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Original Research Article

A COMPARATIVE STUDY BETWEEN SPINAL BUPIVACAINE PLUS CLONIDINE AND ROPIVACAINE PLUS CLONIDINE FOLLOWED BY ROPIVACAINE INFUSION IN PATIENTS UNDERGOING ABDOMINAL HYSTERECTOMY

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Abstract

Background: We performed this study of comparison between spinal bupivacaine plus clonidine vs ropivacaine plus clonidine followed by ropivacaine epidural infusion in both the groups to see their effect on total abdominal hysterectomy patient. **Materials and Methods:** This was a Randomised, controlled, double-blinded, parallel group study at JLNMCH, Bhagalpur Bihar from January 2021 to June 2022. Informed consent was obtained from each patient and a detailed history, systemic examination and laboratory findings were checked on the day before surgery. After proper pre-medication with Inj.ondansetron 4mg and Inj.ranitidine 50mg (both IV) and moist oxygen inhalation through bi-nasal prong at 3L/min, the epidural catheter was inserted at L2-L3 level under complete aseptic precaution and test dose of 3ml of Inj.lignocaine was administered. Then BC group of patients (n=37) received 15mg (3ml) of 0.5% hyperbaric bupivacaine2 along with 30 µg (0.2ml) of clonidine through spinal route at L3-L4 level. The RC group (n=37) received 22.5mg (3ml) of 0.75% isobaric ropivacaine2 along with same dose of clonidine. **Result:** Age, body weight, height and ASA status between the groups were compared. There was no statistically significant difference between the groups in these regards. Regarding time to reach the peak level of sensory block the intra-group mean of the RC group (7.7±1.9 min) is higher than that of the BC group (5.8 ±1.79min). The p value (0.00) is statistically significant. As for the motor block the mean of the RC group subjects (9.8± 2.26 min) is higher than that of the BC group (7.6±2.04 min) and here also the p value (0.000) is statistically significant. **Conclusion:** It is concluded that bupivacaine (with clonidine added) produces a significantly quicker onset of both sensory and motor block when compared with ropivacaine (with clonidine added).

INTRODUCTION

Spinal anaesthesia [subarachnoid block, SAB] was first described by August Bier in 1898, using 3ml of 0.5% cocaine. The technique has been refined since that time and has been evolved into the modern concept of intrathecal, spinal or subarachnoid block. Subarachnoid block is one of the most commonly used regional anaesthesia techniques available today.[1-3]

0.5% hyperbaric bupivacaine is most commonly used drug for spinal anaesthesia. Patients undergoing surgery under spinal anaesthesia with hyperbaric bupivacaine alone occasionally experience varying degrees of intraoperative pain and discomfort in spite of apparently adequate level of sensory block. This requires supplementation with intravenous opioids or administration of general anaesthesia. Various studies have shown that adjuvants used with intrathecal local anaesthetics block affarent nociceptive stimuli at the level of dorsal root axon and the spinal cord by the mechanism distinct from local anaesthetics and potentiates the block or increases its duration. Thus, they not only decrease the required dose of spinal local anaesthetic agent but also their side-effects. In our study we used both 0.5% hyperbaric bupivacaine and 0.75% isobaric ropivacaine alongwith clonidine through spinal route.[4-7]

Epidural anesthesia and analgesia involves administration of drugs into the epidural space using epidural needle and or epidural catheter which would ultimately block the spinal nerves traversing through the epidural space after emerging from the spinal

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medulla. Hypotheses regarding the block of spinal nerves by epidural anesthesia state that it is either due to action of the epidurally administered local anaesthetic (LA) on the spinal nerves traversing the epidural space or slow diffusion of the drug into the sub-arachnoid space and subsequent action on the spinal roots. The main advantage of epidural analgesia is the level of block and duration of analgesia may be controlled by the anaesthesiologist. Since we can administer LA and other drugs through the epidural catheter either as continuous infusion or as top-up doses, this route can very aptly be used for prolonged post-operative analgesia, an added advantage over spinal anesthesia.[8-12]

We performed this study of comparison between spinal bupivacaine plus clonidine vs ropivacaine plus clonidine followed by ropivacaine epidural infusion in both the groups to see their effect on total abdominal hysterectomy patient.[13-15]

MATERIALS AND METHODS

This was a Randomised, controlled, double-blinded, parallel group study at JLNMCH, Bhagalpur Bihar from January 2021 to June 2022. Informed consent was obtained from each patient and a detailed history, systemic examination and laboratory findings were checked on the day before surgery.

Inclusion criteria:

- ASA grade I and II, informed patients with body weight in the range of 40 to70 kgs, aged 25 to 60 yrs.

Exclusion criteria:

- ASA III and above
- Coagulatoin disorders
- Bronchial asthma
- Known hypersensitivity to the study drugs
- Patients with anticipated difficult airway
- Patient refusal

Methodology

This was a Randomised, controlled, double-blinded, parallel group study at JLNMCH, Bhagalpur Bihar from January 2021 to June 2022. Informed consent was obtained from each patient and a detailed history, systemic examination and laboratory findings were checked on the day before surgery. After proper pre-medication with Inj.ondansetron 4mg and Inj.ranitidine 50mg (both IV) and moist oxygen inhalation through bi-nasal prong at 3L/min, the epidural catheter was inserted at L2-L3 level under complete aseptic precaution and test dose of 3ml of Inj.lignocaine was administered. Then BC group of patients (n=37) received 15mg (3ml) of 0.5% hyperbaric bupivacaine2 alongwith 30 µg (0.2ml) of clonidine through spinal route at L3-L4 level. The RC group (n=37) received 22.5mg (3ml) of 0.75% isobaric ropivacaine2 along with same dose of clonidine. After proper positioning and testing the level and adequacy of sensory and motor block the surgery started. After the surgery, continuous epidural infusion of 0.2% ropivacaine at 10ml/hr for 24 hrs was started and continued for 24 hours postoperatively in both the groups.

Pain score on a visual analogue scale was assessed by the patients at 1,3,6,12 and 24 hours after operation. When VAS of any patient was > 40, bolus dose of inj tramadol 1-2 mg/kg IV was administered if pain was not controlled. Dose of rescue analgesic along with time of the initial dose of rescue analgesia was recorded. Levels of sensory block to pin-prick bilaterally was recorded at the same intervals. Besides, appearance of adverse, untoward reactions viz. nausea, vomiting, hypotension and PDPH were also recorded.

Statistical Analysis

Statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by Statistica version 6 [Tulsa, Oklahoma, USA; 2001] and Graph Pad Prism version 5 [San Diego, California: GraphPad Software Inc., 2007] . All analyses were two-tailed and $p<0.05$ was considerd statistically significant.

RESULTS

Demographic profile of subjects: Age, body weight, height and ASA status between the groups were compared. There was no statistically significant difference between the groups in these regards as shown below [Table 1].

Comparison of Mean Arterial Pressure and Heart rate: Mean Arterial Pressure and Heart rate of all the subjects were recorded before administering the block (Baseline) and every 15 minutes thereafter. Although the Group RC had lower MAP, the difference is not statistically significant either in MAP or HR.

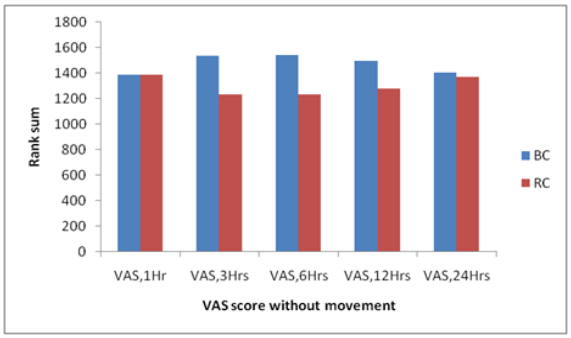

Figure 1: VAS score at rest of both the group

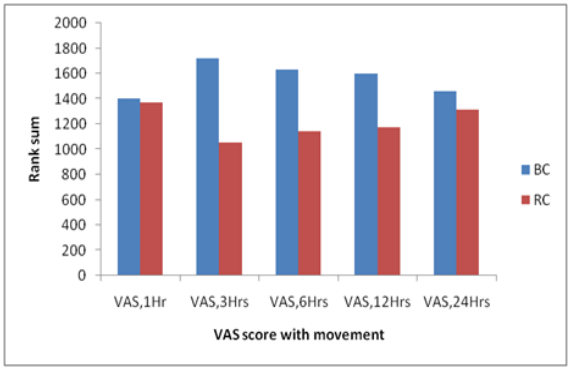

Figure 2: VAS score with movement of both the groups

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Comparison of Peak level of Sensory and Motor Block: Regarding time to reach the peak level of sensory ensory block the intra-group mean of the RC group (7.7±1.9 min) is higher than that of the BC group (5.8 ±1.79min). The p value (0.00) is statistically significant. As for the motor block the mean of the RC group subjects (9.8± 2.26 min) is higher than that of the BC group (7.6±2.04 min) and here also the p value (0.000) is statistically significant.

Comparison of Two Segment Regression Time: In the BC group the two Segment Regression Time is statistically (p= 0.001) longer than in the RC group (193.5+-30.20 min as compared to 172.2 +-24.40min).

Comparison of VAS at REST: VAS score at rest is compared between the two groups at the end of 1st, 3rd, 6th, 12th and 24th post-operatve hours. The mean of each group at these intervals, obviously not equal- the BC group generally having somewhat higher values, shows no statistically significant difference (p value being 1.000, 0.104, 0.093, 0.247 and 0.858 respectively)

Comparison of VAS at MOVEMENT: There were no significant difference between the groups at 1 and 24 hours, the RC group shows significantly lower VAS scores at 3, 6 and 12 post-operative hours (p value being 0.841, 0.000, 0.008, 0.023 and 0.421 respectively).

Comparison of Requirement of Rescue Analgesia: The requirement of rescue analgesia with Inj. Tramadol, IV for the BC group subjects was 32.43% subjects and for RC group it was 29.73%. There was no significant difference between the two groups as far as rescue analgesic requirement is concerned (p = 1.000).

Table 1: Age, Body Weight, Height and ASA Status of both the Groups

Group	Age (Years) (Mean ± SD)	Body Weight (kg) (Mean ± SD)	Height (cm) (Mean ± SD)	ASA status
BC	48.9±4.99	52.5±4.93	153.7±4.04	ASA-I 21 ASA-II 16
RC	48.9±6.75	54.2±5.42	155.1±4.03	ASA-I 20 ASA-II17
p value	1.000	0.169	0.146	1.000

Comparison of Mean Arterial Pressure

Table 2: MAP (Mean Arterial Pressure) of both the Groups

Groups	MAP Baseline (Mean±SD)	MAP-1 (Mean±SD)	MAP-2 (Mean±SD)	MAP-3 (Mean±SD)	MAP-4 (Mean±SD)	MAP (Mean±SD)	MAP-6 (Mean±SD)
BC	88.3	88.1	85.8	83.7	82.6	83.4	84.2
RC	87.9	86.5	83.9	81.9	82.1	83.3	84.3
p value	0.738	0.338	0.233	0.267	0.752	0.968	0.969

Comparison of Heart rate

Table 3: Heart Rate of both the Groups

Groups	HR Baseline (Mean±S.D)	HR-1 (Mean±S.D)	HR-2 (Mean±S.D)	HR-3 (Mean±S.D)	HR-4 (Mean±S.D)	HR-5 (Mean±S.D)	HR-6 (Mean±S.D)
Gr BC	85.9	87.9	88.4	87.8	86.6	86.3	85.1
Gr RC	85.4	88.2	88.0	87.2	85.5	84.4	84.4
p value							

Table 4: Time of peak sensory and motor block of both the groups

Groups	Sensory block (Min) (Mean±S.D)	Motor block (Min) (Mean±S.D)
Group BC	5.8±1.79	7.6±2.04
Group RC	7.7±1.9	9.8±2.26
p value	0.00	0.00

Table 5: Two segment regression time of both the groups

Groups	Two segment regression time (Min) (Mean±S.D)	p Value
Gr BC	193.5±30.20	0.001
Gr RC	172.2 ± 24.40	

Table 6

Groups	Group BC	Group RC	P value
% of subjects requiring analgesia	32.43%	29.73%	1.00

DISCUSSION

Spinal anaesthesia with intrathecal hyperbaric bupivacaine for lower abdominal surgery is a widely accepted technique. Moreover the increased blood flow resulting from the sympathetic blockade of regional anesthesia may play a role in reducing deep vein thrombois formation.[16] There is evidence that

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homeostais of neuroednocrine system and the immune response are better preserved after regional anesthesia than after general anesthesia. This technique may also decrease the length of hospital stay and allow more efficient use of our increasingly stretched health care money.[17,18] Spinal anesthesia was not limited to surgical conditions but was also touted for the treatment of medical conditions (e.g. pulmonary edema) by taking advantage of its venodilatory effect.[19] It also provides good quality early-post operative analgesia and overall reduction in post operative morbidity and mortality.[19]

Bupivacaine is appropriate for procedures lasting up to 2 to 2.5 hour.20 But increased dose of bupivacaine produces severe hypotension and other adverse outcome. To overcome these problems associated with increased dose of bupivacaine different adjuvant like clonidine is added to intrathecal bupivacaine to increase the duration of analgesia and decrease the side effects of increased dose of bupivacaine, this is consistent with a study by Dobridnjov I et al who studied combined spinal epidural anesthesia (CSEA) using spinal bupivacaine either singly or in combination with clonidine followed by epidural ropivacaine either singly or in combination with clonidine in hip arthroplasty.They found that low dose intra-thecal clonidine provided a better quality of anesthesia and longer lasting analgesia.[20]

In this study, group BC patients (n=37) received 15mg (3ml) of 0.5% hyperbaric bupivacaine2 alongwith 30 µg (0.2ml) of clonidine through spinal route at L3-L4 level. The group RC patients (n=37) received 22.5mg (3ml) of 0.75% isobaric ropivacaine2 along with same dose of clonidine. After the surgery, continuous epidural infusion of 0.2% ropivacaine at 10ml/hr for 24 hrs was started and was continued for 24 hours postoperatively in both the groups via the epidural catheter inserted at T10-T11 level before insertion of the SAB. Further, Inj.tramadol 100mg IV was used if pain was still not controlled. In literature review, we did not find any study comparing Inj bupivacaine plus clonidine vs Inj ropivacaine plus clonidine via SAB followed by Inj ropivacaine epidural infusion for postoperative analgesia in patients undergoing total abdominal hysterectomy.[21-24]

Peter Hodgson et al compared ropivacaine and fentanyl to bupivacaine and fentanyl for post-operative epidural analgesia on 43 patients of abdominal surgery for 42 post-operative hours. They used bupivacaine at 0.05% and 0.1% concentration and ropivacaine at 0.05% and 0.1% concentration and added 4µg of fentanyl with each of these four groups. This randomised double-blinded study showed that concentration of bupivacaine and ropivacaine in the range of 0.05% to 0.1% respectively are optimal for epidural analgesia when combined with fentanyl. Such a combination improves dynamic analgesia while minimising motor block and other side effects of local anesthetics.[25] In our study 0.5% bupivacaine and 0.5% ropivacaine were used with clonidine to compare same concentration of the local anaesthetics.

When clonidine was added to intrathecal local anaesthetic, the regression of sensory and motor block is delayed and post-operative analgesia is prolonged in a dose dependent manner.[21] However increased dose of clonidine may lead to significant fall in mean arterial pressure.

In this study both spinal and epidural anesthesia were used, popularly known as CSEA viz. Combined Spinal Epidural Anesthesia, in double inter-vertebral spaces whereupon the profit of both the techniques at a time were availed. Rapid onset sensory plus motor block was achieved with spinal anesthesia while at the same time prolonged post-operative analgesia was provided by the epidural LA infusion having a provision of increasing the duration of block with lower concentration of the local anesthetic epidurally. Epidural anesthesia itself produces the same effects of spinal anesthesia in a slow and gradual manner without much hemodynamic instability frequently seen with spinal anesthesia. The postoperative analgesia was provided by continuous epidural infusion through the epidural catheter with 0.2% ropivacaine at 10ml/hr.

In one such study Roula Mrad et al at Anesthesia and Critical Care Dept, Hotel-Dieu de France Hospital, Achrafieh, Beirut, Lebanon compared CSEA followed by a post-operative patient-controlled epidural analgesia (PCEA) (n=15) to general anesthesia (GA) followed by intra-venous patient-controlled analgesia(PCA) (n=16) in abdominal hysterectomy and found that CSEA+PCEA produce better post-operative analgesia than GA+PCA in abdominal hysterectomy. It is also associated with rapid recovery and less PONV.[22]

In another study Nikhil Swarnkar et al compared sequential CSE with Epidural block for total abdominal hysterectomy with 50 patients in each group. The first group received 0.5% hyperbaric bupivacaine spinally followed after 15 minutes by 0.5% plain bupivacaine epidurally by needle through needle single interspace technique. The second group received 15 ml of 0.5% plain bupivacaine through epidural catheter. The quality of block in terms of degree of analgesia and muscle relaxation was superior with sequential CSE block. The need for supplementary analgesic and sedative were significantly higher in epidural group, thus substantiating the superiority of CSEA over epidural anesthesia alone.[23] Mihic DN and Abram SE found that pain in abdominal hysterectomy can be controlled by regional anesthesia alone and they compared several methods of regional anesthesia for this.They found that sub-arachnoid bupivacaine plus epidural morphine and bupivacaine provided by far the best anesthesia and analgesia. This also shows the forte of CSEA in lower abdominal surgeries like TAHBSO.[24]

In this study, pain score on a visual analogue scale was assessed by the patients at 1,3,6,12 &.24 hours after operation. Dose of rescue analgesic were recorded. Levels of sensory block to pin-prick bilaterally and motor block using four point modified

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bromage scale were recorded at the same intervals. Besides, appearance of adverse, untoward reactions viz. Nausea, vomiting, hypotension and PDPH were also recorded. The main objectives of this study were pain management in terms of pain free period, timings of appearance of pain, need for any rescue analgesic, VAS score at certain periods after operation. The last one is our main parameter. We also studied sensory and motor block, their peak level, time to reach that level, two segment regression time etc. The two groups viz. BC and RC groups were comparable as far as their age distribution, weight, height and ASA status were concerned, as is depicted in Figure 1. Mean age for both the groups were 48.9 yrs, mean weight for BC group was 52.5 kg while that for RC group was 54.2 kg. Twenty one patients of BC group (56.76%) belonged to ASA-I while this percentage is 54.05 (20 patients) for the RC group. The rest of both the groups belonged to ASA-II. The difference is not statistically significant (p=1.000).

Mean Arterial Pressure (MAP) of both the groups per-operatively were not significantly different as is shown in table. The p value ranged from 0.233 to 0.969. This signifies that neither bupivacaine nor ropivacainen is significantly hypotensive with respect to each others. Figure 4 depicts baseline and per-operative mean heart rates of both the groups over time. p value ranges from 0.163 to 0.880, ie. Hear rates of both the groups were comparable and the drugs viz. bupivacaine and ropivacaine have no significantly different actions, either direct or indirect, on the heart. Figure 5 shows difference in reaching the highest sensory and motor level for both the groups. For the BC group this level ranges from T4 downwards to T8 level and for the RC group, from T4 to T9 level. The mean time to reach highest level for the BC group was 5.8 minute and that for the RC group 7.7 minute. As the p value is 0.000, this shows that speed of onset of sensory block for bupivacaine is significantly faster than ropivacaine. The mean of two segment regression time for the BC group was193.5 minutes while that of RC group was 172.2 minutes. The p value (0.001) is statistically significant which implies that recovery from sensory block is significantly faster for ropivacaine, an effect desired for both the surgeons and anesthesiologists. This is in keeping with a similar study by Mcnamee DA et al at the Queen's university of Belfast, UK, who compared between spinal bupivacaine and ropivacaine in case of total hip arthroplasty on 66 patients and found that a more rapid post-operative recovery of sensory and motor function was seen in group ropivacaine compared with group bupivacaine.[22] Mean time to reach highest motor block was 7.6 minute for the BC group while 9.8 minute for the RC group. p=0.000, which signifies bupivacaine produces satisfactory motor block within a significantly shorter duration.

shows the post-operative VAS scores at rest of both the groups at the stipulated time intervals. This is expressed as Rank Sum, a parameter of Mann-Whitney U-test. On no occasion there is significant difference between the groups implyning no one is superior to the orher in respect of pain control. In one similar study H.Jorgensen et al compared effect of continuous epidural 0.2% ropivacaine vs. 0.2%bupivacaine on post-operative pain, motor block etc. after abdominal hysterectomy and found that there were no significant difference between ropivacaine and bupivacaine with respect to pain score.25 However VAS score with movement or on coughing shows significant difference, that too at the end of 3, 6 and 12 post-operative hours only whereupon Rank Sum of the RC group shows statistically significant lower values signifying better analgesic efficacy of ropivacaine.

While comparing rescue analgesic for the groups we resort to the pie-charts shows that 32.43% subjects of the BC group and 29.73% subjects of the RC group needed one or more doses of Inj. tramadol as rescue analgesic. Although total dose needed were higher for the BC group, this was statistically insignificant with p=0.712.

CONCLUSION

From the above discussion it is concluded that bupivacaine (with clonidine added) produces a significantly quicker onset of both sensory and motor block when compared with ropivacaine (with clonidine added). Although their analgesic profile are similar when patient makes no movement post-operatively, pain control is significantly better when patient makes movement post-operatively, at least for a duration of 3 to 12 post-operative hours. Besides, reversal of sensory block occurs significantly earlier for ropivacaine (with clonidine added). However,this reversal dose not cause any increased pain perception.

REFERENCES

1. World Health Organisation. World Pain Day [Media Centre Release]. Geneva:The Institute;2004[Updated 2004 Oct 11] Available from: www.who.int
2. Brown DL, Spina , epidural, and caudal anesthesia. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL. Miller's anesthesia: anesthesia management. 7th ed. Vol 2. Philadelphia: Churchil Livingstone Elsevier; 2010. p 1619-1632
3. Jorgensen H, Fomsgaard JS, Dirks J, Wetterslev J, Dahl JB. Effect of continuous epidural0.2% ropivacaine vs 0.2% bupivacaine on postoperative pain, motor block and gastrointestinal function after abdominal hysterectomy. Br J Anaesth. 2000 Aug 24; 84(2): 144-50. bja.oxfordjournals.org
4. Morgan GE Jr, Mikhail MS, Murray MJ, Larson CP Jr. editors. Clinical Anaesthesiology 4th ed. New York: Lange;2002.
5. Visser L. Epidural Anaesthesia. Update in Anaesthesia. 2001; Issue 13: 01. Available from http://www.nda.ox.ac.uk
6. http://www.mayfieldclinic.com
7. Silviu Brill, MD and Muguel Plaza, MD, Non-narcotic adjuvants may improve the duration and quality of analgesia after arthroscopy : a brief review. Candadian Journal of Anesthesia, 2004, 51 : 975-978
8. Reuben SS, Connelly NR. Postoperative analgesia for outpatient arthroscopic knee surgery with intraarticular clonidine. Anesth Analg 1999; 88 : 729-33.
9. Greene JA: Physiology of Spinal Anesthesia, 4th ed. Williams & Wilkins, 1993.

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10. Zhang X, Aman K, Hokfelt T : Secretory pathways of neuropeptides in rat lumbar dorsal root ganglion neurons and effects of peripheral axotomy.The Journal of comparative Neurology 1995;352:481-500.
11. Mervyn Maze, William Tranquilli . Alpha-2 Adrenoreceptor Agonist :defining the role in clinical anaesthesia . Anaesthesiology. 1991;74:581-605.
12. KD Tripathi. Essentials of Medical Pharmacology: Antihypertensive drugs.; 6th edition ; p-546.
13. I RA S. Segal, David J. JARVIS, Steven .R Duncan et al. Clinical efficacy of oral - Tran dermal clonidine combinations during the perioperative period. Anesthesiology .1999;74:220-225
14. Brain B. Hoffman. Catecholamine ,sympathetic drug and adrenergic receptor antagonist. Goodman & Gilman's ;The Pharmacological Basis of therapeutics:11th edition; 2001 :216-234.
15. Collin Dollery . Clonidine . Therapeutic drug;1999: C294-99
16. Aberg G. Toxicological and local anesthetic effects of optically active isomers of two local anesthetic compounds. Acta Pharmacol Toxicol Scand1972;31:273-86.
17. Hansen TG. Ropivacaine: A pharmacological review. Expert Rev Neurother 2004;4:781-91.
18. Kindler CH, Paul M, Zou H, Liu C, Winegar BD, Gray AT, et al. Amide local anaesthetics potently inhibit the human tandem pore domain background K+ channel TASK-2 (KCNK5). J Pharmacol Exp Ther 2003;306:84-92.
19. Selander D, Sjovall J, Waldenlind L . Accidental i.v injections of ropivacaine: Clinical experience of six cases [abstract]. Reg Anaesth 1997;22:70.
20. Dobridnjov I, Axelsson K, Gupta A, Lundin A, Holmstrom B, Granath B. Improved analgesia with clonidine when added tolocal anesthetic during combined spinal-epidural anesthesia for hip arthroplasty: a double-blind, randomized and placebo-controlled study. Acta Anaesthesiol Scand. 2005 Apr; 49(4): 538-45. PubMed. http://www.ncbi.nlm.nih.gov
21. Mrad R, Naccache N, Narchi P, Antakly MC. Effect of combined spinal-epidural anesthesia followed by patient controlled epidural analgesia in abdominal hysterectomy. American society of anesthesiologists annual meeting abstracts. 2010 Oct 16-20; ASA abstracts. http://www.asa-abstracts.com
22. Mcnamee DA, Mccleland AM, Scott S, Milligan KR, Westman L, Gustafsson U.Comparison between spinal bupivacaine and ropivacaine on total hip arthroplasty outcome. Br J Anaesth. 2003 Jul; 91(1): 155-6; Author reply 156-7. bja.oxfordjournals.org
23. Swarnkar N, Ghosh A, Yadav A. Sequential combined spinal epidural block superior to epidural block for total abdominal hysterectomy in patient and surgeons perspective. Internet Journal of Anesthesi.2009 Feb 13;18(2). www.ispub.com
24. Mihic DN, Abram SE. Optimaional regional anaesthesia for abdominal hysterectomy: combined subarachnoid and epidural block compared with other regional techniques. Eur J Anaesthesiol. 1993 Jul; 10(4): 297-301. PubMed. http://www.ncbi.nlm.nih.gov
25. Hodgson PS, Spencer S, Liu. Comparison between epidural bupivacaine and ropivacaine, both added to fentanyl for postoperative analgesia in abdominal surgeries.Anesthesia and Analgesia, 2001 Apr; 92(4). 1024-1028.

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