Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/12218
DOI URL: http://dx.doi.org/10.21474/IJAR01/12218

RESEARCH ARTICLE

COMPARATIVE EVALUATION OF TRAMADOL AND FENTANYL FOR EPIDURAL ANALGESIA IN LOWER LIMB SURGERIES

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Manuscript Info

Manuscript History
Received: 25 October 2020
Final Accepted: 28 November 2020
Published: December 2020

Key words:-
Fentanyl, Tramadol, Epidural, Bupivacaine

Abstract

Background: Epiduralandspinalblocksaremajorregionaltechniques with along history of effectiveuseforavarietyofsurgicalprocedures and pain relief. Epidural block with the catheter technique gives a better control of the level of analgesia and can be used for providingpost-operativepainreliefbyopioidsorlocalanaestheticagents.The purposeofthepresentstudywastocomparethe safetyandefficacyofepiduraltramadolversusepiduralfentanylas adjuvantstobupivacaineforlowerlimbsurgeries.

Materials and methods:100 patients werer an domisedin to two groups with50 patient sineach group: Group BB-epidural administration of 20mL 0.5% plain bupivacaine with [50 mg (1 mL) tramadol + 1 mL NS= 2 mL].Group BF- epidural administration of 20 mL 0.5% plain bupivacainewith100mcg(2mL)of fentanyl.Settings and Design- Randomised double-blind trial.

Results: The mean onset of sensory blockade and time for maximum sensory blockade was observed to be significantly reduced with the addition of fentanyl to bupivacaine as compared to tramadol and bupivacaine. The results showed statistically significant increase in the duration of analgesia with the addition of fentanyl to bupivacaine as compared to tramadol and bupivacaine.

Conclusion: We can conclude that tramadol and fentanyl were effective adjuvants to bupivacaine when used epidurally in patients undergoing lower limb surgery. Although, epidural fentanyl with bupivacaine produces significantly faster onset of sensory blockadecompared to epidural;however,epiduraltramadolwithbupivacaineproducessignificantlyprolonged durationofanalgesiacomparedtoepiduralfentanyl.

Introduction:-

Background:

Epidural and spinal blocks are major regional techniques witha long historyofeffectiveusefor avarietyof surgical procedures and pain relief. Epidural block with the catheter technique gives a better control of the level of analgesia and can be used for providing post-operative painreliefbyopioidsorlocalanaestheticagents.[1]

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Local anaesthetics are the mainstay of therapy for obtaining analgesia or anaesthesia with an epidural. Specifically, factors such as surgical location and duration desire to have a sensory and/ or motor block or theexpected potency and duration of a specific local anaesthetic agent shouldbeconsideredpriortoplacinganepiduralblock.[2]

Localanaestheticsactbyproducingareversibleblockade of sodium channels in nervous tissue preventing the transmissionofelectricalimpulsesandproducesympathetic blockade.[2]

Adjuvant analgesics (co-analgesics) contribute significantly to pain relief when used either alone or in combination with other analgesics. Neuraxial adjuvants are used to improve or prolong analgesia and decrease the adverse effects associated with high doses of a single local anaesthetic agent. In addition to their dose sparing effects, neuraxial adjuvants are also utilised to increase the speed of onset of neural blockade (reduce latency), improve the quality and prolong the duration of neural blockade. Sedation, stable haemodynamics and an ability to provide prolonged post-operative analgesia are the main desirable qualities of an epidural adjuvant. Tramadol is a potent analgesic with both opioid agonist and antagonist effect. Tramadolanditsmajormetabolitesareagonistatkappa-opioidreceptorsandmixedagonist-antagonistsatmuopioid receptors.[3]

Fentanyl, a highly lipid soluble, pure mu agonist with rapid onset and short duration of action has been used with various local anaesthetics for wide variety of surgicalprocedures.Fentanylishighlylipophilic,rapidlydiffusesout of epidural space and much of fentanyl analgesic effect is mediatedbysystemicabsorptionratherthanspinalreceptor binding. These highly lipid soluble agents as fentanyl are associated with rapid dermatomal spread, rapid onset and lowincidenceofpruritisornauseaandcanbepotentiatedby epinephrine.[4]Epiduralfentanylcausedsegmentalanalgesia when administered as a bolus and non-segmental systemic analgesiawhenadministeredcontinuousinfusion.

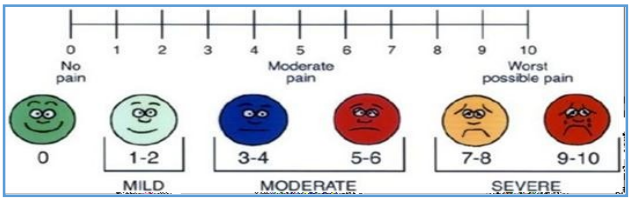
The purpose of present study was to compare the safety andefficacyofepiduraltramadolversusepiduralfentanyl asadjuvantstobupivacaineforlowerlimbsurgeries.

Materials and Methods:-

After Institute's Ethical Committee approval and informed written consent from patients, 100 patients of both genders aged18-60years,ASAgradeIandIIadmittedforlowerlimb surgeries were enrolled into the present study. Those patientswhohadanyanatomicalabnormalitiesofspine,local skininfectionorcellulitis,coagulationdisordersorassociated neurologicalorcardiovasculardisorderswereexcludedfrom thestudy.
Study Design- Randomised controlled double-blind trial.

Randomisation:
Eligible patients underwent randomisation after providing writteninformedconsent.Therandomsequenceofallocation code (Intrathecal analgesia group or systemic analgesia group) was obtained from a random number table of integers. This random number table of integers was constructed using a computer generated random number functioninLibreOfficeCalcversion5.0.3.2.Randomisedand blindedallocationofpatientstothestudydrugswasachieved by assigning concealed random number codes to patients at thetimeofenrolment.Labelsindicatingintrathecalanalgesia group or systemic analgesia group were sealed in opaque, numbered envelopes. The concealed randomised allocation codes (patient's group assignment) was known only to the principalinvestigatorandtheanaesthesiacaregivers,butnot to the post-operative assessors or the patients or the statistician.

100 patients were randomised into two groups with 50 patientsineachgroup:GroupBB-epiduraladministrationof 20 mL of 0.5% plain tramadol with [50 mg (1 mL) tramadol + 1 mL NS = 2 mL].Group BF- epidural administration of 20 mL 0.5% plain bupivacaine with 100 mcg (2 mL) of fentanyl.
Patients were familiarised with the visual analogue scale (VAS) (0- No pain, 10- Worst pain) 1 day before surgeryand askedtogradetheirpainonthisscale.



Visual Analogue Scale (VAS)[5]:

During pre-anaesthetic check-up, a detailed history and thorough general, physical and systemic examination (CVS,chest,CNS,renal)wasdone.Patientswereadvisedovernight fastingandTab.Ranitidine150mgandTab.Lorazepam1mg orallywasgivenaspremedicants6aminthemorningonthe dayofsurgery.Intheoperationroom,afterattachingroutine monitors (Electrocardiogram, non-invasive blood pressure, pulse oximeter), intravenous access was secured with 18-G cannula. All patients were preloaded with 20 mL/kg of Ringer's lactatesolution.

After proper positioning, back was cleaned with antisepticsolutionanddraped.Localanaesthetic1-2mLof 2% xylocaine was injected subcutaneously at L3 - L4 space. Sise introducer was introduced and taken out. The epidural space was identified using 18-G disposable Tuohy's needle with loss of resistance technique at L3 - L4 interspace. Then 18-G Portex epidural catheter will be passed through the epidural needle in upward direction and threaded 3 - 4 cm insidetheepiduralspace.Theneedlewaswithdrawnslowly, andthecatheterwasfixedtothebackusingadhesivetape.A test dose of 3 mL of 2% lignocaine with adrenaline was given after initial negative aspiration for blood and cerebrospinal fluid.Then,20mLof0.5%plainbupivacainealongwithone ofthetwostudydrugswasinjectedintotheepiduralspace.

Group BB- Epidural administration of 20 mL 0.5% plain bupivacaine with [50 mg (1 mL) tramadol+ 1 mL NS= 2 mL].

Group BF- Epidural administration of 20 mL 0.5% plain bupivacaine with fentanyl 100 mcg [2 mL]

Blood pressure (systolic, diastolic and mean), heartrate, respiratory rate and peripheral oxygen saturation (SpO2) were recorded 5 minutes before the epidural injection (0) andat5,10,15,20,25and30minutesaftertheinjection,and subsequently every 15 minutes till the end of surgery. Hypotension (defined as systolic blood pressure of less than 90 mmHg or less than 20% of baseline blood pressure) was treatedwithintravenousfluidinitiallyandappropriatedoses of intravenous mephentermine, if required. Bradycardia (defined as heart rate of less than 60) was treated with intravenous 0.6 mg atropinesulfate.

Sensoryblockwasassessedbypinprickmethod.Thelevel of sensory blockade was assessed every two minutes till blockade at L1 level wasachieved.

Onset of Sensory Blockade:

It was taken from the completion of injection of study drug till the patient does not feel pinprick at L1 level.

Time for Maximum Sensory Blockade:

It was taken as the time from the completion of injection of study drug to maximum sensory blockade attained (i.e. till two consecutive readings of sensory block remain the same,i.e. highest cephalad spread of sensory block occur).

Onset of motor blockade was assessed at 5-minute intervals till 30 mins (i.e. B5, B10, B15, B20, B25 and B30) accordingtotheModifiedBromageScale[6]:

1. Completeblock(UnabletoMoveFeetorKnees). 2-Almostcompleteblock(AbletoMoveFeetOnly).
2. Partial block (Just able to Move Knees).
3. Detectable weakness of hip flexion while supine (Full Flexion ofKnees).
4. Nodetectableweaknessofhipflexionwhilesupine. 6- Able to perform partial kneebend.

Onset of Motor Block:

It was taken from the completion of the injection of study drugtillthepatientdevelopedModifiedBromageScalegrade 4 motorblockade.

Time for Maximum Motor Blockade:
It was taken from the completion of the injection of study drugtillthepatientdevelopedModifiedBromageScalegrade 1 motorblockade.

Grade of sedation during surgery was assessed by the ModifiedRamsay'sSedationScale[7]every5minstill30mins andthenevery15minstillendofsurgery.

Post-operatively, assessment of pain was done with the helpofVASscore,everyhourtill6hrs.andevery2hrs.till24 hrs. and vitals were recorded at the same time intervals. Duration of analgesia was taken as the time from onset of analgesia upto time when VAS reached 5. Patient was then givenrescueanalgesic(tramadol50mgin10mLofnormal salinein BBGroupandfentanyl100mcgin10mLof normal saline in BF Group) through epidural catheter and study in that patient was ceased. The epidural catheter was kept for 24hrs.inpost-operativeperiodandpost-operativeanalgesia will be maintained with epidural top-ups on patient's demand. Complications such as nausea, vomiting, urinary retention, headache, pruritus and respiratory depression were noted and treatedaccordingly.

StatisticalAnalysis:AnalysiswasconductedusingIBMM SPSSStatistics(version22.0).Numericaldatawasexpressed as mean and standard deviation and statistical analysis was doneusingtheindependent't'test,chi-squaretestandMann-WhitneyUtesttocomparethetwogroups.The'p'valueof<0.05wasconsideredstatisticallysignificantandthe'p'value of<0.001wasconsideredstatisticallyhighlysignificant.

Sample size was estimated based on pilot study. We see that mean difference in SBP in 2 groups was 5.3 with SD of 9.05.

Withthisoursamplesizen=46pergroupatapowerof 80%andconfidenceintervalof95%.Forpossibledropouts,it was decided to include 50 patients per group. Alpha= 0.05, z(1-alpha/2)=1.95996, beta= 0.20 Power= 1-beta= 0.80, z(1-beta)=0.84162,sigma=9.05,delta=5.3n=46pergroup. N=(Zalpha/2+Zβ)2*2*σ2/d2,whereZalpha/2isthecritical value of the normal distribution at /2, Zβ is the critical value ofthenormaldistributionatβ,σ2isthepopulationvariance anddisthedifferencebetween2means.

Results:-

A total of 100 patients for lower limb surgery were enrolled for the study and were randomly divided into two groups. Thedemographiccharacteristicsinboththegroupsexhibited marked similarities and did not show any statistical significant difference (p > 0.05). Table 1 shows the demographic profile of variouspatients.

AsshowninTable2,theonsetofsensoryblockwasfaster inGroupBFwithmean4.92±1.14ascomparedtoGroupBB with mean 5.80 ± 0.95 and this difference was statistically highly significant as the 'p' value was < 0.001**.** The time for maximum sensory block was faster in Group BF with mean15.60 ± 1.39 as compared to Group BB with mean 17.60 ±1.76 and this difference was statistically highly significantas the'p'valuewas<0.001.TheonsetinGroupBFwas21.10±1.13minutesandinGroupBBwas20.84± 1.69andtimefor maximummotorblockadewas29.32±2.13inGroupBFand29.56 ± 1.75 minutes and the difference was statistically not significantasthe'p'valuewas<0.05. InTable 3durationof analgesia was 7.64 ± 1.39 in Group BB and 6.04 ± 1.29 in Group BF and it was statistically highly significant as the 'p' value was <0.001.

Table 1:- Demographic Profile.

Demographic Characters	Group BB	Group BF	P value
Age (year)	39.34 ± 12.69	39.16 ± 13.27	0.939
Height (cm)	164.12 ± 4.99	162.57 ± 5.93	0.160
Weight (kgs)	68.74 ± 5.00	67.96 ± 5.74	0.471
Male/ Female	41/9	37/13	0.334
MeanDurationof Surgery (mins)	105.10 ± 15.40	107.40 ± 13.52	0.429

Table 2:- Comparison of Sensory and Motor Block Characteristics.

Block Characteristics	Group BB	Group BF	P value

Onset of sensory block (mins)	5.85 ± 0.95	4.92 ± 1.14	<0.001
Maximum durationof sensoryblock(mins)	17.60 ± 1.76	15.60 ± 1.39	<0.001
Onset of motor block (mins)	20.84 ± 1.69	21.10 ± 1.13	0.553
Maximum duration of motor block (mins)	29.32 ± 2.13	29.56 ± 1.75	0.763

Table 3:- Duration of Analgesia (hrs.).

Groups	Group BB	Group BF	P value
Duration of Analgesia	7.64 ± 1.39	6.04 ± 1.29	< 0.001

Discussion:-

Epidural anaesthesia offers superior pain relief and early mobilisation. It also improves the post-operative outcome and attenuates the physiological response to surgery, in particular significant reductions in pulmonary infections, pulmonaryembolism,ileus,acuterenalfailureandbloodloss. Addition of opioids to bupivacaine leads to faster onset of sensory blockade and prolonged duration of analgesia. The dose-sparing action of local anaesthetics and stable cardiovascularparametersmakeitaveryeffectiveadjunctin regionalanaesthesia.

In present study, mean time for onset of sensory block was 5.80 ± 95 mins In BB Group and 4.92 ± 1.14 mins in BF Group. Statistically, the difference in time of onset of analgesiawashighlysignificant[pvalue<0.001].Ourresults are in concordance with Kaur et al comparing epidural trmadol AND fentanyl as adjuvants in the lower abdominalsurgery.Itwasshownthatmeantimeforonsetof sensory block in BB (Bupivacaine Tramadol group)was5.50 ± .91 mins AND BF was 4.92 ± 1.03 mins.[8] Similar results were obtained by Kumar et al,[9] Sharma et al[10] and Nupoor et al.[11]

In present study, time for maximum sensory block was17.6±1.76minsinBBGroupand13.9±20minsinBFGroup. Statistically, the difference in time for maximum sensory block was highly significant [p value < 0.001]. Kaur et al in 2014comparedtramadol 50 mgandfentanyl100mcgasadjuvants to bupivacaine in lower abdominal surgeries and demonstrated time for maximum sensory blockade (Completion of analgesia) was 11.80 ± 1.63 mins in tramadol group and 10.80 ± 1.25 mins in fentanylgroup. However, their definition of time for maximum sensory blockade is different from our study. They defined it as time from the onset of analgesia to maximum sensory blockade attained, whereas we defined it as time from the completion of injection of study drug to maximum sensory blockade attained.[8] Our results are in concordance with those given by Hunt etal.[12]

In present study, mean time of onset of motor blockade was20.84±1.69minsintramadolgroupand21.10±1.13 in fentanyl group, which was statistically non-significant. Kaur et al in 2014 compared epidural tramadol and fentanyl as adjuvants in lower abdominal surgery andfound meanonsetofmotorblockintramadolgroupwas20.56±2.04minsandfentanyl(100ug)was20.76±1.6mins.[8]The resultsofpresentstudywereconsistentwithKumaretaland Chattopadhyayetal.Thetimeformaximummotorblockade inpresentstudyintramadol groupwas29.32±2.13mins and 29.56 ± 1.75 mins in fentanyl group. The difference in meanvalueofthesetwogroupsisnon-significant.

In study conducted by Kaur et al, the mean time for maximum motor blockade was 8.68 ± 1.06 mins in tramadol group and 8.72 ± 0.79 mins in fentanyl group. The results of our study are not in concordance with the above study, because in Kaur et al study time for maximum motor blockade was taken from onset of motor blockade, while in our study it was taken from injection of study drug.

In present study, mean duration of analgesia in tramadolgroupwas7.64±1.39hrs.andinfentanylgroup was 6.04 ± 1.29 hrs. Statistically, the difference is highly significant with 'p' value (< 0.001). Thus, fentanyl prolongs duration of analgesia more than tramadol. Similar to our study,Kauretalin2014comparedepiduraltramadoland fentanyl as

adjuvants in lower abdominal surgery and concluded mean duration of analgesia in tramadolgroup was7.64±1.41hrs.and5.96±1.30hrs.infentanylgroup.[8]

Our results are in concordance with Naulty et al in 1985 observed duration of analgesia with epidural fentanyl 100 mcg to be about 4.6 hrs.[13]

Conclusion:-

The mean onset of sensory blockade and time for maximum sensory blockade was observed to be significantly reduced with the addition of fentanyl to bupivacaine as compared to tramadol to bupivacaine. The results showedstatistically significant increase in the duration of analgesia with the addition of fentanyl to bupivacaine as compared to tramadol to bupivacaine. However, haemodynamic parameters and level of sedation was comparable in both groups.

So, we can conclude that tramadol and fentanyl were effective adjuvants to bupivacaine when used epidurally in patients undergoing lower limb surgery. Although, epidural fentanylwithbupivacaineproducessignificantlyfasteronsetof sensory blockade compared to epidural tramadol; however, epidural tramadol with bupivacaine produces significantly prolonged duration of analgesia compared to epidural fentanyl.

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