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COMPARISON OF EFFICACY OF EPIDURAL LEVOBUPIVACAINE WITH LEVOBUPIVACAINE PLUS DEXAMETHASONE FOR LOWER LIMB SURGERY

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ABSTRACT

Introduction: Levobupivacaine is a new long acting local anaesthetic an S(-) enantiomer of Bupivacaine. Dexamethasone, a corticosteroid has an anti-inflammatory property too so we want to study effect of Dexamethasone as an adjuvant to Levobupivacaine for epidural anaesthesia in lower limb surgery.

Aims and Objectives: To compare effect of epidural Dexamethasone plus 0.5% Levobupivacaine with 0.5% Levobupivacaine alone on onset and duration of sensory and motor blockade, intraoperative hemodynamic, post-operative analgesia and side effects in patients posted for lower limb surgeries.

Material and method: A prospective, randomized, controlled, double blinded study was conducted in 60 patients posted for lower limb surgery. After identification of epidural space Inj. 0.5% Levobupivacaine 20ml plus Dexamethasone 8mg (2ml) in Group D or Inj. 0.5% Levobupivacaine 20ml plus 2 ml normal saline in Group L.

Onset of Sensory blockade and motor blockade ,recovery from sensory and motor block, intra-operative haemodynamic and post-operative complications were documented and compared

Observation: Mean time required for onset of sensory block was 8.97 ± 1.03 min in Group D while it was 12.77 ± 1.7 min in Group L. Mean time required for onset for motor block was 15.13 ± 1.38 min in group D while it was 21.4 ± 1.75 min in group L. Time required for two segment regression in group D was 165.8 ± 5.05 minutes while in group L it was 125 ± 8.77 minutes. Time required for rescue analgesic was 237.7 ± 6.75 minutes in group D and it was 166.9± 8.37 minutes in group L. There was no statistically significant difference in quality of motor blockade, pulse rate and blood pressure between two groups. In group D, no complications were observed. In group L, 4(13.33%) patients had shivering which was transient, 2(6.67%) patients had nausea, vomiting.

Conclusion

We concluded that dexamethasone as an adjuvant in epidural anaesthesia leads to early onset of sensory and motor blockade with prolongation of postoperative analgesia without side effects.

KEYWORDS : Levobupivacaine, Dexamethasone ,epidural anaesthesia.

INTRODUCTION

Epidural anaesthesia is commonly used for lower limb surgeries. Levobupivacaine is a new long acting local anaesthetic an S(-) enantiomer of Bupivacaine has similar structure, pharmacology and pharmacokinetic to that of Bupivacaine. Anaesthetic and analgesic effects are similar to that of Bupivacaine with a lower risk of cardiovascular and long term central nervous system toxicity than Bupivacaine[1]. Adjuvants like Fentanyl, Clonidine, Magnesium sulphate, Midazolam, Dexmedetomidine are added to local anaesthetic solution to improve quality of anaesthesia.

Dexamethasone, a corticosteroid has a wide range of clinical applications due to its anti-inflammatory properties. Recent studies suggested that Dexamethasone when used as an adjuvant in epidural anaesthesia prolongs the duration of post-operative analgesia[2]. In present study, we compared the effect of adding Dexamethasone 8 mg to Levobupivacaine 20 ml and with Levobupivacaine in patients undergoing lower limb surgeries.

AIMS AND OBJECTIVES

To compare effect of epidural Dexamethasone as an adjuvant to 0.5% Levobupivacaine with 0.5% Levobupivacaine alone on onset of sensory and motor blockade, duration of sensory and motor blockade, intraoperative hemodynamic, post-operative analgesia and side effects in patients posted for lower limb surgeries.

MATERIAL AND METHOD

A prospective, randomized, controlled, double blinded study was conducted after approval of hospital ethical committee. Total 60 patients of age 18-55year posted for lower limb surgery were randomly allocated in two equal groups 30 each, Group D (Levobupivacaine + Dexamethasone) and Group L (Levobupivacaine + Normal saline).

After detail preoperative evaluation and preparation written informed consent was obtained. Patients were kept nil by mouth overnight. Patients were given Tab. Ranitidine 150 mg 2 hours prior to surgery. Intravenous line was secured with 18 G angiocath, Inj. Midazolam – 0.02 mg/kg was given as premedication. Non-invasive blood pressure, Cardiac monitor and pulse oxymeter was used for intraoperative monitoring. Oxygen supplementation was started at rate of 5 Lt / min.

After all aseptic precautions and local anaesthesia with 2ml of 2% Lignocaine , epidural space was identified at L 2-3 or L 3-4 space by using loss of resistance technique with 18 G Touhey's needle and 18 G epidural catheter was advanced for 3 to 5 cm into epidural space. After confirmation of epidural catheter was fixed and 3ml of 2% Lignocaine with Adrenaline was injected as test dose followed by Injection 0.5% Levobupivacaine 20ml plus Dexamethasone 8mg (2ml) in Group D or Injection 0.5% Levobupivacaine 20ml plus 2 ml normal saline in Group L. Sensory block was assessed by pinprick test. Onset of Sensory block was defined as time required to achieve T_{10} level. Motor block was assessed by Bromage scale , Grade 0 No motor block , Grade I Inability to raise extended legs , Grade II Inability to flex knee, able to flex the ankle, Grade III Inability to flex ankle complete motor block

Level of sensory blockade was checked at every 5 minutes for half an hour followed by every 15 minutes till surgical procedure completed. After that it was tested every half an hour. Patients were asked to note the time when he or she feels pain and requested analgesic. If patient complain of pain during surgery, Inj. Fentanyl 1 ug / kg was given as a rescue analgesic. Post-

Operatively intravenous Inj. Diclofenac sodium 75 mg was given when patient starts complaining pain.

Recovery from sensory block will be considered when two segment regression of sensory blockade occurs. Recovery from motor block when patient had lower limb movement with motor power grade II or more. A constant watch will be kept for development of any complications intra and post-operative period. Vital parameters like pulse rate, blood pressure, mean arterial pressure, respiratory rate, Oxygen saturation and sedation will be recorded at every 10 minutes.

Independent samples students **t test** and **Chi square test** was used for evaluation of demographic data and post operative hemodynamic data, time of onset and recovery of sensory and motor block, duration of

operation and tourniquet, duration of analgesia, intra-operative and post-operative analgesic use. P<0.05 will be considered as significant.

OBSERVATION

Mean time required for onset of sensory block was 8.97 ± 1.03 min in Group D while it was 12.77 ± 1.7 min in Group L. Mean time required for onset for motor block was 15.13 ± 1.38 min in group D while it was 21.4 ± 1.75 min in group L. Statistically significant difference was observed in time required for onset of sensory as well as motor blockade in group D and group L (P< 0.05) with early onset in group D.

Time required for two segment regression in group D was 165.8 ± 5.05 minutes while in group L it was 125 ± 8.77 minutes. Time required for rescue analgesic was 237.7 ± 6.75 minutes in group D and it was 166.9± 8.37 minutes in group L. Statistically significant difference was there in time required for two segment regression and requirement of rescue analgesic in both groups (P value < 0.05). This indicates that Dexamethasone as an adjuvant to Llevobupivacaine leads to prolongation of duration of sensory blockade .

We also compared quality of motor blockade. In group D, 9 (30%) patients had motor blockade of Bromage scale III and 21 (70%) patients had Bromage scale II. In group L, 8 (26.66%) patients had Bromage scale III and 22 (73.33%) patients had Bromage scale II. There was no statistically significant difference in quality of motor blockade between two groups (P value > 0.05). In group D, lowest mean pulse rate observed was 74.36 ± 6.99 per minute at around 120 minutes. In group L, lowest mean pulse rate observed was 77.53 ± 6.00 per minute at around 120 minutes. There was no statistically significant difference in pulse rate and blood pressure changes in both groups.

In group D, no complications were observed. In group L, 4(13.33%) patients had shivering which was transient, 2(6.67%) patients had nausea, and vomiting for which injection Odancetron 4 mg was given. Other complications like hypotension, bradycardia, sedation, and headache did not occur in both groups. No patients in either group had transient pain or focal neurological deficit. Hemodynamic stability was seen in both groups.

DISCUSSION

Levobupivacaine an S (-) enantiomer of racemic bupivacaine had similar pharmacokinetics to Bupivacaine with less cardio-toxic and neurotoxic effects.[2] Many drugs have been tried as an adjuvant to epidural local anaesthetic solution but still no ideal adjuvant is found. Opioids may cause nausea, vomiting, itching all over body, sedation and or respiratory depression. Alpha-2 blocker may cause severe bradycardia and hypotension.

Epidural steroid injection is effective in the treatment of chronic backache so we want to study its effect in post-operative pain. Dexamethasone is a highly potent, long acting glucocorticoid with little mineralocorticoid effect that has been used for prophylaxis of postoperative nausea[3]. Dexamethasone microspheres have been found to prolong the block duration in animal and human studies[4,5] and adding Methylprednisolone and Dexamethasone to local anaesthetic increases the duration of axillary brachial block[6]. Preoperative administration of Dexamethasone either oral or intravenous has been reported to reduce postoperative pain through both routes.[7,8] Dexamethasone has been demonstrated to reduce lumber epidural puncture-induced backache,[9] postoperative pain and morphine consumption.[10]

Surgical trauma produces local tissue damage with release of prostaglandins, histamine, serotonin, bradykinin and substance P and generation of noxious stimuli. Local oedema and release of algogenic agents increase nociceptors activity. This leads to increase in afferent input to spinal cord and initiating increase in sympathetic activity. This results in a vicious cycle of pain – muscle spasm – increased sympathetic activity and other reflex changes. Glucocorticoids due to its anti-inflammatory effect might be effective in controlling acute pain

In our study early onset of sensory and motor block was found in Dexamethasone group. Same observation was noted when caudal Ropivacaine with Dexamethasone was used.[11] Though actual mechanism of Dexamethasone in producing early onset of block is not well understood, the reason could be due to local action of Dexamethasone on nerve as well as anti-inflammatory effect , alteration in potassium channel of nerve cell thereby synergistic action with local anaesthetic or the action on corticosteroid receptors present in brain.[12,13] Early onset of sensory and motor blockade was observed not only by epidural administration of Dexamethasone but also in brachial plexus block.[15]

Epidural administration of Dexamethasone in different doses 5mg[10], 6mg[16] or 8mg[17] is effective in prolongation of duration of analgesia with reduced post-operative pain, opioid sparing and antiemetic effect.[2] Also 8 mg Dexamethasone as an adjuvant to Lidocaine for intravenous regional anaesthesia (IVRA) was effective in providing prolonged postoperative analgesia.[19] Dexamethasone with local anaesthetic prolongs postoperative analgesia significantly than Tramadol 50mg or epinephrine or clonidine, and reduces opioid requirement when used in supraclavicular or interscalene block.[20,21]

It was observed intrathecal administration of Dexamethasone 8 mg with Bupivacaine significantly improved the duration of sensory block.[18] Nadia Bani-hashem et al used 8 mg Dexamethasone in spinal anaesthesia and found that duration of sensory block was 119.12 ± 10.69 minutes in dexamethasone group and 89.44 ± 8.37 minutes in control group.[18]

It was observed in our study that the time required for the first rescue analgesic was 237.7 ± 6.75 minutes in Dexamethasone group while it was only 166.9 ± 8.37 minutes in control group. Bahaman Naghipour et al used 8mg Dexamethasone added to Bupivacaine-Fentanyl solution in epidural anaesthesia and found that duration of analgesia was 372 ± 58.1 in Dexamethasone group and 234.6 ± 24.3 in control group.[17] Prolonged duration of postoperative analgesia as compared to our study may be due to addition of fentanyl 50 microgram to Bupivacaine in addition to dexamethasone 8mg . Caudal Ropivacaine 0.15% mixed with Dexamethasone in a dose of 0.2mg/ml provided analgesia for 464±45.5 minutes as compared to 418±48.9 minutes in control group[11]. Jehan M.K. used epidural injection of 0.25% Bupivacaine 12ml, Morphine 2mg and Magnesium sulphate 50mg in group I, 0.25% Bupivacaine 12ml, Morphine 2mg and Dexamethasone 6 mg in group II and 0.25% Bupivacaine 12ml, Morphine 2mg in group III and found that time to first analgesic was 7.5±3.2 hours in Magnesium sulphate group, 8.2±2.4 hours in Dexamethasone group and 2.3±1.8 hours in control group.[16] Similarly, duration of postoperative analgesia was also prolonged when Dexamethasone was added as adjuvant in brachial plexus block [15]

The pathophysiological mechanisms for epidural steroids effects may be related to the anti-inflammatary action, oedema reduction, or shrinkage of connective tissue. Local steroid application was found to suppress transmission in thin unmylienated C-fibres but not in myleinated A-beta fibers.[22] it has been suggested that steroids may bind directly to the intracellular glucocorticoid receptor and their effects are predominantly mediated through altered protein synthesis via gene transcription.[23]

Epidural Dexamethasone may affect intraspinal prostaglandin formation. Acute noxious stimulation of peripheral tissues during surgical stimulation leads to activation of phospholipase A2 and up-regulation of the expression of cyclo-oxygenase-2 in the spinal cord, leading to prostaglandin synthesis and a resultant hyperalgesic state.[24] Inflammatary, metabolic, hormonal and immune responses to surgery are activated immediately after surgical incision, so preoperative administration of steroids may reduce these responses, by virtue of their anti-inflammatary and immunosuppressive effects, by inhibiting both phospholipase A2 and cyclo-oxygenase-2 enzymes[25]. This was obvious with reduction of C-reactive protein levels, pain and fatigue scores in patients who received preoperative Dexamethasone[8]. The mechanism by which glucocorticoids alleviate nausea and vomiting is not fully understood, but the effects are probably centrally mediated via inhibition of prostaglandin synthesis or inhibition of release of endogenous opioids.[26]

Another possible mechanism is abolishment or suppression of inflammatory cytokine release with its subsequent nociceptive effects.[27] Wang et al found epidural Dexamethasone as adjuvant , prevented elevation of maternal temperature and prevented increased serum levels of interleukin-6, one of the potent inflammatory cytokines, compared to control parturient received epidural analgesia free of Dexamethasone.[28]

The use of epidural Dexamethasone had no specific side effects different from other groups of drugs. Although arachnoiditis has been reported in association with accidental intrathecal injection of depo-steroids, this risk is considered to be minimal with Dexamethasone as a result of its water-solubility, and because its particles are significantly smaller than red blood cells with least tendency to aggregate reducing the risk of embolic infarcts. A single epidural injection of 15 mg dexamethasone acetate was found to be associated with transient adrenal suppression, but there were no changes in fasting serum glucose, triglycerides and cholesterol, sodium or potassium levels.[29,30]

Adding a steroid to local anaesthetic solution may not be indicated for all patients. For example, diabetic patients may experience hyperglycaemia and patients with a continuing infectious process may be detrimentally affected by the anti-inflammatory effects of steroids. So, we excluded diabetic patients from our study. This led us to hypothesize that dexamethasone may be useful in situations in which epinephrine must be used with caution (e.g., hypertension, ischemic heart disease).[31]

Thus, we concluded that when dexamethasone is used epidurally as an adjuvant it leads to early onset of sensory and motor blockade with prolongation of postoperative analgesia without significant side effects.

CONCLUSION

We concluded that when dexamethasone is used epidurally as an adjuvant it leads to early onset of sensory and motor blockade with prolongation of postoperative analgesia without significant side effects.

Table no.1 Onset of sensory and motor blockade

Title	Group D n = 30	Group L n = 30	Significance P value
Onset of Sensory block (min)	8.97 ± 1.03	12.77 ± 1.7	< 0.0001
Onset of Motor block (min)	15.13± 1.38	21.4 ± 1.75	< 0.0001

There was statistically significant difference in time required for onset of sensory as well as motor blockade with earlier onset in group D than in group L (P< 0.05).

Table no. 2 Time for two segment regression and rescue analgesia

Title	Group D n = 30	Group L n = 30	Significance P value
Time for two segment regression (min)	165.8 ± 5.05	125 ±8.77	< 0.0001
Time for rescue analgesia (min)	237.7 ± 6.75	166.9 ± 8.37	< 0.0001

There was statistically significant difference in time required for two segment regression and rescue analgesia in both groups (P value < 0.05) with prolongation of sensory blockade and postoperative analgesia in group D.

Table no. 3 Quality of motor blockade

Bromage scale	Group D n = 30	Group L n = 30
0	0	0
1	0	0
2	21 (70%)	22 (73.33%)
3	9 (30%)	8 (26.66%)

There was no statistically significant difference in quality of motor blockade between two groups (P value > 0.05).

Table no. 4 COMPLICATIONS

	Group D	Group L
Perioperative		
Bradycardia	0	0
Hypotension	0	0
Sedation	0	0
Shivering	0	4(13.33%)
Postoperative		
Nausea, Vomiting	0	2(6.67%)
Headache	0	0
Transient radiating pain	0	0

In group D no complications were observed. In group L patients had shivering ,nausea and vomiting for which

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