the start of study period, the baseline value of mean arterial pressure in esmolol and control groups were 88.57 ±8.60 (mmHg) and 91.67 ±9.60 (mmHg) respectively (p >0.05). Mean heart rate of patients in esmolol and control groups were 72.23 ± 7.15 per minute and 73.63 ±6.04 per minute respectively (p >0.05).

Intraoperatively, in esmolol group mean arterial pressure and heart rate variability were less than in control group (p<0.05) (Table-2, 3).

Figure 2

Table No.2- CHANGES IN MEAN ARTERIAL PRESSURE (mmHg) (Mean±S.D.)

TIME	CASE	CONTROL
Baseline	88.57±8.60	91.67±9.60
Intubation	92.20±8.93	103.90±9.17
5 min	87.97±8.34	98.40±8.62
10 min	86.57±8.99	95.50±8.63
15 min	89.80±8.74	99.87±8.47
20 min	87.30±8.27	96.37±9.52
25 min	85.77±8.10	94.03±8.39
30 min	84.73±8.22	92.43±8.25
45 min	84.53±8.71	91.70±7.32
60 min	81.97±9.15	90.73±7.81
75 min	81.80±10.12	90.10±6.73
90 min	79.77±9.17	87.90±16.14
105 min	80.73±8.11	91.00±6.66
120 min	81.40±7.44	96.20±11.14
Extubation	90.33±8.21	101.17±8.48

Figure 3

TABLE No.3 CHANGES IN heart rate (per minute)(Mean±S.D.)

TIME	CASE	CONTROL
BASELINE	72.23±7.15	73.63±6.04
INTUBATION	76.00±7.32	87.47±7.51
5 MIN	73.03±7.88	85.97±8.19
10 MIN	73.30±7.84	85.20±8.90
15 MIN	74.83±7.70	87.63±9.25
20 MIN	73.17±7.64	86.70±8.92
25 MIN	72.20±7.34	83.30±8.86
30 MIN	71.33±7.15	83.57±7.79
45 MIN	70.07±7.61	82.53±7.71
60 MIN	68.33±9.47	81.90±8.22
75 MIN	67.87±8.28	80.50±6.52
90 MIN	68.17±6.36	79.93±7.03
105 MIN	69.10±6.42	76.46±15.69
120 MIN	72.33±9.03	81.83±9.57
EXTUBATION	75.83±7.28	87.83±7.98

Intraoperative use of fentanyl and hemodynamic variations were high in control groups. Requirement of morphine for postoperative pain relief in the first three days was found to be significantly lower in esmolol group (Table -4, graph-1).

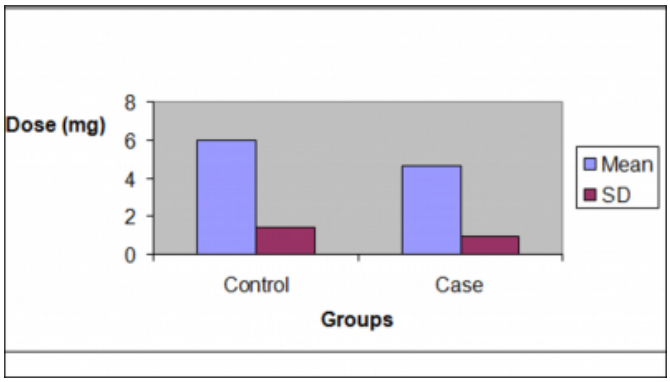
Figure 4

TABLE No:4 postoperative morphine use (mg) (Mean±S.D.)

	case-control	Mean	SD
MORPHINE	Control	5.950	1.3793
	Case	4.650	0.9111

Figure 5

GRAPH- 1: Postoperative Morphine use



It was observed that in esmolol group the average morphine used by PCA pump was 4.65mg and in control group was 5.95mg ($p < 0.05$). The consumption of morphine was low at second and third post operative day.

Postoperative mean visual analogue score at rest (VASR) and movement (VASM) after 48 hours was significantly less in esmolol group (Table-5).

Figure 6

TABLE No.5 :- postoperative mean visual analogue score at rest / MOVEMENT

	VASR		VASM	
TIME	CASE	CONTROL	CASE	CONTROL
0 HR	1.37	1.77	1.37	1.77
1 HR	1.70	2.13	1.70	2.13
2 HR	1.92	2.21	2.73	3.34
3 HR	2.12	2.51	2.20	2.77
4 HR	2.26	2.64	1.93	2.47
5 HR	1.89	2.23	2.30	2.97
6 HR	1.60	1.96	2.73	3.33
12 HR	1.52	1.80	2.90	3.47
24 HR	1.23	1.72	2.60	3.10
48 HR	0.98	1.52	2.20	2.90

Postoperative sedation score in first five hour was less in esmolol group. Incidence of post operative nausea, vomiting, respiratory depression and pruritus were less in esmolol group.

Intraoperative ephridine (6mg) IV was given in one patient of esmolol group but not used in control group.

Intraoperative atropine (0.6mg) IV was used in two patients of esmolol group was not used in control group.

DISCUSSION

Overall results of our study demonstrated that there was difference in requirement of morphine in postoperative period between patients receiving perioperative esmolol and control group. Two major benefits were observed in our study that in esmolol group there were lower incidence of postoperative pain and decreased requirement of fentanyl intraoperatively. Interaction between tetrodotoxin (TTx) and and -adrenergic antagonist compounds were demonstrated [6] and concluded that and -blockers prolong the duration of blockade from sodium channel blocker. The mechanism by which high concentrations of adrenergic antagonist prolong TTx block is unknown. Direct activation of GTPases by molecules with these general physiochemical properties was one potential mechanism[7].

Another possible non specific mechanism by which adrenergic antagonist might prolong TTx block is by increasing the permeability of lipid rich barrier to dry diffusion, such as the epineuruim and perineurium.

Esmolol compared favorably with fentanyl in its ability to obtunded unwanted cardiovascular response to laryngoscopy and tracheal intubation in patient with cardiovascular disease [8].

-adrenergic antagonists possess central nervous system depressant, antinociceptive and anxiolytic effects [9,10,11,12] , thought to be caused by central blockade.

The cumulative pain scores observed for the first 3 days were consistently lower in esmolol group than in the control group. Most of the previously published reports have unanimously agreed to antinociceptive and anxiolytic effects [10 , 11,12] of -blocker . The incidence of postoperative nausea, vomiting and respiratory depression were low in the esmolol group. Intraoperative continuous infusion of esmolol was used and reported a postoperative opioid sparing effect[11]. Verbal Rating Scale for pain (VRS) is also low in esmolol group. Opioid requirement in the esmolol group hold the lowest incidence of nausea and received the least amount of ondansetron in the recovery period. Esmolol treated patient experienced less nausea than the remifentanil group[13] after using intraoperative esmolol and remifentanil infusions. Many previously published reports of meta-analysis and trials analyzed the effect of esmolol in pain modulation. The effect of esmolol in modulation of inhibitory transmission in the trigeminal nociceptive network was studied [14]. The antinociceptive effects of -blockers have been noted in rats and in humans with allodynia[15,16]. It has been speculated that adequate pain relief allows patients to cough, sigh and change position more easily[20].

Another benefit offered by esmolol was shorter time of postoperative stay. In the ambulatory setting, the esmolol-treated patients were discharged home earlier. The faster emergence from anaesthesia and smaller postoperative opioid analgesic requirement may have contributed to the shorter time to discharge home [13,26].

Contrary to this, some authors have demonstrated no significant analgesic effect of esmolol unlike propanolol[18-21] which has very little sedative effect, no analgesic activity and no local anesthetic properties [22,23,24,25].

A thorough review of the existing literature on the role of esmolol in anaesthesia has shown emerging field for postoperative pain relief and decreasing opioid related postoperative complication e.g. nausea, vomiting, sedation, respiratory depression.

In summary, for decades balanced anaesthesia has been a well established technique which allows for comfortable and patient adjusted induction of anaesthesia and unlimited prolongation dependent on the duration of surgery and reduced incidence of complications due to availability of newer short acting anaesthetics and better postoperative pain relief. The study and research material on perioperative use of

esmolol is limited however whatever data is available; it concludes that esmolol decreases the perioperative morphine requirement for pain relief with faster awakening from anaesthesia.[26]

The intraoperative use of esmolol increases the permeability of fentanyl to blood brain barrier and reduces the fentanyl requirement. G-protein coupled receptors (GPCRs) are the largest class of receptors and channel proteins and are widely distributed in the central nervous system and modulate various CNS functions, including nociception. adrenergic antagonist activates G-proteins and it was suggested that this property resembles the mechanism of central analgesia. It also results in low incidence of post operative side effects of opioids as nausea, vomiting, respiratory depression and pruritus. All the patients of the esmolol group had complete recovery from anaesthesia within five hours of completion of surgery.

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