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Original Research Paper

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"A COMPARATIVE EVALUATION OF EFFECT OF INTRA ARTICULAR FENTANYL VERSUS DEXMEDETOMIDINE AS ADJUVANT TO ROPIVACAINE ON POST OPERATIVE PAIN IN KNEE ARTHROSCOPIC SURGERIES"

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ABSTRACT

Background: Knee arthroscopy involves good repair of knee ligaments and menisci with minimal injuries but with variable degree of post operative pain. This pain can be minimal in some but can be very distressing in others. This study aims at evaluating effect of intra articular fentanyl versus dexmedetomidine as adjuvant to ropivacaine on post operative pain in knee arthroscopic surgeries. **Materials and Methods:** Ninety patients of ASA Class I/II, aged 20–60 years posted for arthroscopic knee surgery were randomly divided into Group R (control group),Group RF(fentanyl) and Group RD (dexmedetomidine) with 30 patients in each group. Anaesthetic technique used was spinal anaesthesia in all patients. Group I patients received Ropivacaine 0.75% 22 ml , group II received Ropivacaine 0.75% 20 ml +Fentanyl 1mcg/kg and Group III received 1 μg/kg dexmedetomidine diluted to 20 ml Ropivacaine 0.75% via intra-articular route at end of procedure. VAS score for 24 h, time to first rescue analgesia and total dose of analgesic required in each group was evaluated. **Results:** VAS scores were significantly lower in Group III, time to first analgesic requirement was highest in group III (412.2±34.9mins) and lowest in group I (280.4±18.8mins), P value 0.002. Total dose of analgesic used in Group III (166.667±47.946 mg) patients was significantly lesser compared to patients in Group I (273.33±44.978 mg) and group II (183.33±46.113 mg), P value 0.0226. **Conclusion:** Intra-articular dexmedetomidine as adjuvant to 0.75% ropivacaine is effective in providing prolonged postoperative analgesia and decreases total analgesic requirements without any significant side effects after arthroscopic knee procedures.

KEYWORDS : Analgesia, dexmedetomidine, fentanyl, ropivacaine, intra-articular, knee

INTRODUCTION

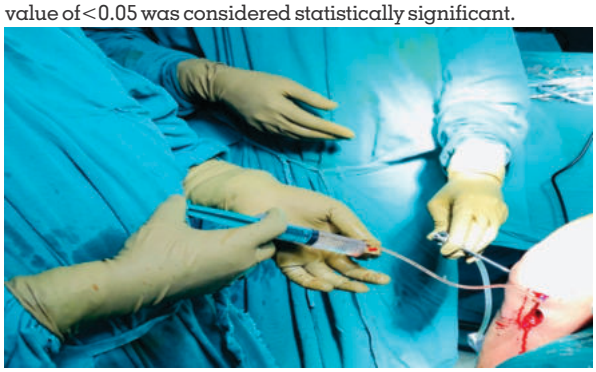
Among the upcoming surgeries in this era, are minimally invasive surgeries eg: arthroscopic knee surgeries in modern orthopaedics setups. This procedure involves good repair of knee ligaments and menisci with minimal injuries but with variable degree of post operative pain. This pain can be minimal in some but can be very distressing in others[1,2]. The pain associated with arthroscopic knee surgery is usually caused by stimulation of the synovial tissue free nerve endings, anterior fat pad and capsule of the joint by either surgical excision or resection[3,4].Since pain around knee can prevent early mobilization and rehabilitation, it reduces patient's satisfaction. Knee arthroscopy is a very short duration procedure, infiltration of local anaesthesia is a well known anaesthetic technique followed for such surgeries. This technique not only reduces cost of procedure but it is also easy to perform that too in day care setup and no anaesthesia related complications are there. Different intra-articular analgesic agents for day care arthroscopy have been studied but search for an ideal agent goes on. It should have rapid onset of action, have a prolonged duration of action, be easy to administer and be without serious adverse effects.[5,6]Many adjuvants have been used with local anaesthetics intraarticularly to enhance duration of analgesia and requirement of postoperative rescue analgesics. Opioids have been used as adjuvants to local anaesthetic since long back. Non histamine releasing opioid fentanyl is preferred over morphine as adjuvant to local anaesthetic intraarticularly[5] Among them the most effective adjuvant is alpha-2 adrenergic agonists eg: clonidine, dexmedetomidine. Several studies have demonstrated that intra-articular injection of α2-adrenoceptor agonists such as clonidine derivative apraclonidine, provided effective analgesia after arthroscopy.[3,7-10]Dexmedetomidine, a highly selective α2-adrenoceptor agonist, binds the α2-receptors up to eight times more avidly than clonidine.[11] Systemic dexmedetomidine has sedative, anxiolytic, analgesic, and anaesthetic sparing effects. Intra articular administration of drugs utilizes peripheral receptors to provide local analgesia with minimum systemic side effects.

The present study was aimed to evaluate the effect of intra articular ropivacaine with fentanyl versus ropivacaine with dexmedetomidine for post operative analgesia in knee arthroscopic surgeries with the objective of evaluating duration and quality of analgesia and any side effect.

MATERIAL AND METHODS

After approval from the Institutional Ethical Committee Subharti Medical College, Meerut, this study was conducted on 90 patients of ASA status I and II, aged between 20 to 60 years, of either sex undergoing elective arthroscopic knee surgery under spinal anaesthesia. Patients of ASA III or greater, severe cardiac or pulmonary disease, bleeding or coagulation disorder, known hypersensitivity to study drugs, infection at site, refusal to technique or enrolment for study were excluded from the study. A sample size of 27 patients in each group was determined on the basis of a pilot study, with α error of 0.05 and β error of 80% to detect a difference of at least 60 minutes in time taken for the request of rescue analgesia between treatment groups. Including 10% dropout rate a total of 90 patients were taken as sample size for the study. Patients were divided into three groups of 30 each using simple randomization technique of card method. Group RF Ropivacaine 0.75% 20 ml +Fentanyl 1mcg/kg, Group RD Ropivacaine 0.75% 20 ml+ Dexmedetomidine1mcg/kg and Group R Ropivacaine 0.75% 22 ml. Total volume of drug in each group was 22ml. All patients were kept fasting for at least 6 hours prior to the surgery. Standard monitors (heart rate (HR), electrocardiogram (ECG), pulse oximetry (SpO2) and non-invasive arterial blood pressure (NIBP) were attached to each patient after arrival in the operation theatre. Intravenous line with 18 G intracath was secured in the non-dominant forearm and lactated Ringer was started at rate of 10 mL/kg over 15 minutes, before initiation of subarachnoid block. Before the initiation of subarachnoid block, all patients were made to understand on the methods of sensory and motor block assessments and visual analogue scale (VAS) scoring system which consists of a 10 cm long horizontal paper strip (marked at 1cm interval) with two end points; 0-no pain and 10–worst possible pain.

The subarachnoid block was performed under all aseptic precaution; 3 ml of 0.5% Heavy bupivacaine solution was injected slowly. After injecting the drug the patient was placed supine, sensory and motor block were assessed before commencement of operation. Tourniquet was applied and inflated on the thigh of operative knee and time was noted. At the end of surgery before skin closure, the study drug was administered by the surgeon through the port site in the intra articular space. Tourniquet was kept inflated for another 20 minutes. Drain put by the surgeon was clamped after administering the study drug and remained clamped for another 20 minutes.HR, MAP, VAS score for pain at rest and movement was recorded at 1^{st},2^{nd},4^{th},6^{th},12^{th} and 24^{th}post operative hours. Injection Tramadol 100 mg iv was given as rescue analgesic ,if VAS>4.Time to first rescue analgesic, total Tramadol used in 24 hours and duration of motor block were recorded .All data was collected by the observer who was unaware of patients' group assignment. Statistical analysis was performed using SPSS (Version23) software. Chi-square test was used for analysis of categorical data and one way analysis of variance (ANOVA) test was used for analysis of numerical data of all the three groups simultaneously. The p-value of <0.05 was considered statistically significant.



Picture: Demonstration of intra-articular injection of study drug for knee arthroscopic surgeries

RESULTS

Patient's age, weight, gender ratio, and ASA physical status were considered as demographic parameters. Age and weight were analysed by one way ANOVA and the chi square test was used to analyse gender ratio and ASA physical status. All the three groups were comparable in terms of age, weight, gender ratio and ASA physical status.(Table 1)

Table 1: Demographic characteristics

PARAMETERS	GROUP R	GROUP RF	GROUP RD	P-VALUE
AGE (IN YEARS)	34.233±7.43	39.267±5.971	41.03±6.795	0.1678
WEIGHT(IN KG)	47.30±7.580	52.300±7.096	54.10±6.96	0.4154
GENDER (M/F)	14/16	14/16	17/13	0.1189
ASA GRADE (I/II)	14/16	13/17	12/18	0.2179

The mean heart rate of patients among the three groups was analysed using one way ANOVA from 1 hour till 24 hours was statistically significant.(Table 2)

Table 2:-Heart rate (beats /mins) comparison at different intervals among the study groups

	Group R	Group RD	Group RF	p value
	Mean±SD	Mean±SD	Mean±SD	
Pre	72.53±6.07	76.60±6.02	74.50±6.11	0.27
Immediate Post-op	87.07±5.59	80.07±5.52	84.60±5.64	0.07
30 min	90.20±6.42	82.20±6.38	90.80±6.47	0.0.66
One Hour	85.07±6.09	62.08±6.18	82.80±6.22	0.001*
1.5 Hour	85.67±6.27	68.67±6.08	84.62±6.31	0.01*
2 hour	87.90±6.07	70.90±6.09	90.74±6.06	0.008*
4th Hour	84.70±6.84	64.70±6.93	88.40±6.90	0.006*
6th Hour	104.03±6.70	62.03±6.73	98.90±6.78	0.001*
10th Hour	102.70±7.03	65.30±6.88	85.48±6.98	0.008*
12th Hour	83.93±6.44	69.90±6.41	94.40±6.47	0.003*
18th Hour	103.40±5.76	72.20±5.70	100.78±5.82	0.004*
24th Hour	84.57±6.42	80.70±6.34	92.76±6.39	0.007*

The mean arterial pressure of patients was statistically analysed using one way ANOVA and was found statistically insignificant post operatively in patients of all the three groups. (Table 3)

Table 3:- Mean Arterial Pressure (mmHg) comparison at different intervals among the study groups

Intervals: MAP	Group R	Group RD	Group RF	p value
	Mean±SD	Mean±SD	Mean±SD	
Immediate Post-op	93.30±5.45	92.67±5.74	94.30±5.45	0.26
30 min	94.03±4.87	94.30±5.45	96.03±4.87	0.19
One Hour	93.63±6.04	95.03±4.87	96.63±6.04	0.12
1.5 Hour	94.27±5.49	94.63±6.04	98.27±5.49	0.08
2 hour	93.67±5.25	95.27±5.49	95.67±5.25	0.31
4^{th} Hour	92.17±5.71	94.67±5.25	96.17±5.71	0.06
6^{th} Hour	92.97±5.74	94.17±5.71	96.97±5.74	0.06
10^{th} Hour	93.10±5.12	94.97±5.74	96.10±5.12	0.10
12^{th} Hour	92.83±4.94	94.10±5.12	95.32±4.94	0.24
18^{th} Hour	92.43±5.19	92.83±4.94	95.43±5.19	0.07
24^{th} Hour	94.67±5.74	94.43±5.19	96.67±5.74	0.13

Mean visual analogue scale (VAS) at rest in three groups of patients at different time intervals.

Comparison between the three groups was done using one way ANOVA at different time intervals i.e. immediate post-op, thereafter every hour till 6 hours and 2 hourly for the period of 12 hours postoperatively and lastly at 24 hours

postoperatively. Difference in the Visual analogue scale (VAS) among the three was found statistically significant ($p<0.05$).

Mean visual analogue scale (VAS) on movement in three groups of patients at different time intervals. Comparison between the three groups was done using one way ANOVA at different time intervals i.e. immediate post-op, thereafter every hour till 6 hours and 2 hourly for the period of 12 hours postoperatively and lastly at 24 hours postoperatively. Difference in the Visual analogue scale (VAS) among the three was found statistically significant ($p<0.05$ The time to first rescue analgesic as injection Tramadol (given when VAS>4) was analysed by one way ANOVA test. All the three groups were compared.(Table 4)

Table 4:- Time To First Rescue Analgesic And Tramadol Consumption Among The Study Groups

Variables	Group R	Group RF	Group RD	p value
	Mean±SD	Mean±SD	Mean±SD	
Time to first rescue analgesic (in min)	280.4±18.8	320.7±32.7	412.2±34.9	0.002*
Tramadol consumption (in mg)	273.33±44.978	183.33±46.113	166.667±47.946	0.0226*

The three groups were compared in which time to first rescue analgesic in group R (ropivacaine) were 280.4±18.8minutes, 320.7±32.7 minutes in group RF (fentanyl) and 412.2±34.9 minutes in group RD (dexmedetomidine). It was observed that time to first rescue analgesic was highest in group RD (dexmedetomidine) and lowest in group R (ropivacaine). The difference in the time to first rescue analgesic in all the three groups was statistically significant. (P-value =0.002).

The three groups were compared in which the total analgesic consumption in group R(ropivacaine) were 273.33±44.978mg, 183.33±46.113 mg in group RF(fentanyl) and 166.667±47.946 mg in group RD(dexmedetomidine). The difference in the total analgesic consumption amongst all the three groups was statistically significant. (P-value = 0.0226).

There were no complications or any other study drug related serious side effects among the study groups

DISCUSSION

Arthroscopic surgeries are day care procedures and are frequently done for both diagnostic and therapeutic purposes but if patient suffers pain then the whole purpose of a day care surgery is defeated. Since there can be minimal to moderate pain after arthroscopy depending upon the tissue handling ,techniques of providing complete analgesia are always looked out.

Both dexmedetomidine and fentanyl when given intravenously produces profound analgesia but such patients need monitoring due to associated side effects.

So, intrarticular route of using analgesic agents came up gradually, as a simple and cost effective method. Drugs used intraarticularly act on peripheral receptors and provide analgesia locally with minimal systemic side effects. Intrarticular surfaces are poorly vascular and hence, very slow rate of absorption of drug is there which in turn decreases the amount of rescue medication[12,13] In present study we found that intra articular usage of these drugs along with local anaesthetic is associated with good analgesia and minimal side effects.

In present study we found that the mean time for first rescue analgesia during postoperative period in ropivacaine group was least (280.4±18.8 minutes),(320.7±32.7minutes) in group fentanyl and highest in dexmedetomidine group (412.2±34.9 minutes). The total analgesic consumption in Group ropivacaine was (273.33.4±44.978 mg), (183.33±46.113 mg) in group fentanyl and (166.667±47.946 mg) in group dexmedetomidine which was also statistically significant.(p value 0.0226) and VAS scores were lower in patients of dexmedetomidine and fentanyl group than the patients of ropivacaine. Difference in VAS among the three groups was found significant ($p<0.05$).

Local anaesthetics reduce chondrocyte viability, so produces chondrotoxicity. Hence, their use intraarticularly after arthroscopic surgeries is a matter of concern[12] Breu A et al. in their study concluded that in a time dependent and concentration dependent manner, bupivacaine, ropivacaine and mepivacaine are more chondrotoxic in degenerated compared with intact human cartilage. Chondrotoxic substance specifically increases from ropivacaine to mepivacaine to bupivacaine, without clearly correlating with analgesic potency[14]

Opioids too can produce analgesic effects by acting on peripheral opioid receptors, which are activated in the presence of tissue inflammation producing analgesia by local action whereas dexmedetomidine an α2 adrenoreceptor agonist acts on presynaptic α2 adrenergic receptors and inhibits the release of norepinephrine at afferent nociceptors and another action of local anaesthetic is due to inhibition of conduction of nerve signals through C and Aδ fibres[12]

Akca B et al. in their research studied the effect of intrarticular dexmedetomidine injection on articular cartilage and synovium in animals and concluded that in low concentration like (1 μg/ml) intrarticular use of dexmedetomidine seems safe in relation of histopathological analysis[15]

Intra-articular injection of local anaesthetics with adjuvants not only reduces pain scores on rest but also on movement because of which patient can easily undergo their postoperative physiotherapies and ambulation and that too with least side effects that generally occurs with these adjuvants when given by systemic route Samoladas EP et al. in their study compared 10ml and 20 ml of 0.75% ropivacaine for control of post knee arthroscopy pain and found that none of the patients developed any adverse reactions and that intra-articular dose of ropivacaine upto 150 mg is safe and intra-articular injection of local anaesthetic seems to provide an alternative and effective solution in pain control after knee arthroscopy[16]

Mostafa El-Hamasy et al. in their study compared intra-articular 30 ml 0.25% bupivacaine with dexmedetomidine (1 μg/kg) and intra-articular 30 ml 0.25% bupivacaine with fentanyl 1 μg/kg and concluded that both dexmedetomidine and fentanyl with bupivacaine equally prolong the duration of analgesia post operatively in comparison to bupivacaine alone[5]

Volume and concentration of drug used in the present study is similar to previous studies. 22 ml of volume was used in the study, this volume when given in intra-articular space may increase intra-articular pressure leading to increased absorption but due to application of tourniquet , absorption is delayed and duration of action can increase. In the present study tourniquet application after study drug injection was continued till 20 minutes which could be another reason for prolonged effect of study drugs[17,18,19]

Devi MM et al. in their study compared 20 ml 0.25% bupivacaine ,20 ml 0.25% bupivacaine with 0.5 μg/kg of dexmedetomidine and 20 ml 0.25% bupivacaine with 10 mg/kg magnesium sulphate intraarticularly and concluded

that IA bupivacaine with adjuvants prolongs duration and improves quality of post operative analgesia as compared to bupivacaine alone.[12]

Panigrahi R et al. compared 18 ml 0.2% Ropivacaine with 1μg dexmedetomidine and 18 ml 0.2% Ropivacaine with 2 μg dexmedetomidine in knee arthroscopy patients and concluded that 2 μg/kg dexmedetomidine group has superior analgesic efficacy and decreased need for rescue analgesia with no adverse effects.[17]

Mitra S et al. in their study compared intra-articular bupivacaine, bupivacaine plus fentanyl and bupivacaine with tramadol after knee arthroscopic surgeries and concluded that bupivacaine with fentanyl appears to be best combination for pain relief in knee arthroscopic surgery patients when given intraarticularly.[20]

Present study has similar findings that both dexmedetomidine and fentanyl as adjuvant with ropivacaine prolongs post operative analgesia but dexmedetomidine prolongs the effect more.

CONCLUSION

In conclusion, intra-articular 0.75% 20ml ropivacaine with 1μg/kg dexmedetomidine is effective in providing postoperative analgesia of 6 to 7hrs and decreases total analgesic requirement without any significant side effects in comparison with ropivacaine plus fentanyl and both being superior to ropivacaine alone in patients undergoing arthroscopic knee surgeries under spinal anaesthesia.

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