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A Randomized Double-Blind Placebo-Controlled Clinical Trial To Assess The Efficacy Of Dexamethasone To Provide Postoperative Analgesia After Cervical Plexus Block In Patients Undergoing Elective Thyroid Surgery.

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ABSTRACT

Background: In an attempt to improve the patient comfort after thyroidectomy, various methods of pain-relief have been tried to prolong the duration and to improve the quality of postoperative analgesia. Cervical plexus block using steroids like dexamethasone, administered as an adjuvant along with local anaesthetic agents, could be of particular interest. **Methods:** Fifty patients undergoing elective thyroidectomy were randomly assigned to one of the following groups containing twenty five patients each. Group D patients received 8 mg (2 ml) of dexamethasone added to 13 ml of 0.25% levobupivacaine as cervical plexus block (total volume 15 ml). Group L patients received 13 ml of 0.25% levobupivacaine and 2 ml of isotonic saline (15 ml in total) as cervical plexus block. Analgesic effect was evaluated by measuring pain intensity (VAS score) and duration of analgesia. **Results:** A longer delay was observed for first requirement of supplementary analgesic in group D (572.24±68.42 minutes) compared to group L (402.46±52.34 minutes). Total consumption of diclofenac sodium in first 24 hours in postoperative period was significantly less in group D. No significant side effects were noted. **Conclusion:** Dexamethasone, used as adjuvant to levobupivacaine for cervical plexus block in patients undergoing thyroidectomy, improve the quality and prolong the duration of post operative analgesia.

Keywords: Dexamethasone, Levobupivacaine, Thyroidectomy, Cervical Plexus block.

INTRODUCTION

Peripheral nerve blocks are gaining popularity because of superior quality of postoperative analgesia with fewer side effects, greater patient satisfaction and faster functional recovery after surgery. Cervical plexus blocks can be performed in patients undergoing thyroid surgery and prolonged postoperative analgesia can be provided by administering local anaesthetic solutions with or without adjuvant.[1]

Dexamethasone is potent and highly selective glucocorticoid with minimal mineralocorticoid effect. It blocks the nociceptive impulse transmission along the myelinated C fibres.[2] So when used in association with local anaesthetics, dexamethasone prolongs the duration of local anaesthetic block.[3,4] This placebo controlled, double blind, prospective study is designed to assess the efficacy of dexamethasone administered as adjuvant to local anaesthetic levobupivacaine for single bolus injection of cervical plexus block in patients undergoing elective thyroidectomy.

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MATERIALS AND METHODS

The randomized trial was performed between December 2016 and September 2017. The study protocol was approved by the ethical committee of Calcutta National Medical College, Kolkata and informed consent was obtained from every patient. Fifty ASA I –II euthyroid patients of either sex, aged 18-65 years, undergoing elective thyroid surgery were randomly assigned to one of the two groups, containing twenty five patients each. Group D patients received 8 mg (2 ml) of dexamethasone added to 13 ml of 0.25% levobupivacaine as cervical plexus block (total volume 15 ml). Group L patients

received 13 ml of 0.25% levobupivacaine and 2 ml of isotonic saline (15 ml in total) as cervical plexus block. [Group size of twenty five patients was determined by power analysis study, which is mentioned as follows: the primary outcome of interest is dichotomous (success/failure, yes/no, etc). For example, 25% of the subjects on the standard therapy had a successful outcome and it is of clinical relevance only if we observe a 40% (effect size) absolute improvement for those on the study therapy (i.e. 65% of the subjects will have a successful outcome). How many subjects do we need to observe a significance difference? For a two-sided test of 5%, a simple formula to calculate the sample size is given by m (size per group) = c X $\pi1(1 - \pi1) + \pi2(1 - \pi2) / (\pi1 - \pi2)2$ where c = 7.9 for 80% power and 10.5 for 90% power, $\pi1$ and $\pi2$ are the proportion estimates. Thus from the above example, $\pi1 = 0.25$ and $\pi2 = 0.65$. For a 80% power, we have m (size per group) = 7.9 X [0.25 (1 – 0.25) + 0.65 (1 – 0.65)] / (0.25-0.65)2 = 20.49. Hence 21 X 2 = 42 subjects will be needed. Due to availability of subjects, we selected 50 patients for our study divided into two equal groups].

Patients having known bleeding diathesis or known diaphragmatic motion abnormalities, history of cardiovascular, neurological, respiratory diseases, patient receiving chronic pain treatment and patients with history of anaphylaxis to local anaesthetics were excluded from the study. On preoperative round, patients were explained regarding the procedure and were also taught to interpret the visual analogue scale (VAS) (graded from 0 = no pain to 10 = maximum pain).

All patients were given tab. diazepam 10 mg and tab. ranitidine 150 mg orally on the night before surgery and tab. ranitidine was repeated on the day of surgery two hours before induction with sips of water. On the operation table, routine monitoring (ECG, pulse-oximetry, NIBP) were started and baseline vital parameters like heart rate (HR), blood pressure (systolic, diastolic and mean) and arterial oxygen saturation (SpO2) were recorded. An intravenous line was secured.

After preoxygenation for 3 minutes, induction of anaesthesia was done by fentanyl 2 µg/kg and propofol 2 mg/kg administered intravenously(i.v.). Patients were intubated with appropriate size endotracheal tube after muscle relaxation with vecuronium bromide in a dose of 0.08 mg/kg. Anaesthesia was maintained with 33% oxygen in nitrous oxide and isoflurane 0.6%. Muscle relaxation was maintained by intermittent i.v. bolus doses of vecuronium bromide.

After endotracheal intubation, bilateral cervical plexus block were performed by using drugs as per grouping. Deep cervical plexus block was performed by a technique suggested by Winnie et al5. A 23 gauge short beveled needle was inserted behind the lateral border of sternocleidomastoid muscle, 3 cm distal to the mastoid process. After negative aspiration, 9 ml of solution was injected. The superficial block was performed by using same needle inserted at the midpoint of the lateral border of sternocliedomastoid muscle. After negative aspiration, 6 ml of solution was injected in four directions (1.5 ml in each direction) to block the main branches (lesser occipital, greater auricular, transverse cervical and supraclavicular nerves) of the plexus. Sealed envelops containing one syringe with levobupivacaine and saline or levobupivacaine and dexamethasone were prepared The injection was given with unlabelled syringes prepared by an anaesthesiologist not involved in the perioperative management and pain assessment of the patients.

Surgical incision was given twenty minutes after the cervical plexus block and changes in haemodynamics were noted down. Increase in heart rate more than 20 bpm and systolic arterial pressure more than 20 mm Hg in response to surgical incision was considered as failure of cervical plexus block and was excluded from the study.

At the end of the surgical procedure, ondansetron 4 mg was administered for prophylaxis against nausea and vomiting. Residual neuromuscular paralysis was reversed using intravenous glycopyrrolate and neostigmine and subsequently extubation was done. Intensity of pain was assessed. VAS score 4 or more was considered as failure of block and was excluded from the study.

All patients were observed postoperatively by resident doctors who were unaware of the study group. Patients were transferred to postanaesthesia care unit and intensity of pain was assessed after thirty minutes and then an hourly interval for 24 hours. Diclofenac sodium (75 mg) was administered i.v. as analgesic supplement if the recorded VAS pain score was 4 or more and was repeated every 8 hour, if required. Tramadol 100 mg i.v. was used as a rescue analgesic, if the patients continued to have pain even after diclofenac administration. The time to the first analgesic requirement and the total diclofenac consumption during first 24 hour after operation were also recorded.

Statistical analysis:

The results obtained from the study are presented in the following section in a tabulated manner. The results are expressed in Mean ± SD. Comparison between groups were performed with the Kruskal-Wallis one way ANOVA by ranks or Fisher's exact test for small samples with a 5% risk. Mann-Whitney-Wilcoxon tests were performed when tests of normal distribution have failed. P value<0.05 was considered to be statistically significant [Graph Pad In Stat version 3.05, Graph Pad Software, SanDiego, CA]

RESULTS

Two patients from group D had significant rise in heart rate and systolic blood pressure following surgical incision. One patient of group L complained of severe pain (VAS>4) following reversal of anaesthesia. The failure rate was 8% (2 patients) in Group D and 4% (1 patient) in Group L. These three patients were excluded from the study. Therefore data from 47 patients were available for analysis; group D (n=23) and Group L (n=24).

The two groups were comparable with regard to age, sex, body-weight, height and duration of surgery (P>0.05) [Table 1]. Intensity of pain was significantly less in Group D compared to Group L at 30 minutes (P<0.01), 1 hour (P<0.01), 2 hour (P<0.05) and 6 hour (P<0.05) following surgery. However from 10 hour, intensity of pain was comparable in both groups [Table 2].

The duration of analgesia (time period between the cervical plexus block and the first postoperative analgesic demand) was significantly more in group D compared to group L (572.24±68.42 minutes vs. 402.46±52.34 minutes; P<0.01) [Table 3]. Total diclofenac consumption in first 24 hours was significantly less in group D compared to group L (P<0.01) [Table 3]. None of the patients received tramadol.

Table 1: Patients Characteristics (mean±SD)

Variables/Groups	Group L (n=24)	Group D (n=23)	P value
Age (Year)	36.6 ±8.6	38.6 ±9.2	0.43
Sex (M/F)	8/16	8/15	
Weight (kg)	48.3 ± 10.4	50.6±10.6	0.57
Height(cm)	154.76±13.6	153.36±12.6	0.37
Duration of surgery (minutes)	72.62. ± 17.6	74.24 ± 18.6	0.63

Table 2: Intensity of Pain in Postoperative Period Intensity of Pain(VAS)

Postoperative Period	Group L(n=24) (Mean±SD)	Group D (n=23) (Mean±SD)
30 min	2.72±0.68	1.82±0.47**
1 hour	2.83±0.77	1.93±0.54**
2 hour	3.03±0.83	2.3±0.63*
6 hour	4.03±1.03	3.17±0.72*
10 hour	3.73±0.9	3.63±1.02
14 hour	3.53±0.9	3.43±1.02
18 hour	3.65±1.04	3.56±1.04
24 hour	3.68±1.1	3.62±1.07

* = P< 0.05 ; ** = P< 0.01

Table 3: Duration of analgesia and diclofenac consumption in the postoperative period (Mean± SD)

	Group L(n=24)	Group D(n=23)
Duration of Analgesia (minutes)	572.24±68.42	402.46±52.34**
Diclofenac consumption in 24 hours (mg)	153.6±26.4	106.4±18.4**

* = P< 0.05 ; ** = P< 0.01

DISCUSSION

Combined superficial and deep cervical plexus block is a technique that was initially developed to avoid general anaesthesia for carotid end arterectomy.[6] This block has been successfully used to perform thyroid surgery as well as other neck surgries.[7,8] Subsequently many clinicians used cervical plexus block to provide postoperative analgesia following thyroid surgery.[9i] Diendonne et al.[10] reported the advantages of bilateral cervical plexus block administered immediately after thyroid surgery in terms of postoperative pain relief. They observed that 45% and 34%% patients did not require opiate analgesics during first 2 hours and 24 hours after surgery. Similarly in another study by Aunac S and Carlier M7, 73% and 69% of patients with bilateral cervical plexus block were free from pain without any opiates during the first 2 and 24 hours after surgery. Unlike previous reports, all patients in the present study felt pain during first 24 hours following surgery and received i.v. diclofenac sodium. Reasons might be the routine use of paracetamol 2 gm, immediately after surgery by the previous workers which possibly reduced the requirement of opiates in postoperative period.

Dexamethasone a 9α-derivative synthetic glucocorticoid was selected because of its highly potent anti-inflammatory property (about 25-30 times as potent as hydrocortisone) and with minimal mineralocorticoid activity, thus found to be safer and devoid of potential side effects. Steroids have block prolonging effect according to their anti-inflammatory potency. Local anesthetic agents can provide analgesia for limited period of time when used as single injection. To extend the analgesia period beyond the operation rooms, various adjuvants have been tried with the aim of prolonging the duration and improving the quality of analgesia.

Because steroids block the transmission of impulse in nociceptive C fibres, it prolongs the action of local anesthetics when used together.[2] Few preliminary studies reported that steroids significantly prolong the duration of analgesia in extremity nerve blocks.[3,4] A study in supraclavicular brachial plexus block reported that dexamethasone when added as adjuvant to local anesthetic bupivacaine resulted in significant prolongation of anesthesia.[11] We assumed the similar probable mechanism regarding dexamethasone and levobupivacaine combination as bupivacaine and levobupivacaine were comparable regarding quality and duration of blockade when used in three-in-one blocks in a study by Urbanek B and colleagues.[12] The dense and prolonged block in the dexamethasone group is due to the synergistic action with local anesthetic levobupivacaine on blockade of nerve fibres2. The block prolonging effect of dexamethasone is due to its local action, not a systemic one.[13,14] It has been found that this effect of steroid is mediated via steroid receptors.[15] When steroids alone were used in regional blocks, the blockade is not produced. Steroids might bring about this effect by altering the function of potassium channels in excitable cells.[16]

In our study, the means of assessing postoperative analgesia was the time to first analgesic administration, the total amount of analgesic consumed in the first 24 hour period after surgery and the VAS scores at different time in first 24 hour. The delay between cervical plexus block with levobupivacaine and dexamethasone and supplementary analgesic administration in the form of i.v. diclofenac was 572.24±68.42 minutes in our study compared to cervical plexus block using levobupivacaine alone (402.48±52.34 minutes) and the difference was statistically significant. Mean requirement of diclofenac sodium in the first 24 hour was also lesser in group D as compared to group L. Dexamethasone has never been administered in combination with levobupivacaine for increasing the duration of postoperative analgesia after thyroid surgery in any previous study. In a study by Pal R and Ray M,[17] it was found that time period for first analgesic request after cervical plexus block with bupivacaine and dexmedetomidine was 8.19±1.6 hours and this finding was comparable to our study.
The potential serious complications associated with cervical plexus block include vertebral artery, subarachnoid or epidural injections followed by transient motor weakness18 and phrenic nerve palsy. Patients were closely monitored for any complications in postoperative period. No serious complication was observed in our study.

Limitations:

This study is aimed at describing the postoperative analgesia after total thyroidectomy. Here, we have performed general anaesthesia followed by bilateral cervical plexus block. As a result of which, we could not evaluate the immediate effect of the sensory block except for the change in heart rate and blood pressure. In post-operative period, we could not assess the sensory block due to presence of adhesive bandage that protected the surgical wound and the suction drains.
In this present study, we have randomly selected fifty patients of ASA1 and ASA2 for undergoing total thyroidectomy. The sample size being small, we need further evaluation with larger sample size.

CONCLUSION

In conclusion, dexamethasone administered as adjuvant to local anaesthetic levobupivacaine for cervical plexus block improves the quality and duration of postoperative analgesia and reduces the consumption of diclofenac sodium in patients undergoing elective thyroid surgery.

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