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Astudy to Compare the Analgesic Efficacy of Intra-Articular Levobupivacaine, Fentanyl And Clonidine Following Arthroscopic Knee Surgery

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Abstract: Arthroscopic knee surgery can produce pain postoperativelywhich can be very distressing. Many drugs in variousways have been tried to overcomethis pain. But none found to be most effective.So we have done a study for correlating with the analgesiclevobupivacaine efficiency, fentanyl, & clonidine into intra-articular therapy associated with arthroscopic surgeries. This study was conducted from Nov 2019 to April 2020, in which 90 patients undergoing arthroscopicsurgery of knee split in 3classes of 30 each. (L,F,C). ClassL were injected 10 millilitrein levobupivacaine of 0.26% e, where ClassF wereinjected 50 mcg fentanyl, and Class Cwere injected 50 mcg of clonidine in intra-articular therapyafter surgery. Time of first analgesia request, no of analgesic dose required and total rescue analgesic required in postoperative 24 hours were assessed. Pain was assessed using visual analogue scale. Demographic characteristicsweresimilaramong allthe three Classs. Time for need of 1stanalgesic request in ClassL was 381.57 ± 24.63 min, in ClassF was 328.67 ± 20.42 min and in Class C was 238.47 ± 21.93 minutes.(p<0.06)Overall amount ofdoses of analgesic needed was fewer in ClassL (1.21 ± 0.57) in comparison to ClassF (1.95 ± 0.42) and Class C (2.12 ± 0.34). (p<0.05) Total dose of paracetamol used was reduced in ClassLcorrelated withClassF and C in 1st 24 hrs postoperatively. (p<0.05) Class F & C has highest average score of VAS at various time points in 1st 24 hrs correlated withClass L.(p<0.05) Intra-articular levobupivacaine obtained better control of pain inpostoperative period with delayed time of need of 1st analgesicdose and reduced the need of total dose of rescue analgesicin comparison to intra-articular clonidineandfentanyl.

Keywords: Intra-articular, fentanyl ,clonidine,levobupivacaine, knee arthroscopy

1. INTRODUCTION:

Arthroscopic knee surgeryare commonly done for various ligament injuries. Now a days it is done as day care procedures.But it may be associated with significant amount ofpainin postoperative period, which is usuallyproduced by the stimulation of joint capsule, anterior fat pad&synovial tissue (their nerve endings). [1] Postoperative pain always has influence on psychology of patientswhich prevents early mobilization, and discharge in day care surgery.So effective pain relief is very importantwhich can reduce surgical stress response leading to early recovery. Multimodalstrategies like systemic drugs, peripheral nerve blocks, and drug administrationin intra-articular routehave been used to block the pain pathway for

effective pain relief.But, no technique has been found ideal.[2] The intra-articular injection of drug for postoperative pain has gained popularity. It provides analgesia locally by blocking peripheral receptors with no or minimal sideeffects. Variousdrugs have been tried in intra-articular route for postoperative pain management but none has been found ideal.[3] Levobupivacaine is a local anaestheticwhichobstructs the peripheral afferents and act on Na + channels(voltage-dependent). Now a days this is commonly used,as it is less cardio and neuro toxic than bupivacaine.[4] Fentanyl is a synthetic opioid which has been used in many routes for providing analgesia.It can also produce an analgesic effect through coming in contact with receptors associated with periphery of opioid. [5] α2 receptors that are adrenergic is associated with its predominant part called Clonidine, whichhas not only pain relieving, calming, blood pressure reducing properties but also reduces anaestheticrequirement. [6] We have carried out atrial to compare the analgesic potency of levobupivacaine, fentanyl, and clonidine within inter-articular postoperative analgesic after surgery of knee.

2. METHODS

This trialwas carried out at a tertiary care hospital in Odisha from Nov 2019 to April 2020 after obtaining permission from institutional ethical committee. This trialwas conducted among patients of age between 18-60yrs of either sex,postedfor arthroscopic knee surgery for procedures like synovectomy and ligament reconstruction under spinal anaesthesia. Patients with alteredkidney and liver function, heart disease and use of opioid or nonsteroidal anti-inflammatory drug in 24 hrs before surgery were excluded from the study.

Sample size:

Sample size was calculated using time of first analgesic request as primary endpoint of the study.On the basis of a previous study[5], the mean time to 1st postoperative rescue analgesia and standard deviation values were assumed. Assuming a standard deviationof 30 minutes within Class and variation in mean time to need of 1st analgesic request be 40 minutes,with α error of 0.05 and power of the study (1− β) at 80%,26 sample per Class is required.We have included 30 subjects in each Class expecting possible dropouts.

Study design:

Prospective randomized double blinded parallel Class open labeled study

Sample design:

Patients of 90ASA grade1st& 2nd waiting forarthroscopic surgery of knee were selected and classified in 3Classes(L, F,C).

ClassL- got 10 millilitre of 0.26% Levobupivacaine.

ClassF -got 50 mcg of Fentanyl (added to NS to make up volume to 10ml).

Class C -received 50 mcg of Clonidine (added to NS to make up volume to 10ml).

Anesthesiologists,who prepared study drug,remained unaware of the nature of the study and was not involved in further data collection.Patients were clarified with Visual analogue scale (VAS)at the time of pre anesthetic checkup. (o-pain less and 10- maximum pain). Baseline noninvasive blood pressure, ECG, and SpO2 was recordedin the operating room. Intravenous line was secured and ringers lactate started.Puncturing of lumber was performed in sitting condition utilizing aseptic safeguardsover L4- L5 internalvoid utilizing 26G needle having Quincke spinal &3milliliter of 0.6% bupivacaine (heavy) was administered.Surgery was allowed when blockade of sensation was upto level T12 and motor blockadeinBromagescale was>2 . At the completion of surgery, trial drugpreparedwas injectedinto inter-articular voidby the surgeon. For 20minutes, Tourniquet was left

inflating.Surgeon put by the drain,which was clamped prior to injection of drug&remain clamped for 20minutes. For pain VAS was recorded at 1st, 2nd, 4th, 6th, 12th & 24th post-operative hrs.Injection paracetamol(1gm)wasinjected IV as analgesia if the VAS>4.Time to 1strescue analgesia,and total analgesicconsumption in 1st 24hours were assessed. All data was recorded by an anesthesiologist who was not awareabout Classallocationof patients.

Raw data of study parameters was putwithin the sheet prepared in Excel& evaluated using version 20 of SPSS. Information associated with categories was evaluated utilizing the testing method of chi square test as applicable. Nonnormalcontinuousvariableswas analyzedusing the KruskallWallisH test.Categorical data was expressed in percentages.Value of $p< 0.05$ considered to be important in statestic.

3. RESULT

Table 1: Patientvariables

Variables	ClassL	ClassF	Class C	*P* value
Age (yrs.)	39.12 ±15.6	38.45±16.9	39.85±15.7	0.554
Sex(M/F)	26/4	27/3	25/5	0.451
Height(cm)	161.22±11.47	159.13±11.9	160.75±11.2	0.348
Weight(kg)	60.84±9.85	59.38±9.24	59.15±10.12	0.429
ASA status(I/II)	16/14	15/15	16/14	0.498
Duration of surgery(mins)	120.45±12.85	118.94± 14.44	119.18±13.82	0.342

Information collected demographicallylikegender, weight, ages, height,statusof ASA &surgerytime between the three Classs were similar (Table 1). Time of need for1strescue analgesic in ClassL(381.57 ± 24.63minutes) was longer compared to ClassF(328.67±20.42minutes)and Class C (238.47 ± 21.93minutes)($P < 0.05$). Rescue analgesicneeded in1stt 23 hours was also lower in Class L (1.21 ± 0.57) in comparison to Class F (1.95 ± 0.42) and Class C (2.12 ± 0.34) ($P < 0.05$). Total dose of Paracetamol needed was fewer in Class L in comparison toClass F and C in 1st 24 hrs postoperatively. ($p<0.05$) (Table 2) In comparison toClassF and Class C, ClassL had lower mean VAS score at various time points in postoperative 24hours.(Table 3)

Table 2: Analgesic characteristics

Variables	ClassL	ClassF	Class C	P value
Time of first rescue analgesia requirement (min)	381.57 ± 24.63	328.67±20.42	238.47±21.93	< 0.05
Total number of rescue analgesia	1.21 ± 0.57	1.95 ± 0.42	2.12 ± 0.34	< 0.05
Total dose of Paracetamol used(mg)	1008.24± 540.25	1360.0± 515.6	1850.45± 438.14	< 0.05

Table 3:VAS score in postoperative 24hrs

Time of follow up	Class L(VAS)	Class F(VAS)	Class C(VAS)	P value
1hr	1.2± 1.1	1.8 ± 1.1	1.7 ±1.3	< 0.05
2 hr	1.3± 1.2	1.9± 0.9	1.9± 1.2	< 0.05
4 hr	1.9± 1.8	2.7± 0.8	1.9± 1.6	< 0.05
6 hr	2.3± 1.9	3.9 ±0.7	3.8± 1.8	< 0.05
12 hr	2.±5 1.8	4.2± 0.9	3.7± 0.9	< 0.05
24 hr	3.1± 1.4	4.5± 0.4	4.7± 0.6	< 0.05

4. DISCUSSION

Any arthroscopic surgery can be associated with significant amount of pain postoperatively. The intra-articular drug can provide postoperative analgesia after the arthroscopic surgery. Different drugs like bupivacaine, ropivacaine, fentanyl, and dexmedetomidine hadproved their analgesic efficacy when used in intra-articular route. We haveconcluded that

intra-articular injection of levobupivacaine provided prolongedanalgesia compared to fentanyl and clonidine. Intra-articular administration of local anaesthetics act on peripheral receptors andproduce adequate pain relief after surgery andtherebydicreasethe requirement of oral and intravenousanalgesic drugs.[4] Analgesia was offered locally without causing any mojor side-effects. Levobupivacaine wasusually referred over bupivacaine.This S-enantiomer of bupivacaine is a newerlocal anaesthetic which has less cardiac and neural toxicity but similar efficacy to bupivacaine.[7] Different trials had found that intra-articular injection of levobupivacaine is safe and devoid of any side effects. Das et al. in his trial opined that intra-articular levobupivacaine reduced the need of rescue analgesic in 1st 24 hrs postoperativelyand increases the duration of analgesia.[8] Kazak Bengisun et alin his study concluded that that intra-articular bupivacaine and levobupivacaine provided prolonged analgesia,reduced rescue analgesic requirement, which resulted in shorter hospital stay, and higher patient satisfaction score.[9]Both the above studies are in agreement with our study.Clonidine,an α2 adrenergic agonist alone has proved its efficacyfor postoperative analgesia when used in intra-articular route. Reuben SS et al in their study concluded that clonidine, when used as adjuvant to bupivacaine in intra-articular route, provided prolongedanalgesia. Time of need for1st analgesic dose was deferred and requirement of postoperative analgesics was reduced.[10] In this study1 mcg/kg of intra-articular Clonidine was used to observe maximum effectwith minimum side effects.Buerkle H et al in his study found that intra-articular clonidine provided prolonged analgesia in patients 24 h postoperatively.[11] Sun et al in his meta-analysis opined that duration of analgesic effect of clonidine is short which indicates- inter-articularinsertion of clonidine may not allow to be free from suffering which is in agreement with our study.[12]Fentanyl is a synthetic opioid which is very commonly used now a days by anaesthetistin various routes.[13] After surgery of knee, few trials have shown thatintra-articular use of opioids can produce analgesia.[14,15] Researchers stated that intra-articular fentanyl can delay requirement of rescue analgesia and produce prolonged postoperative analgesia. Heconcluded that intra-articular 50mcg fentanyl can provide postoperative analgesia.[16] Several researchers al studied inter-

articularfentanyl&dexmedetomidinehaving bupivacaine(0.25%).They opined that bothfentanyl and dexmedetomidine when combined with bupivacaine,delayed the time forneed of 1st rescue analgesic and reduced the requirement of analgesia postoperatively.[17] Prolonged postoperative pain relief in the intra-articular routeis due to the fact that drugs are absorbed slowlythrough poorly vascular intra-articular surface.Further studies are needed to be done to find out theideal dose of all the intra-articular study drugs which can provide prolonged analgesia without any side effects.

5. CONCLUSION

Intra-articular levobupivacaine delayed the time of need for1st rescue analgesia,reduced the requirement of rescue analgesia and prolonged the duration of analgesia in postoperative period.

REFERENCES

[1] KaramanY, Kayali C, Ozturk H et al. A comparison of analgesic effect of intra-articular levobupivacaine with bupivacaine following knee arthroscopy.SaudiMedJ.2009May;30(5):629-32
[2] Alagol A, Calpur OU, Usar PS. Intra-articular analgesia after arthroscopic knee surgery. Comparison of neostigmine, clonidine, tenoxicam, morphine and bupivacaine. Knee Surgery, Sports Traumatology. Arthroscopy 2005;13:658-63.
[3] Rosseland LA, Stubhaug A, Skoglug A, Skoglund A, Breivik H. Intraarticular morphine for pain relief after knee arthroscopy. Acta AnaesthesiolScand1999;43:252-7.
[4] Moiniche S, Mikkelsen S, Wetterslev J, Dahl JB. A systematic review of intra-articular local anesthesia for postoperative pain relief after arthroscopic knee surgery. Reg Anesth Pain Med 1999;24:430-7.
[5] Varkel V, Volpin G, Ben-David B, Said R, Grimberg B, Simon K, et al. Intra-articular fentanyl compared with morphine for pain relief following arthroscopic knee surgery. Can J Anaesth1999;46:867-71.
[6] Gentili M, Juhel A, Bonnet F. Peripheral analgesic effect of intra-articular clonidine. Pain 1996;64:593-6.
[7] Foster RH, Markham A. Levobupivacaine: A review of its pharmacology and use as a local anaesthetic. Drugs 2000;59: 551-79.
[8] Das A, Majumdar S, Kundu R, Mitra T, Mukherjee A, Hajra BK, et al. Pain relief in day care arthroscopic knee surgery: A comparison between intra-articular ropivacaine and levobupivacaine: A prospective, double-blinded, randomized controlled study. Saudi J Anaesth2014;8:368-73.
[9] Kazak Bengisun Z, AysuSalviz E, Darcin K, Suer H, Ates Y. Intraarticular levobupivacaine or bupivacaine administration decreases pain scores and provides a better recovery after total knee arthroplasty. J Anesth2010;24:694-9.
[10] Reuben SS, Connelly NR. Postoperative analgesia for outpatient arthroscopic knee surgery with intraarticular clonidine. AnesthAnalg1999;88:729-33.
[11] Buerkle H, Huge V, Wolfgart M, Steinbeck J, Mertes N, Van Aken H, et al. Intra-articular clonidine analgesia after knee arthroscopy. Eur J Anaesthesiol2000;17:295-9.
[12] Sun R, Zhao W, Hao Q. Tian H, Tian J. LiL, et al. Intra-articular clonidine for post-operative analgesia following arthroscopic knee surgery: A systematic review and meta-analysis. Knee Surg Sports TraumatolArthrose2014;22:2076-84.
[13] Stein C, Schafer M, Cabot PJ, Carter L, Zhang Q, Zhou L, et al. Peripheral opioid analgesia. Pain Rev 1997;4:173-87

[14] Pooni JS, Hickmott K, Mercer D, Myles P, Khan Z. Comparison of intra-articular fentanyl and intra-articular bupivacaine for postoperative pain relief after knee arthroscopy. Eur J Anaesthesiol1999;16:708-11.
[15] Soderlund A, Westman L, Ersmark H, Eriksson E, Valentin A, Ekblom A. Analgesia following arthroscopy- a comparison of intra-articular morphine, pethidine and fentanyl. Acta AnaesthesiolScand 1997;41:6-11
[16] Mondal P, Saudagar AH. Intra-articular Fentanyl for analgesia following arthroscopic knee surgery. Indian J Anaesth2002;46:107-10.
[17] El-Hamamsy M, Dorgham M. Intra-articular adjuvant analgesics following knee arthroscopy: Comparison between dexmedetomidine and fentanyl. Res J Med Sci 2009;4:355-60.