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EFFECT OF GENERAL ANESTHESIA WITH EPIDURAL VERSUS GENERAL ANESTHESIA ALONE ON REQUIREMENT OF INHALATIONAL AGENTS AND PERI OPERATIVE ANALGESIC IN PATIENT UNDERGOING MAJOR ABDOMINAL SURGERY

A ORIGINAL CASE STUDY

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ABSTRACT:

Background: Abdominal onco surgeries are of longer duration and patients may experience severe pain peri operatively. We have hypothesized that patient will require more IV analgesic drugs like opioids, if only general anaesthesia is given, but need for IV analgesic will be reduced if Epidural anaesthesia is combined with General anaesthesia. Here we have compared 32 patients (sixteen from each group) undergoing major abdominal onco surgery under general anaesthesia alone versus epidural along with general anaesthesia with use of Ropivacaine and Fentanyl for epidural infusion, and observed that patient with general and epidural anaesthesia required smaller dose of IV opioids and minimal use of inhalational agent intra operatively.

Methods:

- Objectives are: Need of inhalational agent, to asses perioperative pain relief and need of iv analgesic drugs in patient undergoing major abdominal onco surgeries under epidural with general anesthesia as compared to general anesthesia only.
- After Institutional Ethics committee approval (IEC/BU/133/FACULTY/2/251), CTRI registration (CTRI/2022/02/039912) and patient's consent, 32 patients were randomly allocated in Group GA (n=16) and Group EG (n=16), undergoing major abdominal onco surgeries. Group GA receiving general anaesthesia only, Group EG receiving epidural with general anaesthesia. Parameters mentioned in aims and objectives were compared.

Results: Study revealed statistically significant difference between two groups, with mean value for use of Sevoflurane was 26.88 in EA with GA group and 44.94 in GA only group with P value <0.001.

Conclusions: EA with GA group required less inhalational anaesthetic agent and iv analgesic agents as compared to GA group only.

Keywords: Abdominal onco surgeries, Epidural anaesthesia with Ropivacaine, Inhalational agent.

INTRODUCTION

Generally major surgeries are performed under general anaesthesia, but in view to reduce central sensitization after tissue injury in humans, the concept of pre-emptive analgesia has evolved. As a broader definition of pre-emptive analgesia, preventive analgesia includes any perioperative analgesic regimen able to control pain induced sensitization of the central nervous system, hence to decrease both the development and the persistence of pathological pain. Adequate analgesia aids to restore normal function including respiration, ventilation, coughing and mobility, thereby facilitating early rehabilitation, early mobilization, less chance of deep vein thrombosis, pulmonary complications and shortened hospital stay. However, epidural analgesia, wherever possible, using local anaesthetic with or without additives, provides distinct advantages over other modalities, and prove to be gold standard. In some studies, pharmacological blockade of the somatosensory pathways before surgery, by means of opioid premedication, incisional and peripheral nerve blocks with local anaesthetics, and neuraxial blockade with local anesthetic or opioids, have been shown to decrease perioperative pain. Opioids are an essential part of perioperative pain management of cancer surgeries. ⁽¹⁾ Perioperative pain is a potent trigger for the stress response, which activates the autonomic system, and is thought to be an indirect cause of adverse effects on various organ systems. ⁽²⁾ The aim of the current study is to compare perioperative pain and analgesic demand and need of inhalational agents intraoperatively in patient receiving general anaesthesia alone and patient receiving epidural anaesthesia with Ropivacaine and Fentanyl in combination with general anaesthesia in patients undergoing major abdominal onco surgeries. We hypothesized that epidural anaesthesia in combination with general anaesthesia, may decrease intra operative and postoperative pain along with analgesic demand and inhalational agent, when compared with patients operated under general anaesthesia alone. Exposure to inhalation anaesthetics was associated with increased risk of recurrence after colorectal cancer surgery. ⁽³⁾ Opioids are often associated with systemic complication like nausea, vomiting, respiratory depression, sedation, delayed recovery of bowel and bladder function and hyperalgesia. And as per studies no improvement was observed in post operative pain control after pre-emptive administration of systemic opioids ⁽⁴⁾ and perioperative analgesia with opioids can reduce myocardial morbidity and mortality ⁽⁵⁾. Thus, to reduce the need and adverse effects of systemic opioids, the perineural use of local anaesthetics has gradually evolved over time. Intraoperative stress may suppress the adaptive immune system of the body and abolished pro inflammatory lymphocyte function is linked with high risk of infection, and this is reduced by thoracic epidural anaesthesia ⁽⁶⁾. The combination of epidural opioids and local anesthetic provides synergistic analgesia as per the study ⁽⁷⁾.

MATERIAL AND METHOD

- **Source of data**

Samples consist of patients undergoing surgeries in SHREE KRISHNA HOSPITAL, KARAMSAD, ANAND

- **Methodology**

(A) Inclusion criteria

- 1) Patients ASA (American society of anesthesia) I-IV physical status
- 2) Age 30-80 year of either sex
- 3) Patients undergoing major abdominal onco surgery

(B) Exclusion criteria

- 1) Patient's refusal
- 2) Infection at site of epidural needle insertion
- 3) Coagulopathy or bleeding disorder
- 4) Increased intracranial pressure
- 5) Allergy to local anesthetics
- 6) Pregnancy
- 7) Severe hypotension, hypovolemia
- 8) History of known allergy to drugs used in the study
- 9) Any other relative contraindication of epidural anesthesia
- 10) Blockage or intrathecal migration of epidural catheter during intraoperative or post operative period.
- 11) Post operatively if patient shifted to intensive care unit unreversed and intubated.

(C) Study Design

After obtaining approval from the internal ethical committee of Shree Krishna Hospital, Karamsad, Anand, Gujarat (registration no: IEC/BU/133/FACULTY/2/251 and CTRI registration (CTRI/2022/02/039912) and obtaining written and informed consent, patients of ASA (American society of anesthesia) I to ASA IV physical status who were undergoing surgery were recruited to participate in the randomized control trial. Thirty-two patients were randomized to either GA only (group GA) or EA with GA (group EG) using stata 14.2 software. Pre anesthetic checkup was carried out in all patients with detailed clinical history, general history, as well as general and systemic examination. After checking the overnight fasting of 6-8 hours, arrival to pre anesthetic room, an IV line was taken. A blood pressure cuff and pulse oximetry probe were attached. All anesthetic procedures were performed by the 2nd and 3rd year resident with experience under the supervision of an experienced anesthesiologist.

Patients were randomly assigned into two anesthetic groups by closed envelope method containing two groups- general anesthesia (GA n=16) and combined epidural and general anesthesia (EG n=16). Randomization was carried out in 32 patients.

ANESTHETIC PROTOCOL

GENERAL ANESTHESIA

General anesthesia was induced with INJ Fentanyl 2 mcg kg⁻¹, INJ Glycopyrrolate 0.2mg and INJ Midazolam 0.2mg kg⁻¹, induction with INJ Propofol 2-3mg kg⁻¹ or INJ Etomidate 0.2-0.6 mg kg⁻¹ and muscle relaxation achieved with short acting muscle relaxant INJ Succinylcholine 1mg kg⁻¹ and long acting muscle relaxant INJ Vecuronium 0.1mg kg⁻¹, and maintained with oxygen+ air +inhalational agent and post intubation muscle relaxation was maintained with intermittent muscle relaxant INJ Vecuronium 0.05mg kg⁻¹ according to TOF. Perioperative analgesia was maintained by combination of opioid and nonopioid analgesic (intra op all the patients received INJ Fentanyl intermittently and before emergence from anesthesia INJ Diclofenac- 75mg iv stat

COMBINED EPIDURAL AND GENERAL ANESTHESIA (EG GROUP)

Anesthesia was given in all patients by an epidural catheter insertion at thoracic or lumbar interspaces according to type and site of surgeries. Before induction of anesthesia, an epidural test dose of 3ml 2% INJ Lignocaine with 1:200000 Adrenaline ($C_{23}H_{35}N_3O_4$) was given to all patient of EG group, to exclude intravascular or intrathecal catheter location, and wait for 5 min and check bilateral lower limb movements and sensation.

After epidural insertion patient was given supine position, and activation and confirmation with test dose, INJ Ropivacaine ($C_{17}H_{26}N_2O$) 0.5% (30ml) + Normal saline 0.9% (18ml) + INJ Fentanyl 50mcg ml⁻¹ (2ml) =total 50ml infusion was administered via epidural infusion, and infusion rate was decreased or stopped if systolic BP is < 80mmhg.

After giving IV pre medication with half the dose of INJ Fentanyl (1mcg kg⁻¹), INJ Glycopyrrolate 0.2mg and INJ Midazolam 0.2mg kg⁻¹, induction with INJ Propofol 2-3 mg kg⁻¹ or INJ Etomidate 0.2-0.6 mg kg⁻¹ and muscle relaxation achieved with short acting muscle relaxant INJ Succinylcholine 1mg kg⁻¹ and long acting muscle relaxant INJ Vecuronium 0.1mg kg⁻¹, and maintained with oxygen+ air +inhalational agent (Sevoflurane), and post intubation muscle relaxation was maintained with intermittent muscle relaxant INJ Vecuronium 0.05mg kg⁻¹ according to TOF.

POSTOPERATIVE MANAGEMENT

In the immediate postoperative period, patients were asked about the occurrence and the intensity of pain at the site of surgery according to VAS score, and regarding awareness during operative procedure if any before shifting patient from PACU to ward. All patients were assessed post operatively every 2-3 hourly for initial 6-8 hours and questioned about complications like headache, vomiting, lower limb movement and sensation, vas score, bladder tone and sensation. All the patients were assessed and need of iv analgesics in both the group in postoperative period was compared.

POST OPERATIVE ANALGESIA PROTOCOL

Patients from both the groups were assessed based on vas score and need for epidural top up post operatively, and other iv analgesic drugs. When patient complain of pain in post operative period, we gave epidural top up (INJ Ropivacaine 0.15%+INJ Fentanyl 1mcg/ml) according to patient's vitals and vas score and if need arises again (VAS score 3-4) then we gave INJ Paracetamol 1g iv with prior INJ Ondansetron ($C_{18}H_{19}N_3O$) 4mg iv in both the groups, and in GA only group post operative analgesia was managed by INJ Diclofenac 75mg and INJ Tramadol ($C_{16}H_{25}NO_2$) 50mg twice a day.

Plan of statistical analysis

Data was analysed using stata 14.2 statistical software. Descriptive statistics mean (SD), median (IQR), frequency (%) was calculated to portray the demographic and clinical, biochemical and characteristics of the study population. Independent T-test was used to compare perioperative requirements of analgesia and inhalational agent between two groups.

SAMPLE SIZE

We require 16 patients in each group to achieve 80% power allowing for 5% type 1 error. This sample size calculated by Winpepi software.

Software output.

REQUIRED SAMPLE: total 32 (16 in Group GA, 16 in group EG)

EXPECTED PRECISION:

Approx. 95% CI for difference between means (D)= D-3.526 to D +3.526

In formula $\{2*1.96+0.8422*5252, n =15.70 =16 \text{ approx.}\}$

OBSERVATION AND RESULT:

- We have observed the need of inhalational anesthetic agent (sevoflurane) in 32 patients undergoing major abdominal onco surgery under EA with GA and GA only and we found statistically significant difference between two groups.

TABLE I: Need for sevoflurane (inhalational agent) intraoperatively

Need for sevoflurane	Mean value	Std deviation	P value
EA+GA	26.88	5.886	<0.001
GA	44.94	10.804	>0.995

- We have observed the need of muscle relaxant in 32 patients undergoing major abdominal onco surgery under EA with GA and GA only and there is no statistically significant difference between two groups.

TABLE II: Need for muscle relaxant (injection vecuronium) intraoperatively

NEED FOR MUSCLE RELAXANT	MEAN VALUE OF MUSCLE RELAXANT	Standard deviation	P value
EA+GA	15.56	5.886	>0.001
GA	13.81	10.804	<0.001

- Here we have observed need for intravenous analgesic agent that is I.V. opioids, and compared in both the groups and according to mean value bar graph is made, which shows statistically significant difference between two group.

TABLE III: Need for analgesic drug intraoperatively (IV opioids)

NEED FOR ANALGESIC DRUG INTRAOP (OPIOIDS)	MEAN VALUE	Chi square test value	P vale
EA+GA	0.5	8.167	<0.001
GA	1.93	10.667	>0.001

- Adverse events like vomiting, hypotension were observed which showed statistically significant difference between two groups.

TABLE IV: Adverse events

ADVERSE EVENT	EA+GA	GA
YES	2	5
NO	14	11
TOTAL	16	16

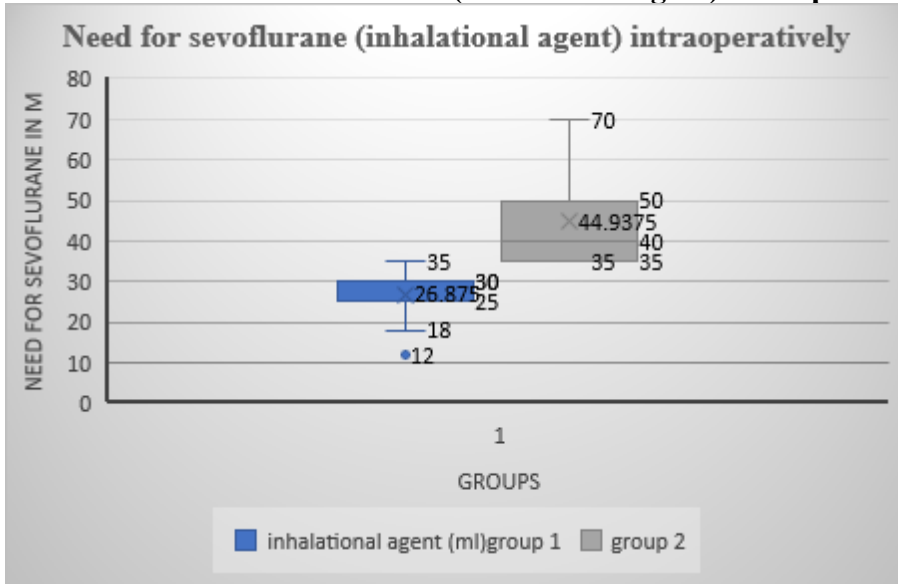
- The need of iv opioids and NSAIDS post operatively was studied and depicted as a bar graph with statistically significant difference between two groups.

TABLE V: Need for iv analgesic agent (opioids) post operatively

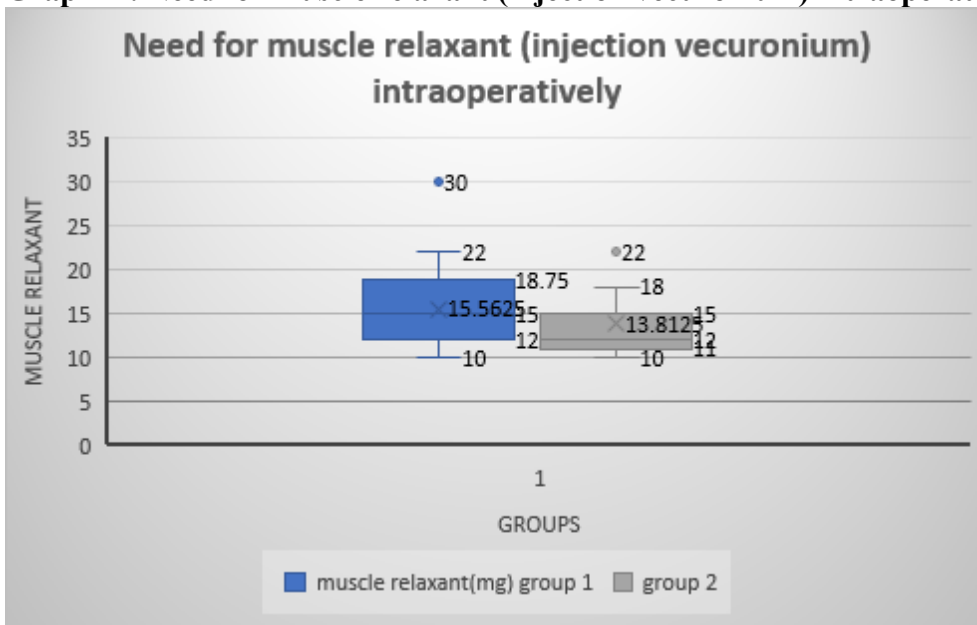
NEED FOR IV ANALGESIC AGENT (POST OP)	EA+GA	GA
YES	1	16
NO	15	0
P value	<0.001	>0.001

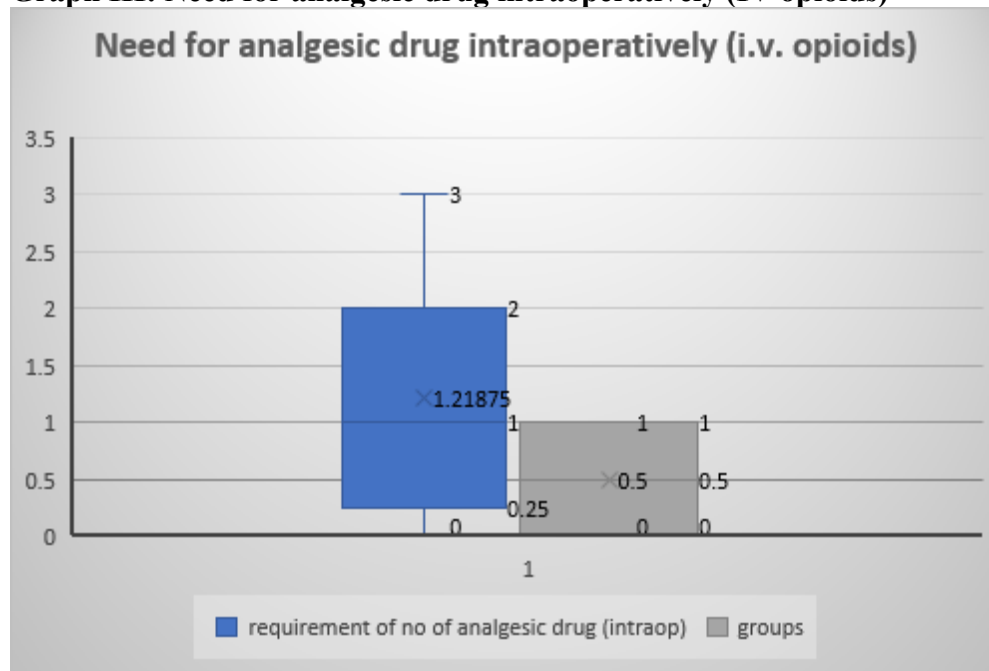
- Intra op and post op hemodynamic like pulse, blood pressure, respiratory rate, etco2, spo2 and post op visual analogue scale (vas score) is assessed in both the groups with statistically significant difference and here we depicted it as tabulated form
GRAPHS:

- **GRAPH I: Need for sevoflurane (inhalational agent) intraoperatively**



- **Graph II: Need for muscle relaxant (injection vecuronium) intraoperatively**



Graph III: Need for analgesic drug intraoperatively (IV opioids)

DISCUSSION

Epidural anaesthesia and analgesia are an old and gold standard method often combined with general anaesthesia to enhance onco abdominal surgeries. The essence of good postoperative analgesia using a local anesthetic lies in pain relief without loss of motor power. This is important to allow physiotherapy, facilitate early mobilization, and prevent deep vein thrombosis⁽⁸⁾. In the recent years, there has been an increasing amount of research over newer local anesthetic ropivacaine which is less toxic and safer than bupivacaine with similar pharmacodynamic properties⁽⁹⁾⁽¹⁰⁾

By this study we have tried to decrease the use of inhalational anesthetic agent which is our primary goal and by decreasing the use of it we can decrease the Operating room environmental pollution where scavenging system is not available. And secondary goal is pain relief in patients undergoing supra major surgeries like onco surgeries. Previous studies suggested that epidural anaesthesia with INJ Ropivacaine and opioids proved to be beneficial in onco abdominal surgeries.

For this study 32 patients were randomly assigned into 2 groups fulfilling inclusion and exclusion criteria. In the operative room on the day of surgery before giving general anaesthesia, under all aseptic precautions epidural catheter was inserted and 3 ml INJ Lignocaine with Adrenaline given as test dose immediately and then before giving IV induction agents epidural infusion of local anesthetic drug INJ Ropivacaine 0.3% and INJ Fentanyl 2mcg/cc-total 50cc volume- started acc to hemodynamic of the patient. Continuous infusion of local anesthetic leads to increase in protein binding (α 1-acid glycoprotein) and decreased clearance of the drug⁽¹¹⁾. We had chosen this group of drugs as rightly said by **Wheatley and colleagues**, who analysed four studies and reported that the group that received a combination of local anesthetic and lipophilic opioid as a continuous epidural infusion had much better analgesic effect as compared to groups that received either drug alone⁽¹²⁾. A lipophilic opioid such as fentanyl is preferred as it gets rapidly absorbed in the spinal cord and nearby vessels. Therefore, there is rapid decrease in the cerebrospinal fluid concentration and reduced cephalad spread⁽¹³⁾. After extubation the epidural infusion was stopped and immediately after extubation VAS score was assessed. Patients were asked about awareness under anaesthesia if any after shifting patient from operative room to post anaesthesia care unit (PACU). In GA only group analgesia was

managed by IV opioids and NSAIDS (INJ Diclofenac 75MG and INJ Tramadol 50MG). Post operatively in both the groups rescue analgesia was managed by INJ Paracetamol 1gram.

As per our data analysis need for inhalational agent, Sevoflurane requirement is less in patient undergoing surgery under general with epidural anesthesia with mean value of 26.88 and standard deviation of 5.886 with standard error mean of 1.472, as compared to patient undergoing surgery under general anesthesia only with mean value of 44.94 and std deviation of 10.804 and standard error mean of 2.701, with p value of <0.05, these results are same as studied by **Shir Y and colleagues** where they suggest that- EA patients have less post operative pain and an efficient intraoperative blockade of noxious afferent signals to the CNS is fundamental in reducing post operative pain ⁽²⁾. Patient's hemodynamics like pulse, blood pressure, etco2 are more stable in patients undergoing major abdominal surgery under general with epidural anesthesia with significant P value of <0.05 as compared to general anesthesia only similarly suggested by **Scott DA, Blake D and colleagues** and epidural infusion of Ropivacaine 2 mg/mL with fentanyl 4 microgram/mL proved to be most effective ⁽¹⁴⁾. The mean oxygen saturation in the postoperative period was 99% in both the groups, A lipophilic opioid such as fentanyl is less likely to cause respiratory depression. Post op 15 patient from EA with GA group did not require any IV analgesic agent but only one patient required IV analgesic agent as rescue analgesia, whereas all the patients operated upon general anaesthesia required rescue analgesia along with IV opioids and NSAIDS.

Rigg JR, Jamrozik K and colleagues studied Epidural anaesthesia and analgesia and outcome of major surgery: a randomized trial with adverse outcome and we also found similar results with 2 patients from EA with GA group had adverse event like hypotension whereas in GA only group 5 patients had adverse events like post op vomiting and hypotension. The improvement in analgesia, reduction in respiratory failure, and the low risk of serious adverse consequences suggest that many high-risk patients undergoing major intraabdominal surgery will receive benefit from general anesthesia combined with epidural anaesthesia intraoperatively with continuing postoperative epidural analgesia. ⁽¹⁵⁾. The side effects could also occur because of the drugs causing autonomic blockade and hemodynamic disturbance and/or effect of intravascular absorption of the drug reaching toxic levels- local anesthesia systemic toxicity. We did not have any of the above complications related to the procedure similarly studied by **Patil SS and colleagues** ⁽⁸⁾.

In our study visual analogue scale is also statistically significant with P value of <0.05 resembling the results of **Guay J and colleagues** suggesting that thoracic epidural containing a local anesthetic reduces the incidence of renal failure. Epidural analgesia may thus offer many advantages over other modes of postoperative analgesia ⁽¹⁶⁾. The results are similar to study conducted by **de Leon-Casasola OA and colleagues**, both forms of therapy were titrated to provide patients with a dynamic visual analog pain score of 5 or less on a 10-point scale throughout the study period. ⁽¹⁷⁾. The epidural bolus infusion was associated with a significant decrease of VAS (P < 0.001) and stable blood pressure and heart rate in all groups ⁽¹⁸⁾.

A combination of general anaesthesia and peri-operative epidural use decreases immunosuppression in gastric cancer resection ⁽¹⁹⁾. In patients undergoing lower abdominal surgery, the neuraxial blockade and surgical anesthesia achieved by epidural local anesthetics was associated with decreased postoperative analgesic demands. ⁽²⁾

It requires multidisciplinary approach for providing adequate analgesia and anaesthesia during these onco surgeries with minimal side effects and complications, where anaesthetist leads the pivotal role. In toto, our approach of using regional anaesthesia along with GA emphasis, reduction of environmental pollution by using less inhalational agent thus proving safe for patients and anaesthetists as well.

Further scope of the study:

- We can routinely practice these in all the long duration surgeries for pain relief and for better

outcomes. Moreover, regional anaesthesia can decrease cancer recurrence.

- We can compare two different local anesthetic drug potency with or without different additives.
- We can compare epidural anaesthesia with different facial plane block

LIMITATION OF THE STUDY:

- 1) BIS (bispectral index) monitor was not available.
- 2) Less no of patient were included in the study.
- 3) Blinding was not done.

CONCLUSION:

- We denouement that patient required less sevoflurane intraoperatively in EA with GA group and decrease use of perioperative opioids as compared to GA only group in today's scenario of opioid free anesthesia.

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Conflict of Interest:

Nil

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