

Cervical epidural analgesia combined with general anesthesia for head and neck cancer surgery: A randomized study

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Abstract

Background and Aims: The role of cervical epidural analgesia in head and neck cancer surgery is not fully explored. The aim of this study was to evaluate cervical epidural analgesia in terms of opioid and anesthetic requirements and stress response in patients undergoing head and neck cancer surgery.

Material and Methods: After institutional ethical committee approval and written informed consent, 30 patients undergoing elective head and neck cancer surgery were randomized into two groups: Group E (cervical epidural analgesia with general anesthesia), and group G (general anesthesia alone). In group E, an 18 gauge epidural catheter was placed at cervical (C) 6 – thoracic (T) 1 level. After test dose, a bolus of 10 ml of 0.2% ropivacaine was given followed by continuous infusion. Technique of general anesthesia and post-operative management was standardized in both the groups. Opioid and anesthetic drug requirement was observed. Blood glucose and serum cortisol levels were measured at baseline; post-incision and after surgery.

Results: There was significant reduction in the requirement of morphine ($P < 0.001$), isoflurane ($P = 0.004$) and vecuronium ($P = 0.001$) in group E. Post-operative, blood glucose and serum cortisol levels were significantly reduced ($P = 0.0153$ and 0.0074 , respectively). Early post-operative pain was reduced with the lesser requirement of post-operative morphine.

Conclusions: The use of combined cervical epidural analgesia with general anesthesia reduces opioid, anesthetic drug requirement and stress response as compared to general anesthesia alone in patients undergoing head and neck cancer surgery.

Keywords: Anesthesia techniques, cancer surgery, cervical epidural, stress response

Introduction

General anesthesia is the technique of choice for head and neck cancer surgery. Regional anesthesia techniques for head and neck cancer surgery include the use of cervical epidural anesthesia as a sole technique^[1-3] or cervical epidural analgesia for pain management.^[4]

Recent studies indicate that the use of regional anesthesia techniques may benefit patients undergoing laryngeal and

hypo-pharyngeal cancer surgery.^[5] Proposed mechanisms include reduced anesthetic requirements and neuro-endocrine stress response.^[6]

However, randomized trials evaluating the role of cervical epidural anesthesia/analgesia on opioid, anesthetic requirements and stress response in head and neck cancer surgery are lacking. Our hypothesis is that the use of cervical

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epidural analgesia may reduce opioid, anesthetic requirements and stress response in head and neck cancer surgery and these parameters were evaluated in this study.

Material and Methods

This study was approved by institutional ethics committee, and written informed consent was taken from all the patients.

This study included American Society of Anesthesiologist status I and II patients of either sex, aged between 18 and 65 years undergoing elective head and neck cancer surgery. Patients having infection at local site and coagulopathy were excluded from the study.

This was an open label study. Patients were allocated randomly into two groups of 15 patients each: Group E (received combined cervical epidural analgesia with general anesthesia), and group G (received general anesthesia alone). Method of randomization used was computer-generated random number sequence. Method of concealment used was sequentially numbered opaque envelopes.

All patients were pre-medicated with ranitidine 150 mg and alprazolam 0.25 mg the night before surgery and 2 h before surgery with sips of water. Inside the operation theatre, an intravenous line was secured and ringer lactate infusion was started. All patients were monitored with electrocardiogram, non-invasive blood pressure, oxygen saturation, end-tidal carbon dioxide (EtCO₂), temperature, end-tidal isoflurane concentration analyzer and neuromuscular monitoring done using nerve stimulator.

In group E, cervical epidural catheter was inserted in an operating room. Cervical epidural was placed at C 6 – T 1 level in a sitting position with neck flexion. Epidural space was identified by using the loss of resistance to air technique. Epidural catheter (18 G) was placed 3-4 cm into the epidural space. A test dose of 3 ml of 2% lignocaine with epinephrine (1:200,000) was given for confirmation. For analgesia, 10 ml of 0.2% ropivacaine was given as bolus dose followed by 0.2% ropivacaine infusion at a rate of 5 ml/h. After 10 min of injection of ropivacaine, general anesthesia was induced.

Patients in both the groups received general anesthesia using the same technique. Anesthesia was induced with morphine 0.1 mg kg⁻¹ followed by propofol 1.5-2 mg kg⁻¹ till the loss of verbal response. To facilitate naso-tracheal intubation, succinylcholine 1.5-2 mg kg⁻¹ was given. Maintenance of anesthesia was done using nitrous oxide in oxygen and isoflurane (end tidal concentration 0.8-1.2%). For top-up

doses of vecuronium, neuromuscular monitoring was done using train of four responses.

Intra-operative, systolic blood pressure (SBP) and heart Rate (HR) >20% of the baseline was treated by morphine 3 mg intravenous (IV) bolus and/or increasing depth of anaesthesia (end tidal isoflurane concentration 1.5-2%).

Morphine, vecuronium and anesthetic agent requirements (end tidal isoflurane concentration) were noted.

If any of the patients developed bradycardia (HR <40 per min), injection atropine was used for treatment. In the case of hypotension (SBP <40% of baseline), fluid bolus was given. If necessary, mephentermine 3 mg bolus was given. Atropine and mephentermine requirement were noted.

A venous sample (5 ml) was taken for blood glucose measurements and serum cortisol levels at baseline, 30 min after incision, 60 min after surgery.

Fluid management was done as per standard protocol being followed for these procedures. Blood transfusion was given when blood loss exceeded the allowable blood loss for the particular patient.

Study lasted till 6 h post-operatively and during this period, patients were nursed in the high dependency unit. Vital signs (heart rate, blood pressure and respiratory rate) were monitored. Epidural infusion was discontinued in group E, and all patients received background morphine infusion at the rate 0.01 mg kg⁻¹ h⁻¹. All patients received IV paracetamol 1g at the end of surgery and thrice a day, thereafter. Patients were assessed for pain at 2, 4 and 6 h using a standard visual analogue scale (VAS). Morphine 3 mg IV bolus was given when VAS >3. Post-operative morphine requirement was recorded. Patient's were monitored for any sedation and/or respiratory depression.

Statistical analysis

Sample size calculation was based on morphine requirement in the two groups. In the pilot study, morphine requirement in the group G was found to be 7.6, and in the group E, it was 6.5 with a standard deviation of 0.95. By taking power at 85% and alpha error at 0.5, a sample size of 14 patients each was calculated.

To even out the sample size, 15 patients in each group were enrolled. Data were summarized as mean and standard deviation. T-test and Mann-Whitney test was used to analyse morphine, vecuronium and isoflurane requirement (Primary outcome). Blood glucose and serum cortisol

levels (secondary outcomes) were analysed by two-way analysis of variance (ANOVA) test for repeated measures with post-hoc Bonferroni correction. Graph pad prism version 15 software was used to analyze the data.

Results

A total of 30 patients were enrolled for the study. Out of which, 15 patients in group G and 14 patients in group E completed study. One patient in group E could not complete the study due to failure to place epidural catheter. Type of surgery included oral, hypo-pharyngeal and laryngeal cancers. Patient characteristics are summarized in Table 1.

There was significantly lower consumption of morphine ($P < 0.0001$), isoflurane ($P = 0.004$) and vecuronium ($P = 0.001$) in group E compared with the group G as shown in Table 2.

Mean dose of ropivacaine used in group E was found to be 87.13 ± 9.28 [Table 1].

No statistically significant difference was found in baseline and post-incision blood glucose levels. Post-operative glucose levels were found to be lower in group E [Figure 1].

No statistically significant difference was found in baseline and post-incision serum cortisol levels. Post-operative serum cortisol levels were found to be lower in group E [Figure 2].

Mean VAS scores were found to be 2.84, 2.94, 2.7 (group E) vs. 3.58, 3.32, 3.12 (group G) at 2, 4 and 6 h post-operatively. Difference was found to be statistically

significant at 2 h ($P = 0.004$). Post-operative morphine IV bolus requirement was found to be significantly lower in group E [Figure 3].

No statistically significant difference was observed in the hemodynamic parameters. In group E, incidence of bradycardia was 6.6%. Hypotension at induction was seen in 13.3% of the patients.

Discussion

Promising effects of regional anesthesia techniques in cancer surgery have revived interest in cervical epidural anesthesia and analgesia techniques for head and neck cancer patients. Use of regional anesthesia techniques as a part of balanced anesthesia may help to counteract immunosuppressive effects of pain and neuro-endocrine stress response.^[7]

Our study compares combined cervical epidural analgesia and general anesthesia with general anesthesia alone in patients undergoing head and neck cancer surgery.

Our study demonstrates that the use of cervical epidural analgesia reduces morphine, isoflurane and vecuronium requirements. Stress response in terms of blood glucose and serum cortisol levels was seen to be less in the immediate post-operative period. Early post-operative pain is reduced with the lesser requirement of post-operative morphine.

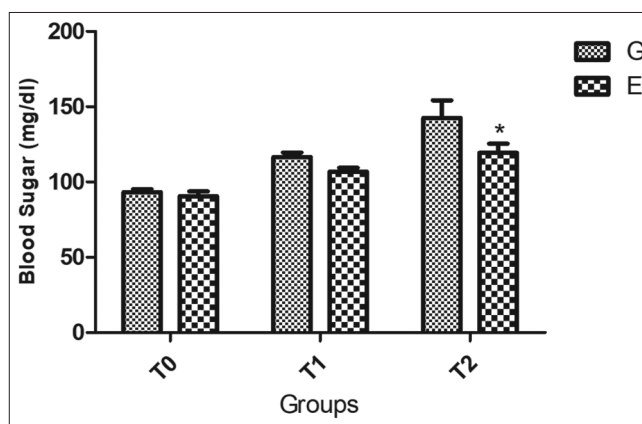


Figure 1: Blood sugar levels measured at three different time points (T0 – baseline, T1 – 30 minutes after incision, T2 – 60 min after surgery). Difference found to be significant at T2 (* $P = 0.015$)

Table 1: Patient characteristics, surgical and epidural data*

	Group G	Group E
Age (yr)	51.6±7.1	49.8±8.9
Weight (kg)	63.8±7.0	62.1±7.1
Sex (M/F)	10/5	9/5
Oral/Hypopharyngeal/Laryngeal cancer	4/9/2	5/8/1
Duration of surgery (h)	5.96±0.51	6.06±0.94
Ropivacaine used (mg)	Not applicable	87.13±9.28

*Data expressed as mean±SD and n. No significant difference observed between the two groups

Table 2: Opioid and anesthetic agent requirement data*

	Group G	Group E	Mean difference (95% CI)	P
Morphine (mg)	8.9±0.95	7.1±1.02	1.8 (-2.41 to 1.18)	<0.0001
End-tidal Isoflurane (%)	1.7±0.3	1.4±0.2	0.3 (-0.45 to 0.14)	0.004
Vecuronium (mg/h ⁻¹)	2.9±0.79	1.4±0.48	1.5 (-1.90 to 1.09)	0.001

*Data expressed as mean±SD

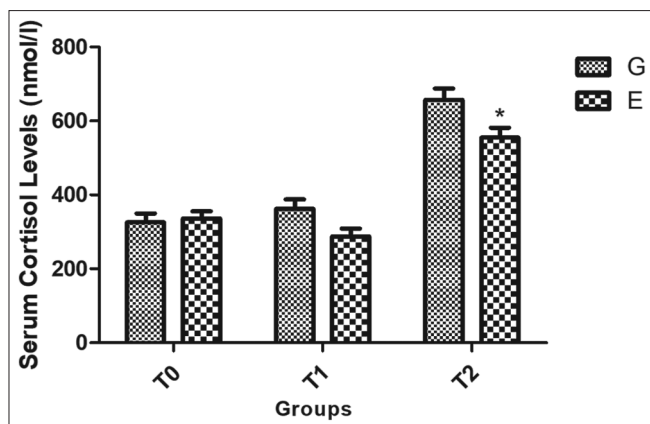


Figure 2: Serum cortisol levels measured at three different time points (T0 – baseline, T1 – 30 min after incision, T2 – 60 min after surgery). Difference found to be significant at T2 (* $P = 0.0074$)

The combined use of cervical epidural and general anesthesia in the carcinoma of neck has been studied and results show that it helps to stabilize hemodynamics during cervical surgery.^[8]

Results of our study are comparable to previous studies that demonstrate reduced neuro-endocrine stress response with the use of thoracic epidural techniques in patient undergoing major abdominal surgeries. Use of thoracic epidural led to reduced consumption of opioids, inhalational agent along with inhibition of stress response (blood glucose and serum cortisol levels) in the peri-operative period.^[9-11]

Effect of cervical epidural anesthesia on stress response was evaluated by Nakamura *et al.* in patients undergoing upper arm surgeries. There was incomplete abolition of stress response with cervical epidural anesthesia in terms of blood glucose levels and insulin secretion.^[12]

In our study, we used ropivacaine as the local anesthetic as it produces less intense motor block as compared to bupivacaine. Lower concentration of ropivacaine (0.2%) was used as intended for analgesia purposes.

Effects of bupivacaine and ropivacaine have been compared in patients undergoing modified radical mastectomy under cervical epidural anesthesia. Authors concluded that ropivacaine is a safer option in view of less motor blockade and less effect on respiratory parameters.^[13] Use of 0.2% ropivacaine has been found to be very effective in continuous thoracic epidural anesthesia in patients undergoing modified radical mastectomy for breast cancer.^[14]

A bolus of 10 ml of ropivacaine was given based on previous reports that show that a volume of 10 ml of ropivacaine through cervical epidural at C 6-7 level achieves block at C 2-T 10 levels.^[15]

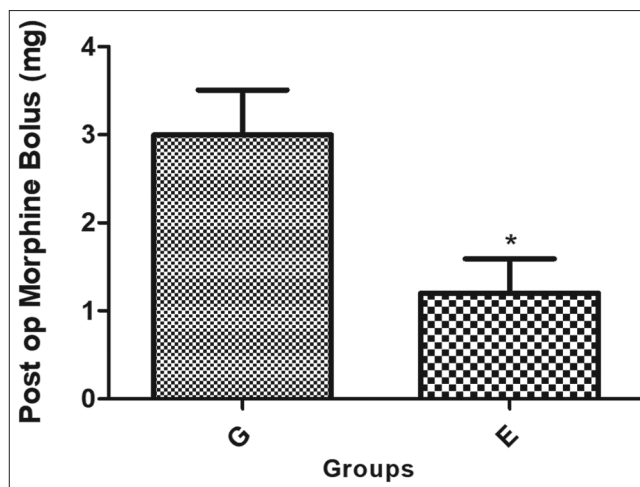


Figure 3: Post-operative morphine requirement (* P value 0.01)

Hong *et al.* studied effects of local anesthetics and opioids in cervical epidural anesthesia. They observed that combining local anesthetics and fentanyl can produce hemodynamic and ventilatory side effects. Hence, the use of epidural opioids was avoided in our study.^[16]

In our study, both the groups received IV morphine and IV paracetamol for post-operative analgesia. Post-operative VAS score was found to be reduced at 2 h with reduced post-operative morphine requirement in group E.

In a previous study, authors demonstrate better analgesia at rest (reduced VAS score) in the first 6 h after surgery with administration of fentanyl using cervical epidural route as compared to IV route in patients undergoing pharyngolaryngeal surgery. Total fentanyl dose requirement was found to be similar in both the groups.^[6]

Lower post-operative morphine requirement observed in our study may be due to use of multi-modal analgesia (epidural analgesia, opioids and paracetamol) in the epidural group. Epidural use was pre-emptive and was not continued in the post-operative period.

Above findings of our study match with the results of a study by Amiri *et al.* suggesting that the use of multi-modal analgesic technique using combination of drugs reduce post-operative pain scores and opioid consumption in patients undergoing radical neck dissection.^[17]

In the cervical epidural with general anesthesia group (group E), one patient developed bradycardia, which responded to atropine and two patients developed hypotension at induction which responded to fluid boluses. There were no other side effects associated with the use of cervical epidural.

Previous studies using cervical epidural anesthesia for neck and arm surgery show that the incidence of hypotension and bradycardia is 20-30% and is easily treatable.^[18]

Anesthetic dose of local anesthetics is associated with motor block of upper extremities with decrease in ventilatory parameters in the post-operative period. This decrease is proportionate to concentration of local anesthetic used.^[19,20]

In our study, although we did not measure ventilatory parameters, they are unlikely to be affected as only lower concentration of local anesthetic intended for analgesia was used, no opioids were added and epidural infusion of ropivacaine was discontinued in the post-operative period.

Limitations of our study include small sample size, titration of anesthetic drugs was based on hemodynamic parameters (non-invasive blood pressure and heart rate) and observer bias cannot be ruled out as blinding was not possible in this study. Also, epidural use was limited to intra-operative period and no follow up was done for cancer recurrence or metastasis.

Conclusion

The use of combined cervical epidural analgesia with general anaesthesia reduces opioid, anesthetic drug requirement and stress response as compared to general anesthesia alone in patients undergoing head and neck cancer surgery.

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Conflicts of interest

There are no conflicts of interest.

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