

COMBINED REGIONAL-GENERAL ANESTHESIA:  
EVALUATION OF REMIFENTANIL BASED  
GENERAL ANESTHESIA AND POSTOPERATIVE  
EPIDURAL ANALGESIA

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**Summary**

**Objectives:** To evaluate whether remifentanil based general anesthesia combined with epidural analgesia for postoperative pain, has any advantages with respect to consumption of drugs, blood loss, quality of pain control, hemodynamic profile, in major abdominal surgery, as compared to other combined techniques.

**Methods:** A retrospective study based on chart reviews of patients who have undergone colectomy, radical cystectomy and radical prostatectomy over one year period in our Institution, operated under combined regional-general anesthesia. Twenty-six patients were analyzed and were divided into three groups according to the type of anesthesia received. Group A: combined general-epidural for per-operative and post-operative pain (10 patients). Group B: combined spinal-general anesthesia (8 patients) post-operative analgesia consisted of parenteral mepiridine and paracetamol. Group C: remifentanil based general anesthesia followed by epidural for postoperative analgesia (8 patients).

**Results:** The demographic data, age and M/F distribution were comparable in the three groups.

The remifentanil group showed less utilization of muscle relaxant (Cisatracurium) with respect to other groups ( $p < 0.001$ ).

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The amount of intraoperative blood loss was not significantly different among the three groups.

The efficacy of the postoperative epidural analgesia was demonstrated by the minimal utilization of analgesics ( $p < 0.05$  and  $0.01$ ) in group A and C as compared to group B.

In the group of remifentanil, the blood pressure was more stable and maintained at a systolic of 80-100 mmHg as compared to initial hypotension mainly in group C.

**Conclusion:** The use of remifentanil based general anesthesia offers the advantage of non-accumulation of drugs and hemodynamic stability. Post-operative analgesia can be provided by epidural route which proved to be satisfactory in the remifentanil group.

The effect on blood loss was not conclusive in this study.

**Keywords:** combined general regional anesthesia, remifentanil.

## Introduction

Postoperative epidural analgesia has been extensively studied and it is believed to have beneficial effects in terms of improved bowel motility, microvascular circulation, decreased stress response and early ambulation<sup>18</sup>.

The aim of the present study is to compare the different techniques of combined regional-anesthesia in terms of the need of drugs, blood loss, and the need of analgesics in the immediate post-operative period, hemodynamic stability, as well as to evaluate the benefits if any, of remifentanil based general anesthesia.

## Patients and Methods

The study is based on chart review of twenty-six patients who had undergone major abdominal surgery (colectomy, radical prostatectomy, and radical cystectomy) under different combinations of anesthetic techniques. Approval of the Institution Research Board, Ethics

Committee, and written permission from the attending physicians were obtained.

Patients were classified into three groups (A, B and C) according to the combination of anesthetics received.

- A. Combined epidural-general anesthesia. (10 patients)
- B. Combined spinal-general anesthesia. (8 patients)
- C. Remifentanyl based general-anesthesia followed by epidural analgesia. (8 patients).

The demographic data is shown in Table 1.

*Table 1*  
*Demographic data of patients in A, B and C groups*

Group	A Epid-GA	B Spinal-GA	C Remif-Epid (postop.)
Mean age (Years)	57.2 (56-72)	62 (52-82)	56 (40-75)
Male/Female	9/1	7/1	8/0
ASA classification	(III x 1)	II	(III x 1)

### **Anesthetic Management**

Patients were premedicated with hydroxyzine 25 mg one hour before the operation. In groups A and C an epidural catheter was installed before the induction of general anesthesia.

The anesthetic management of the three groups varied with respect to onset of the loco-regional anesthesia, and the adjuvants used intra and post-operatively.

In group A (Epid-GA), local anesthetic was administered directly after induction (10 ml of xylocain 2% and 10 ml of bupivacaine 0.5% plus 100 micrograms of fentanyl) in four installments 5 ml each over a period of one hour. The patients were topped up by 7-10 ml of local anesthetics mixture according to the length of the operation. One hour before the end of the surgery, patients were given an additional 10-15 ml of 0.125% of bupivacaine with 5 micrograms/cc of fentanyl.

In group C (Remif-Epid), the administrations of the local anesthetics (bupivacaine 0.125% + fentanyl 100 micrograms, infusion of 15 ml/hr) were given before the end of the operation, to relay analgesia before discontinuation of remifentanyl.

In group B (Spinal-GA), the patients underwent spinal anesthesia at the L4-L5 level using a pencil point needle 25g. Heavy bupivacaine (3.5-4 ml) associated with catapress of 0.25 microgram/Kg and morphine PF 200 micrograms, were administered intrathecally, before the induction of general anesthesia.

The induction of general anesthesia was similar for groups A and B.

1. Na thiopentone 4-5 mg/kg.
2. Cistracrium 0.2 mg/kg, maintenance at 2 microgram/kg/min.
3. Fentanyl 100-150 micrograms.
4. Propofol continuous infusion at 2-3 mg/kg/hr.

For Group C, the induction was similar to the other groups; however, the maintenance was with remifentanyl 0.25-0.4 micrograms varying with the level of hemodynamic stability.

Intra-operative routine monitoring on all patients consisted of: non-invasive blood pressure, pulse oximetry, electrocardiogram, end tidal CO<sub>2</sub>, and neuromuscular monitoring. Few patients had additional CVP monitoring. Blood gases were drawn at least twice during operation for each patient.

Postoperatively all patients of groups A and C were put on epidural analgesia of 0.125% bupivacaine and fentanyl 5 microgram/ml at an infusion rate between 5-10 ml depending on the pain assessment (verbal pain rating)\*, while group B was managed by parenteral mepiridine and paracetamol using same scale.

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\* Subjective questioning of patients:

1. No pain.
2. Mild pain.
3. Moderate pain.
4. Severe pain.

### Statistical analysis

The data was analyzed using the following methods of statistics.

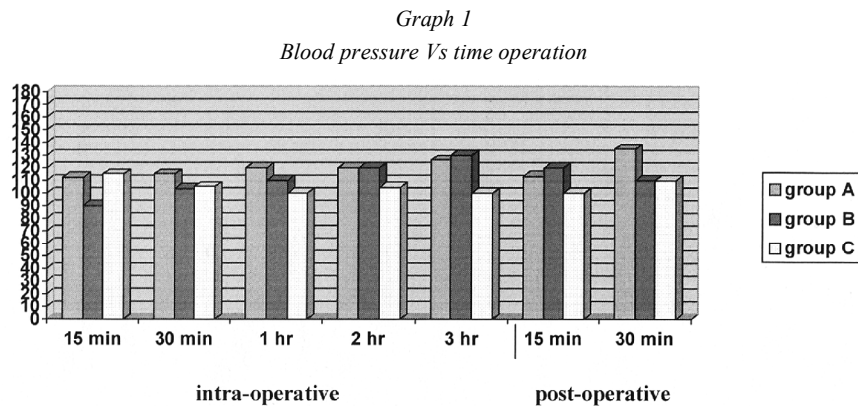
1. Comparison of the means using student test.
2. Analysis of variance test (ANOVA) with the  $t < 2.069$  and  $p < 0.05$  denoting significance.
3. Chi-square test used as a test of independence.

### Results

The variables evaluated in the groups A, B and C were: hemodynamic stability, the need of muscle relaxant, intra-operative blood loss, and the need of postoperative analgesic (within the first 26 hours).

### Hemodynamic Stability

A comparison of blood pressure variation among the groups A, B and C is plotted vs. time during preoperative period and continuing till thirty minutes post-operatively is shown in Graph 1.



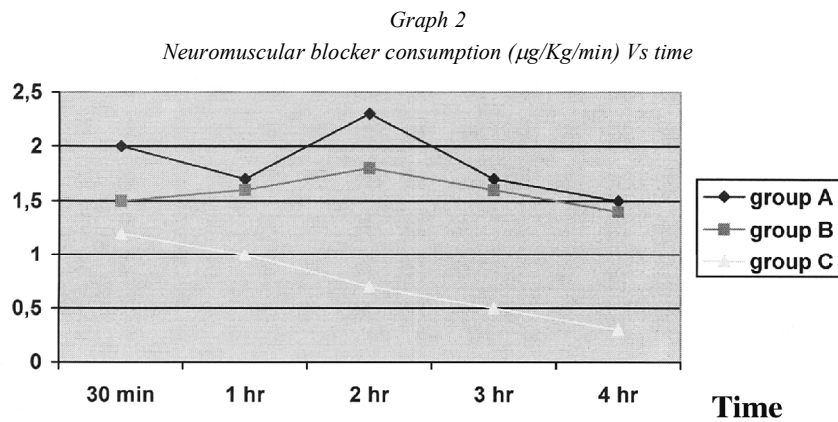
In this graph the mean blood pressure for groups A, B and C was compared in the per-operative period (first 15 minutes, 30 min, 1 hour, 2

hours and 3 hours) and the post-operative period (first 15 min and 30 minutes).

- The preoperative systolic blood pressure for the three groups was in the range of 155-165 mmHg.
- All techniques used were associated with drop in blood pressure, most profound in the spinal group and the least in the remifentanyl group.
- The remifentanyl group also showed more stability of blood pressure.
- Statistical analysis did not show any significance.

### Peroperative Consumption of Neuromuscular Blockers

The consumption of neuromuscular blockers in group A, B and C throughout the operation is shown in Graph 2.



The induction dose was similar for the three groups; cistracrium 0.15-0.2 mg/kg. The maintenance dose (mean) was recorded at the following intervals (30 minutes, 1 hr, 2 hrs, 3 hrs, and 4 hrs). The utilization of neuromuscular blocker was highest in group A followed by group B and the least in group C ( $p < 0.001$ ).

### Evaluation of the Per-operative Bleeding

The amount of intra-operative blood loss (cc) in each group is shown in Table 2.

*Table 2*  
*The intraoperative blood loss*

Group A (n = 10)	Group B (n = 8)	Group C (n = 8)
600	750	1000
750	750	1200
650	340	600
600	450	1200
650	500	400
800	1000	600
750	500	500
600	850	100
1000		
1000		

X	740	642.5	700
SD	154.2	227.77	396.41
SEM	48.76	80.53	140.15
N	10	8	8
A vs B	p > 0.05	t = 0.761	Not significant
A vs C	p > 0.05	t = 0.312	Not significant
B vs C	p > 0.05	t = 0.426	Not significant

The test of significance used is the analysis of variance test (ANOVA) with the condition that if  $t < 2.069$  and  $p < 0.05$ , then there is a significance.

As shown in Table 2, the difference in blood loss in the three groups did not reach statistical significance.

### Assessment of Postoperative Analgesia

The fourth objective in this study was the assessment of post-operative analgesia. The need of additional salvage medication

(paracetamol and meperidine) was utilized as an indicator of pain. The three groups were compared with respect to the amount of analgesic received in the post-operative period (Table 3).

*Table 3*  
*Assessment of post-operative analgesia, number of patients, and analgesic received*

	Group A Epid-GA	Group B Spinal-GA	Group C Remi-Epid
After 2 hours	1 P*	6 P	2 P
After 8 hours	9 P	6 P, 4 M	0
After 14 hours	3 P, 1 M**	8 P, 5 D	1 P
After 20 hours	1 P, 1 M	8 P	1 P
After 260 hours	9 P, 1 M	8 P	0
<b>Total</b>	<b>26</b>	<b>45</b>	<b>4</b>

\* paracetamol.

\*\* meperidine.

(Example: 1P means that one patient from 10 patients of group A has utilized one dose (1 gm) of paracetamol at the specific hour).

These results demonstrate that the use of salvage medication for post-operative pain was most in group B with respect to group A and C ( $p < 0.05$ ) and ( $p < 0.01$ ) respectively. The difference in the need for salvage medication was not significant ( $p = 0.25$ ) between groups A and C who had epidural for post-operative analgesia.

## Discussion

Per-operative hemodynamic stability and post-operative symptoms and complications can be ameliorated by a suitable choice of anesthetic and analgesic techniques tailored to the specific procedures such as abdominal surgery. Combining regional analgesic technique with general anesthesia not only improves analgesic efficacy but also reduces opioid demand and side-effects. Epidural blockade also has beneficial effects in terms of reducing the stress response.

The assessment of the impact of anesthetic and analgesic techniques on the per-operative hemodynamic stability regarding the variation in

blood pressure, blood loss, drug burden used to effect anesthesia and post-operative analgesia, is the objective in view of improving patient recovery<sup>1,2</sup>.

Although a considerable amount of literature has been published on the effect of anesthetic techniques and postoperative analgesia on postoperative morbidity and mortality, the evidence on long term outcome remains controversial. Our main aim, by comparing three anesthetic techniques, is to find out their relative impact on optimization of the perioperative hemodynamic stability, and the postoperative analgesic efficacy.

The variables monitored in this study were evaluated with three different types of anesthesia and their influence on the per and post-operative stability of the blood pressure, the use of muscle relaxants, the amount of per-operative bleeding, and the need of post-operative additional analgesia.

Qualitative analysis of the data showed that the blood pressure, the mainstay of patient hemodynamics, was maintained lower than baseline in the three groups.

In group A, (epidural-general anesthesia) where the epidural provided intra-operative analgesia, this drop was in the order of 20% and there was no immediate increase post-operatively.

In group B, (spinal-general anesthesia) where the spinal anesthesia provided per-operative analgesia, there was a greater drop in blood pressure initially in the order of 25-30%. Blood pressure increased with time (2-3 hours) to stabilize at 20% less than the baseline. There was a further increase in blood pressure in the first hour post-operatively.

In group C, (remifentanil-epidural anesthesia) where the per-operative analgesia was provided with remifentanil and post-operatively with the epidural analgesia, the initial drop in blood pressure was 20%, but during all the operation it was maintained at 25% less than the baseline.

The occurrence of hypertension in response to surgical stimuli was controlled effectively by remifentanil as compared to the other groups. In

addition, remifentanil provided greater hemodynamic stability mainly during induction and throughout the operation<sup>3</sup>. Remifentanil has also been used in monitored anesthesia care with greater cardiovascular stability due to the intense analgesia it produces and decreased sympathetic response to surgical stimuli<sup>4</sup>.

All the above results are in accordance with blood pressure reductions obtained by the regional techniques and remifentanil<sup>6</sup>. However, statistical analysis did not show any significant differences between the three groups.

Several studies have demonstrated lower blood loss with the use of remifentanil in cardiac surgery, neurosurgery, and liver surgery<sup>16,17</sup>. In a recent study, Uroglo *et al*, compared the hypotensive effect of epidural anesthesia and remifentanil intravenous anesthesia on intra-operative blood loss during total hip replacement<sup>5</sup>; In spite of the similar mean arterial pressure levels noted between the two groups, epidural anesthesia resulted in less intra-operative blood loss than remifentanil during primary total hip replacement. This outcome may be associated with distribution of blood flow, and lower mean intra-operative central venous pressure in the epidural group<sup>5,6</sup>.

In view of the above, our expectation was of lower blood loss in the remifentanil group, however the difference among the three groups was not significant. It is worth mentioning that the majority of the patients in group C underwent radical prostatectomy with nerve sparing to preserve erectile function; this resulted in long surgical time and entailed more dissection and bleeding in group C, probably enough to offset any beneficial effect of remifentanil in that respect. Study limitations (retrospective nature of the study, small sample size...), are to be considered.

The use of muscle relaxants was lowest in the remifentanil group. It was also lower in the spinal vs epidural group since the previous provides more profound muscle relaxation. The difference for this variable was extremely significant for group C ( $p < 0.01$ ). Titration of remifentanil appeared to provide sufficient control and maintained anesthesia with minimal requirement of muscle relaxant<sup>3</sup>.

Our last objective in this study was to assess the postoperative analgesia in the three groups<sup>10,14</sup>.

Although single or multiple doses of paracetamol was found to be effective in the treatment of acute postoperative pain<sup>9</sup>, it is well known that adjunctive analgesia with intravenous paracetamol does not reduce morphine related adverse effects events<sup>10,14</sup>. Opioid sparing by epidural analgesia was clearly demonstrated in our study.

Post-operative analgesia, as judged by the need of supplemental pain medications, revealed the following:

In group A, more than 70% did not need additional analgesia post-operatively up to 26 hours.

In group B more than 90% of patients needed additional anesthesia post-operatively.

In group C, patients needed post-operative analgesia only occasionally.

Thus groups A and C have demonstrated the additional benefit of epidural analgesia as shown by decreased total amount of analgesics needed and therefore the incidence of opioid side-effects.

Respiratory depression is not the only side-effect related to opioid administration. Patients more frequently complain of nausea, vomiting, urinary retention, pruritus, and delay in recovery of bowel function especially after abdominal surgery<sup>7,8,11,12</sup>.

We did not explore the incidence of postoperative pulmonary complications. However multiple studies have proved a decrease in the incidence of postoperative pulmonary complications and myocardial infarction with the use of epidural anesthesia and analgesia<sup>15</sup>.

## Conclusions

Considering all variables together, it is concluded that epidural analgesia for post-operative pain proved effective. The remifentanil group C was comparable in per-operative hemodynamic stability, blood loss,

and post-operative comfort to group A; however, it showed the least utilization of muscle relaxant, and no local anesthetic during the operation was used.

A single dose spinal (as in group B) failed to provide post-operative pain and same level of hemodynamic stability.

The use of remifentanyl for maintenance of anesthesia followed by epidural for post-operative analgesia in major lower abdominal surgery is recommended for the following advantages:

- Adequate hemodynamic stability and blood loss profile.
- Satisfactory post-operative analgesia.
- Minimal use of muscle relaxants.
- No use of local anesthetic per-operatively.
- Virtually drug free patient at the end of surgery, due to maintenance by rapidly eliminated agents.

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