EPIDURAL KETAMINE FOR POSTOPERATIVE ANALGESIA AFTER ABDOMINAL HYSTERECTOMY

FINAL REPORT OF THE RESEARCH STUDY

SUBMITTED TO RESEARCH COMMITTEE OF SRI 5 INDRA RAJYA LAXMI
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SUBMITTED BY
Dr. C.B. Karki
Dr. S.B. Karki
Department of Anaesthesia

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Dr. C.B. Karki
Dr. S.B. Karki

Content

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Dr. C.B. Karki, S.B. Karki

INTRODUCTION

Pain is an experience, which is one of the complaints for which a patient visits the hospital.

According to International Association for the study of pain "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" (Wilson-1980)

Postoperative pain is a complex of psychological and physiological factor, so only a simple method of analgesia may not be effective equally for all patients. But adequate pain management in postoperative period is most important for the success of surgical treatment and prevention of complications.

All methods of pain control have some risk, but it has been shown that, instead of using single method of pain management, combined methods are more effective with less undesirable effects.

A number of techniques are being used for post operative pain relief such as narcotics, NSAIDs, local/regional analgesia, intrathecal epidural or combined spinal epidural analgesia etc.

In recent times, among the various post operative techniques for analgesia epidural analgesia has been found to be extremely effective in controlling post operative pain relief for abdominal & thoracic operations.

This study was undertaken to study the efficacy of Ketamine with Bupivacaine given by lumber epidural route for intraoperative and postoperative pain relief after abdominal hysterectomy.

After epidural administration, larger amount of epidural dose is absorbed into the systemic circulation and only small fraction about 2-10% diffuses across the dura to bind the spinal receptors, depending upon the characteristics of the administered drug. (Lauretti-1999)

Ketamine has well known analgesic and anesthetic properties. Intrathecal administration of preservative free ketamine in animal shows no neurotoxic effect & similar study done in human also shows ho neurotoxicity.

In some clinical studies epidural administration of Ketamine provided potent and safe analgesia & has been proposed as an alternative to opioids in addition to local anesthetics.

This double blind study was designed to compare the effects of epidural bupivacaine-ketamine or bupivacaine alone on duration and requirement of postoperative analgesia after abdominal hysterectomy.

Review of Literatures:

Ketamine when used alone for epidural analgesia found to be inadequate (Peat-1989), but Naguib in a study used 30 mg of Ketamine in 10 mls of NS and achieve post operative analgesia for 24 hours in more than 50% patients after cholecystectomy.

Yanli et al used Ketamine with Bupivacaine and found post operative analgesia for 8-10 hours.

Naguib also used Ketamine with Bupivacaine and found better analgesia in comparison with Bupivacaine alone.

Use of Ketamine before noxious stimuli also work as a preemptive analgesia to prevent or to reduce the development of a memory of the pain stimulus in the nervous system, there by lessening the postoperative analgesic requirements. (Rainer-1998)

Use of Ketamine with local anesthetic cause both preemptive and post operative analgesia and also fulfill the analgesic requirment during surgery.

Usually Bupivacaine when given epidurally provide analgesia for 2-4 hours (Barash-1997) & in this study we tried to prolong the analgesic effect of Bupivacaine after addition of Ketamine.

Objectives of the Study

General Objective:

To study postoperative analgesia after epidural analgesia with bupivacaine and ketamine.

Specific Objective:

To prolong postoperative analgesia after addition of ketamine in local anesthetic bupivacaine in epidural analgesia.

To compare postoperative analgesia and requirement of additional postoperative analgesic between bupivacaine alone and bupivacaine - ketamine group in epidural analgesia.

Methodology:

In this randomized double blind prospective study of 40 patients, we studies post operative analgesic effect of Ketamine with bupivacaine & compared two regimen of epidural analgesia: 10 mls of 0.25% Bupivacaine alone and similar amount & concentration of Bupivacaine with 25 mg of Ketamine.

Study was conducted amoung the patients under going TAH selected already by gynecologists for surgery.

In preoperative evaluation, at first patients were evaluated whether patient was fit for study or not & after that properly tought about visual analogue scale.

Epidural catheter was placed in OT at the day of surgery and study solution was administered before induction of general anesthesia. GA was administered for all patients & after reversal & extubation patient send to post operative room after recovery. Patient's pain status was assessed after 2, 6 & 24 hours of surgery and analgesic solution 0.25 % bupivacaine 8 - 10 mls injected via epidural catheter according to requirement.

Duration of post operative analgesia, no. of post operative analgesic requirement assessed in post operative ward. Epidural catheter removed in postoperative ward befor transfer of patient to general ward.

Results:

Patients in each of 2 groups were comparable in age and body weight (Table1). The mean pain score and the total dose of analgesic administered to each patient during 24 hours period were shown in table II and III respectively. The duration of post-operative analgesia was 2.8 hours in bupivacaine group and 3.7 hours in ketamine-Bupivacaine group.

Table I

Patient Characteristics

	Bupivacaine-Ketamine (n = 20)	Bupivacaine (n = 20)
Age: Yrs.	41.8	44.5
Weight; Kg	50.4	53.4
Preoperative SBP; mm Hg	125.5	133.5
Preoperative Heart rate Beat. min^{-1}	93.8	92.7

The mean pain score in both groups was less than 2 and analgesia was adequate and no any significant differences seen between 2 groups.

The number of injections needed in 24 hours in Bupivacaine-Ketamine group was 2.6 and in Bupivacaine group was 2.8. The difference was little, but still Ketamine-Bupivacaine group got less analgesic than bupivacaine group.

Table II

Mean pain score during first 24 hours following surgery

Postoperative Period	Bupivacaine-Ketamine	Bupivacaine
2 hours	1.3	1.0
6 hours	1.3	1.3
24 hours	1.2	1.1

Patients had no complain during introduction of investigation solution via epidural catheter, most of the patient felt only sensation of cold and was due to the cold analgesic solution.

Table III

Number of additional postoperative analgesic requirement and duration of post-operative analgesia.

	Bupivacaine-Ketamine	Bupivacaine
Additional analgesia (epid. bupiv)	2.6	2.8
Duration of Post-operative analgesia in Hrs.	3.7	2.8

Table IV

Details of systolic blood pressure (SBP) and heart rate (HR) in Bupivacaine-Ketamine group and bupivacaine-group.

Time	SBP mm Hg		HR beat per min.	
	Bupiv-Ketam	Bupivacaine	Bupiv-Ketam	Bupivacaine
Preoperative	125.5	133.5	93.8	92.7
Post intubation	130.6	134.7	102.6	102.5
Post incision	126.2	124.2	96.7	96.2
Post extubation	121.3	121.8	92.9	95.2

Patient's analgesia was maintained intra-operatively with N_2O and epidural analgesia and was adequate in both groups, because there was no significant change in

blood pressure and pulse rate between preoperative values and post extubation readings.

Nausea and vomiting were common in both groups, but 5 patients were treated with IV metoclopramide in bupivacaine ketamine group.

Complications such as bladder dysfunction, hallucination and vivid dreams were not seen in ketamine bupivacaine group.

Table V

Number of side effects and medications

Side effects and treatment	Bupivacaine-Ketamine	Bupivacaine
Nausea-vomiting	14	12
Metoclopramide	5	0

Discussion:

Ketamine, a phencyclidine derivative with marked analgesic properties, which are mediated by a number of mechanisms. Ketamine binds to opioid receptors, but its significant contribution to analgesic efficacy come from interaction with cholinergic, adrenergic and 5 HT system. Ketamine also can prevent action potential conduction by an effect on sodium and potassium channels in nerve membranes and is considered as local anesthetic property. Finally, Ketamine can selectively block the NMDA (N-Methyl-D-aspartate) excitation of central neurons. This combination of analgesic activities leads to Ketamine's use by epidural administration for post operative pain relief.

In the present study, we used Ketamine 25mg with 10mls bupivacaine 0.25% solution for epidural analgesia in comparison with 10ml of bupivacaine 0.25%. The results of our study indicate that addition of Ketamine to bupivacaine slightly increased the duration of post-operative analgesia. The post-operative analgesic requirements and incidence of side effects were also comparable between two groups.

Summary

In randomized double blind prospective study of 40 patients, undergoing TAH we have compared two regimen of epidural analgesia: 10 mls of Bupivacaine 0.25%, 25 mg ketamine and 10 mls of bupivacaine 0.25%, 0.5 mls of 0.9% normal saline. The main out come measures were duration of postoperative analgesia & requirement of additional analgesia in Ketamine - bupivacaine group compared with bupivacaine - normal saline group. Duration of postoperative analgesia was longer in katamine - bupivacaine group, similarly requirement of additional analgesia was also less in comparison with bupivacaine - normal saline group. But the difference was not remarkable, side effects were also similar in both groups. The addition of ketamine to bupivacaine given epidurally was better than bupivacaine alone, but the difference was not much remarkable.

Conclusion:

In Conclusion addition of ketamine in analgesic solution bupivacaine for postoperative analgesia was better then bupivacaine alone. Mixed analgesic solution showed longer duration of postoperative analgesia & less additional analgesia was required in postoperative room in comparison to bupivacaine alone. Advantage of addition Ketamine was still not remarkable. About the side effects, in both groups incidence of nausea & vomiting was approximately equal, but in ketamine group 5 patients were treated with IV Metoclopramide for management.

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PROFORMA

CODE NO:_____

A. Pre-anesthetic assessment

a) Identification of the patient

Name:	age / sex:	occupation:
Address:	I.P. No:	Ward \ Bed No:
Diagnosis:	Operative procedure:	
Date of admission:	Date of examination:	

YES NO

b. History of a patient

1. Have you had any anesthetics previously ?
2. Have you had any complication from an anesthetic ?
3. Have any member of your family had any complication form an anesthetic ?
4. Have you had or any of your family members have reaction with local anesthesia ?
5. Do you have any allergies ?
6. Do you ever have any of the following disease ?
   - Diabetes
   - Tuberculosis, asthma
   - High blood pressure
   - Heart disease, heart attack
   - Rheumatic fever, rheumatism
   - Thyroid disease
   - Jaundice or liver disease
   - Kidney disease
   - Mental or nervous disease
   - Arthritis or muscular disease
   - Diseases of vertebral column and spinal cord
   - Bleeding disorders

7. Do you have any other disease, which periodically requires treatment ?

8. Do you get shortness of breath when you walk ?

   If so, how much ? _____

9. Do you get pain or tightness in you chest ?

   If so, when ? _____

10. Do you smoke ?

    If yes, how many ? _____

11. Do you drink alcohol ?

    If yes, how much ?_____

12. Do you use drug or been a drug user ?

13. Do you take any medicines regularly ?

14. Do you have loose teeth, capped teeth, and carries denture, fixed bridge or other dental problem ?

15. Are you having a cough or cold at present ?

16. Menstrual history

17. Obstetric History

18. Does she understand the visual analogue scale (VAS) ?

c. Clinical examination

General examination

General condtions.....
Temperature .....
Cyanosis.....
Lymphnodes .....
Clubbing .....
Weight.....Kg.

Pulse .....
Pallor .....
Oedema.....
Peripheral veins .....
Anemia .....

Blood pressure.....
Jaundice .....
Nutrition.....

Local examination

Mouth opening
TMJ: Free \ Restricted
Neck: i) mobility: Free / Restricted
ii) Swelling
Lumber spines:

Systemic examination

Cardiovascular system

Heart sound

Heart rate.....\ min.

Rhythm: Regular / irregular

Additional sounds

Murmurs

Respiratory system

Lungs: R L

Air Entry

Breath sound

Ronchi

Creps

Others

Gastro intestinal system:

Genito urinary system:

Central nervous system:

Musculo skeletal system:

Skin:

d. Laboratory investigation

Blood:

Hb .....g \ 100ml, TLC..... DLC:N.....L.....E.....M.....B.....ESR.....mm\h

Blood sugar: F..... p.p.....R..... Serum bilirubin: T....., D.....

SGPT;..... SGOT:..... Alk phosphatase:.....

Electrolytes: Na' .....K' .....

Blood group.....

Blood urea..... S Creatinine..... Plateletes .....

BT ..... CT ..... PT .....

Urine for RE .....
Chest X-ray PA .....
ECG .....
USG abdomen .....
Others .....

e. ASA Grading: (I) (II) (III) (IV) (V)

f. Level of placement of epidural catheter :
L_2 / L_3 L_3 / L_4 L_4 / L_5

g. Epidural administration of investigating solution:
- Time of administration:
- Volume:

C. Post operative

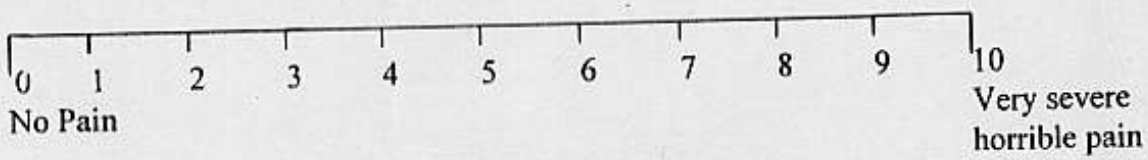
a. When pain was first perceived

Date ..... Time .....
Pulse ..... / min
Blood pressure ..... / mm of Hg.
Resp. Rate ..... / min

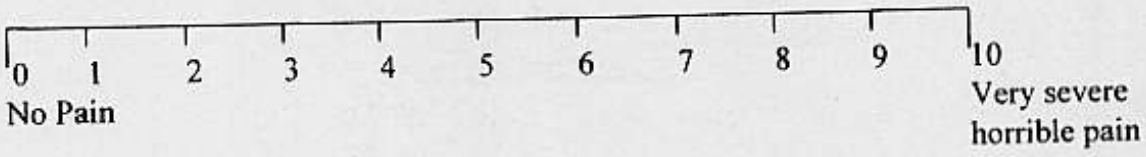
b. After 2 hours of surgery:

Pulse ..... / min
Blood pressure ..... / mm of Hg.
Resp. Rate ..... / min

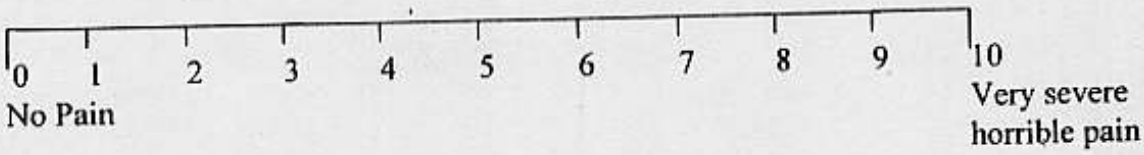
Line below to indicate the intensity of pain at ***rest. (VASR).***



Line below to indicate the intensity of pain during your ***cough (VASC).***



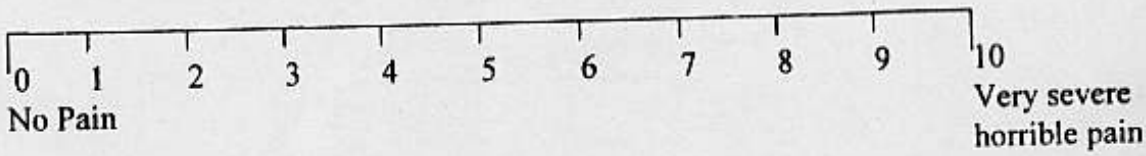
Line below to indicate the intensity of pain during ***pressure*** over the wound ***(VASP).***



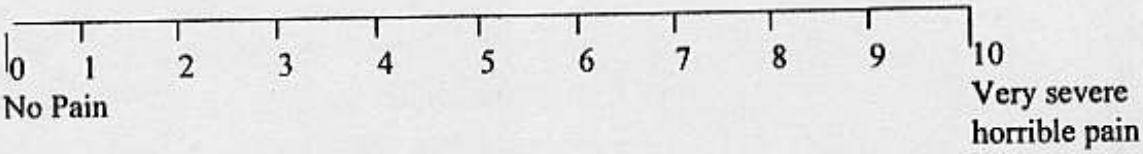
c. After 6 hours of surgery

Pulse ..... / min
Blood pressure ..... / mm of Hg.
Resp. Rate ..... /min.

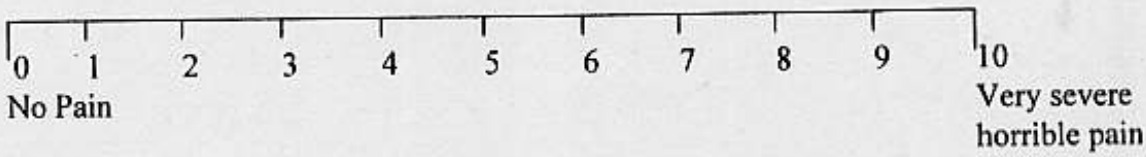
Line below to indicate the intensity of pain at ***rest. (VASR).***



Line below to indicate the intensity of pain during ***cough (VASC).***



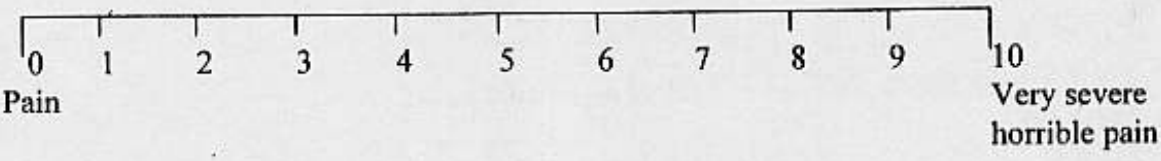
Line below to indicate the intensity of pain during ***pressure*** over the wound ***(VASP).***



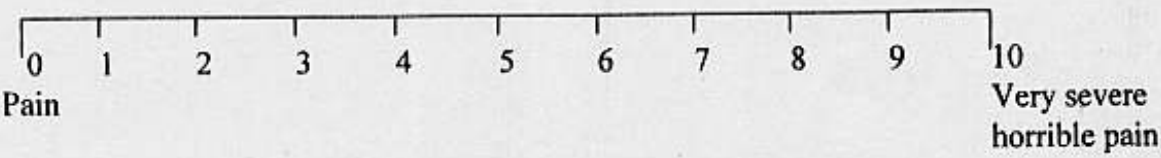
d. After 24 hours of surgery

Pulse ..... / min.
Blood pressure ..... / mm of Hg.
Resp. Rate ..... / min.

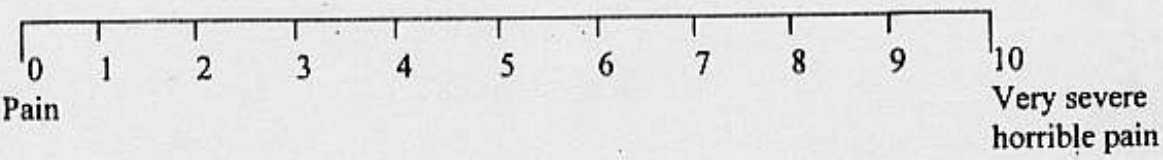
Line below to indicate the intensity of pain at ***rest (VASR).***



Line below to indicate the intensity of pain during ***cough (VASC).***



Line below to indicate the intensity of pain during ***pressure*** over the wound ***(VASP).***



D. Supplementary analgesia

S.N.	Date	Time	Epidural Bupivacaine 0.25 % - 10 mls	Pethidine in mg	Promethazine in mg.	Diclofenac Na in mg.
1.						
2.						
3.						
4.						
5.						
6.						

E. Any Postoperative complications, and treatment:

a. nausea
b. vomiting
c. itching
d. headache
e. hallucination
f. sedation
g. any other .