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Original article:

Post-operative analgesia following arthroscopy: A comparative outcome of intra-articular Neostigmine and Dexamethasone

Dr Prerna Punj[1], Dr Tushar D Bhavar[2], Dr Himanshu Khanapurkar[3]

[1]Senior Resident, Dr Ram Manohar Lohia Hospital, New Delhi. [2] Associate Professor, Department of Anaesthesia and Critical Care, RMC, Loni, [3]Junior Resident, Department of Anaesthesia and Critical Care, RMC, Loni

Corresponding author: Dr Tushar D Bhavar: Associate Professor, Department of Anaesthesia and Critical Care, RMC, Loni; Email: tganesh55555@gmail.com

Abstract

Introduction: Post-operative analgesia after arthroscopic knee surgeries is important for early recovery, mobilisation and decreased hospital stay. So we conducted a study comparing the duration of post-operative analgesia after intra-articular injection of bupivacaine with dexamethasone and with neostigmine.

Aim and objectives: Our aim was to evaluate the effect of intra-articular neostigmine compared to dexamethasone for post-operative analgesia following arthroscopic surgeries with respect to duration of analgesia and additional diclofenac requirement.

Methodology: 40 ASA I and II patients of both sexes in the age group of 18 - 60 years scheduled for arthroscopic knee surgeries were divided into two groups. Group D was given intra-articular 0.5% bupivacaine with 8mg dexamethaosone. Group N was given intra-articular 0.5% bupivacaine with 0.5 mg neostigmine. Duration of post-operative analgesia and additional diclofenac requirement on POD1 and POD2 was observed and side-effects were noted.

Results: Mean duration of post-operative analgesia was significantly more in group D as compared to group N with *p* value of 0.0001. The requirement of additional diclofenac on POD 1 and 2 was significantly less in group D as compared to group N with *p* values of 0.0422 and 0.0103 respectively.

Conclusion: Intra-articular bupivacaine with dexamethasone significantly prolongs postoperative analgesia and has minimal side effects as compare to bupivacaine with neostigmine.

Keywords: Arthroscopy, post-operative analgesia, bupivacaine, dexamethasone, neostigmine

INTRODUCTION

Recent growth of arthroscopic surgeries has led to new challenges for post-operative analgesia which helps in early mobilisation, rehabilitation and discharge. Intra-articular administration of local anaesthetics with different adjuvants is being evaluated for post-operative analgesia. Recent research indicates modulation of pain perception by cholinergic system, anticholinesterases like neostigmine are being evaluated for potential efficacy in post-operative pain relief.[1,2] Dexamethasone is potent and highly selective glucocorticoid which blocks the nociceptive impulse transmission along the myelinated C fibres, suppresses ectopic neuronal discharge.[3] In our study the duration of post-operative analgesia was compared between dexamethasone and neostigmine as adjuvants to intra-articular bupivacaine.

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Aims and Objectives:

Aim: To evaluate the effect of intra-articular neostigmine compared to dexamethasone for post-operative analgesia following arthroscopic surgeries.

Primary objective: To evaluate - duration of analgesia and requirement of rescue analgesia till second post-operative day

Secondary objective: To evaluate complications in perioperative period

Methodology:

The prospective case control study was conducted in the Department of Anesthesiology & Critical Care, P.R.H. Loni, after approval from the ethical committee and written informed consent from the patients. Sample size for the study was calculated using open-EPI software, applied to the study by Yadav RK et al., comparing mean duration of analgesia, for the power of study to be 80 % and confidence interval 95%. The minimum sample size calculated was 38 (19 in each group). Considering attrition and procedure failure, the sample size for this study was decided as 40 (20 in each group). Study group included patients aged between 18 to 60 years, belonging to ASA I/II patients without any co-morbidity undergoing elective arthroscopic ACL reconstruction surgeries at P.R.H. Loni. Patients receiving any other modality for pain relief, with known hypersensitivity to study drugs, psychiatric disorder, pregnant or breast feeding female were excluded from the study. Patients were randomly divided into two groups using block randomization -

GROUP D- Patients received intra-articular 8 mg dexamethasone with 0.5 % bupivacaine with total volume 20cc, after the procedure before removing the scope.

GROUP N- Patients received intra-articular 0.5 mg neostigmine in 0.5% bupivacaine with total volume 20cc, after the procedure before removing the scope.

All solutions were free of preservatives, opened just prior to injection. The day before surgery, the study groups were introduced to VAS with 0 as an indication of no pain at all and 10 as an indicator of the worst possible pain.

Spinal anaesthesia was scheduled for all the patients with intrathecal injection of 15-20 mg 0.5% bupivacaine with dextrose, as per the built and sex of the patient. Intrathecal and parenteral opioids and NSAIDs were avoided pre-and intra-operatively. Patients with inadequate effect were of spinal anaesthesia were given general anaesthesia and were omitted from the study. All patients underwent arthroscopic surgery after inflation of a thigh tourniquet to 300-350 mmHg. At the conclusion of surgery, the appropriate study drug was administered in a randomized manner from a coded syringe into the joint space via an 18G needle. The tourniquet was deflated and the patient was taken into the post-operative room and subsequently to the ward.

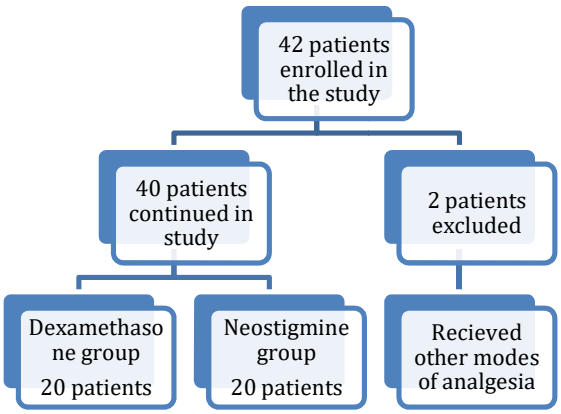
An observer, blinded to the group assigned to the patient, noted the hemodynamic monitoring, VAS scoring at every 2nd hourly till 14 hrs. Administration of study drug was considered as time zero for calculating the duration of analgesia. The time for administration of rescue analgesia was considered as end-point of duration of analgesia.

Patients were administered 75mg diclofenac sodium iv diluted in 100ml normal saline on patient demand or at VAS score >5 and total dose given till second post-operative date was noted.

Evaluation of adverse effects included assessment of the occurrence of post-operative emesis and nausea and incidence of nocturnal pain, bradycardia and urinary retention.

All data was entered into a proforma in Excel sheet (MS Office 2016) and statistical analysis was done using SPSS software (Statistical Package for Social Science [SPSS] version 19.0 for Windows, SPSS, Inc). P value < 0.05 was considered statistically significant. Chi-square test was used to compare qualitative data. Students unpaired t test was used for quantitative data to compare mean and standard deviation. Repeated variables were analyzed with repeated measure ANOVA. Post hoc multiple comparison test was done using the Tukey-Kramer method.

Figure 1 : Study Design



Results:

Table no. 1. Demographic Data

Variables	Group D	Group N	Test Applied	P value	Significance
Age (Years)	42.06 ± 8.56	46 ± 8.82	Students unpaired t test	0.06030	Not Significant
Gender (Male/Female)	13/7	11/9	Chi-Square test	0.4167	Not Significant
Height (cm)	164.52 ± 5.62	167.03 ± 8.34	Students unpaired t test	0.1562	Not Significant
Weight (kg)	70.69 ± 6.99	73.03 ± 7.25	Students unpaired t test	0.1731	Not Significant
Duration of Surgery (min)	119.26 ± 38.84	126.97 ± 49.83	Students unpaired t test	0.4752	Not Significant

Table no. 2. Assessment of Pain

Variable	Group D	Group N	P value
Duration of analgesia (min)	636.24 ± 95.62	496.51 ± 102.68	0.0001
Additional Diclofenac (POD-1) (mg)	96.4 ± 24.36	116.6 ± 36.18	0.0422
Additional Diclofenac (POD-2) (mg)	169.28 ± 33.57	196.18 ± 29.34	0.0103

Figure 2 : Duration of Analgesia

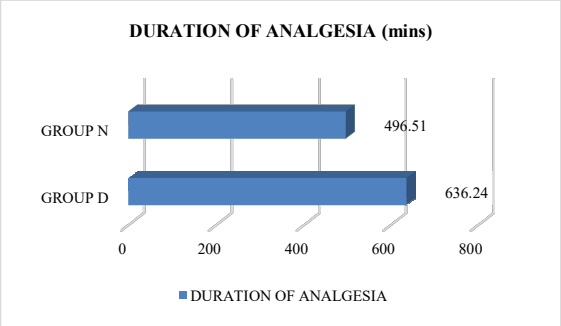


Figure 3 : Additional Diclofenac Requirement

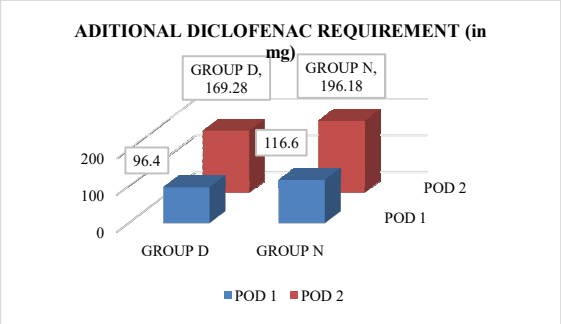


Table no. 3. Side Effects

Variables	Group D	Group N	P value
Nausea/Vomiting	1	7	0.1514
Nocturnal Pain	3	8	0.0766

42 patients were enrolled in the study, of which two patients were excluded was they received opioids intraoperatively. Remaining 40 patients were divided into two groups by block randomisation, as shown in figure 1 and a blinded observer monitored the patients. Mean age, weight, height and duration of surgery were statistically insignificant so both groups were comparable demographically, as seen in Table no.1. As described in table no.2 and figure 2, the mean duration of analgesia was 636.24 min with SD of 95.62 min in group D and 495.61 min with SD of 102.68 min. The duration of post-operative analgesia in group D was significantly more than group N with *P* value of 0.0001. As shown in table no.2 and figure 3, rescue analgesia requirement of Diclofenac was significantly lower in group D compared to group N on first and second post-operative days with *P* values of 0.0422 and 0.0103 respectively. As stated in table no.3, nausea vomiting and nocturnal pain was more in group N with *P* values of 0.1514 and 0.0766 respectively. No incidence of bradycardia and urinary retention was noted.

Discussion

Surgical excision and resection in knee arthroscopy produce postoperative pain which is caused by irritation of free nerve ending of synovial tissue, anterior fat pad, and joint capsule.[4] Post-operative analgesia is a crucial part of rapid recovery from arthroscopic knee surgeries. Adequate analgesia will help patients in early mobilization and possible early discharge and lead to decreased post-op morbidity and lower cost of hospitalization. Minor procedures can even be done on day-care basis if adequate analgesia enables same day discharge. Hence various modalities are being evaluated including intra-articular local anesthetics with adjuvants as in our study.

Acetylcholine acts as an analgesic agonist at muscarinic receptor type I or II. The likely mechanism of action includes hyperpolarization of neurons, decrease in pro-nociceptive neurotransmitters and activation of the nitric oxide-cyclic guanosine monophosphate pathway.[1,2] Administration of the cholinesterase enzyme inhibitor, neostigmine will increase the endogenous acetylcholine levels at the peripheral nociceptors and may cause analgesia. Yang et al compared neostigmine doses of 0.125, 0.25 and 0.5 mg for intra-articular use for post-operative analgesia and found 0.5mg superior to other doses.[5] Hence we have used 0.5mg neostigmine with 0.5% bupivacaine in group N.

In a study conducted by Datta et al, the mean duration of post-operative analgesia with 0.25% bupivacaine and 0.5 mg neostigmine was around 350 minutes which was significantly more than patients receiving either drug alone.[6] The duration of analgesia using a combination of 0.25% bupivacaine with neostigmine was 257.60± 47.243 mins in a study conducted by Amani H et al.[7] In our study, the mean duration in group N was 496.51 ± 102.68 mins which is more than the above study findings. This increased duration could be due to higher

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concentration of bupivacaine (0.5%) used in our study.

Intra-articular glucocorticoid has been used previously to improve pain relief after meniscectomy and synovitis.[8] Dexamethasone, a 9α-derivative synthetic glucocorticoid that has highly potent anti-inflammatory action with minimal mineralocorticoid activity, can inhibit prostaglandin synthesis and increase the release of endorphins, thus it is safer and free of many potential side effects.[9] Additionally, it prolongs the action of local anesthetics when used together, while significantly prolonging the duration of analgesia in extremity nerve blocks.[10] Dexamethasone given as a sole agent intra-articular does not provide analgesia and has shown to increase analgesic requirement and prolong time to mobilization as demonstrated in a study conducted by Saryazad et al.[11]

In a study conducted by Heshmati F et al, the duration of post-operative analgesia after intra-articular 0.5% bupivacaine with 8mg dexamethasone was 574 ± 41 mins and that of intra-articular bupivacaine was 310 ± 30 min.[12] In our study the mean duration in group D was 636.24 ± 95.62 mins.

In our study the mean duration of analgesia in group D was 636.24 ± 95.62 mins, while in group N was 496.51 ± 102.68 mins. The duration of analgesia was significantly more in dexamethasone group as compared to neostigmine group with *P* value of 0.0001. There are no direct studies comparing the efficacy of post-operative analgesia using intra-articular bupivacaine with dexamethasone vs. bupivacaine with neostigmine. In a study conducted by Kunal KS et al comparing the post-operative analgesia after caudal injection of ropivacaine with dexamethasone and with neostigmine, the duration was significantly greater in dexamethasone group which is similar to the observations in our study.[3]

The total analgesic requirement was significantly less in group D on first as well as second POD with *P* values of 0.0422 and 0.0103 respectively. The analgesic requirements were more in our study as compared to a randomized study conducted by Moeen et al, in which there was no requirement of analgesics for up to 72 hours post-op in patients receiving intra-articular dexamethasone with bupivacaine.[13] In a study by Datta and Madhusudanan, the incidence of nocturnal pain was significantly less in bupivacaine with neostigmine group compared to placebo.[14] In our study, the incidence of nausea vomiting was more in neostigmine group compared to dexamethasone group this may be because of systemic effects of adjuvants i.e. antiemetic effect of dexamethasone and side effect of neostigmine as nausea and vomiting. Incidence of nocturnal pain was more in neostigmine group, which may be because of its short duration of postoperative analgesia. Side effects like urinary retention and bradycardia were not seen in both groups which is consistent with observations of Datta and Madhusudanan.[6]

Conclusion

Intra-articular bupivacaine with dexamethasone significantly prolongs postoperative analgesia and has minimal side effects as compare to bupivacaine with neostigmine.

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