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ORIGINAL RESEARCH

Preemptive Local Infiltration of 0.5% Levobupivacaine HCl *vs* 0.5% Ropivacaine HCl for Postoperative Pain Control in Lumbar Laminectomy Patients

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ABSTRACT

Introduction: Achieving effective postoperative analgesia in postlaminectomy patients is a cumbersome task for the anesthesiologist. The need is to provide effective analgesia with minimal systemic side effects, cost-effectively, as laminectomy surgeries are associated with paramount postoperative pain. The purpose of this study was to compare the effectiveness of preemptive local infiltration of 0.5% levobupivacaine HCl *vs* 0.5% ropivacaine HCl for postoperative pain control in lumbar laminectomy patients.

Materials and methods: A total of 96 patients who were scheduled to undergo elective lumbar laminectomy were included in the study. Patients were randomly allocated to three groups. In groups I, II, and III, incisional site was infiltrated with 20 mL of 0.5% levobupivacaine HCl, 20 mL of 0.5% ropivacaine HCl, and 20 mL of 0.9% normal saline respectively. Demographic data, vital parameters, postoperative visual analog scale (VAS) scores, and total tramadol consumption were recorded.

Results: Time to first rescue analgesia was earliest in group III (8.72 ± 6.19 minutes), followed by group II (155 ± 39.53 minutes) and group I (208 ± 27.02 minutes) ($p < 0.05$). Group I has least total consumption of tramadol (253.1 ± 50.78 mg) at the end of 24 hours postoperatively when compared with group II (312.50 ± 33.60 mg) and group III (396.8 ± 40 mg) ($p < 0.05$). The overall VAS score in 24 hours was significantly lower in group I as compared with groups II and III. No significant adverse effects of local wound infiltration were observed.

Conclusion: This study suggests that preemptive infiltration of the incision site with levobupivacaine provides significantly better postoperative analgesia with minimal side effects.

Keywords: Central sensitization inhibition, Local infiltration, Lumbar laminectomy, Postoperative analgesia, Preemptive analgesia, Preincisional, Tramadol.

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INTRODUCTION

Wound infiltration by local anesthetic (LA) has become increasingly common for postoperative pain owing to its simplicity, safety, effectiveness, and ability to reduce the need for additional analgesics and their respective side effects, thus decreasing hospital stay and cost.[1]

With recent lifestyle adaptation, lumbar disk surgeries are on the rise. Postoperative pain after laminectomies is the worst subjective experience to tolerate, as it is associated with considerable pain,[2] when the effect of analgesics given intraoperatively has weaned off. Thus, management of postoperative pain plays an important role in neurological recovery.[2,3] After laminectomy, a poorly managed pain may inhibit the early ability to mobilize the patient. Good pain relief is important for patients undergoing laminectomy, and it may considerably influence the overall outcome.[4]

Moreover, inadequate management of postoperative pain leads to several pathophysiological changes in pulmonary and cardiovascular system. In fact, pain can cause an increase in metabolic catabolism and may impair normal muscle functioning.[5]

A number of studies have reported the use of preemptive LA to relieve postoperative pain from several surgical procedures because of its beneficial effect.[1] Infiltration with LA acts directly on the pain-producing mechanism and is effective in postoperative pain relief after lumbar laminectomies.[6] Various LAs have been utilized for postoperative analgesia via infiltration. Here we compare the effectiveness of levobupivacaine and ropivacaine for postoperative pain relief as preemptive analgesic.

Ropivacaine is also a long-acting amide-type LA that causes reversible blockade of impulsive propagation along nerve fibers. It has an intrinsic vasoconstrictor property that delays absorption outside the infiltration, which is responsible for the better cardiovascular and central system side-effects profile of ropivacaine. At higher concentration, it produces surgical anesthesia, whereas in lower concentration it produces analgesia.[7]

Levobupivacaine (S-enantiomer of bupivacaine) is a member of the hydrochloride amino acid class of LA. It reversibly blocks the transmission of action potential in sensory, motor, and sympathetic nervous fibers by inhibiting the passage of sodium through voltage-sensitive ion channel in the neuronal membrane.

Levobupivacaine has been shown to be equally effective as bupivacaine at comparable doses and concentrations and has been found to produce similar anesthetic characteristics.[8] Levobupivacaine has a lower risk of cardiovascular and central nervous system (CNS) toxicity than bupivacaine. Levobupivacaine has a less negative inotropic effect and produces less prolongation of corrected QT interval (QTc); also the electroencephalogram shows less CNS depression.[9]

In this study, we designed a prospective, double-blind, randomized control study to compare the analgesic efficacy of levobupivacaine and ropivacaine when administered via preoperative local infiltration as preemptive analgesia technique, in reducing the postoperative pain in lumber laminectomy patients.

MATERIALS AND METHODS

After approval by the institutional ethics committee, a prospective, randomized, double-blind study was conducted on 96 patients scheduled for lumbar laminectomy aged 18 to 60 years of either gender, and American Association of Anesthesiologists (ASA) I and II were included in the study. Patients with known allergy to LAs, cardiovascular, hepatic, renal, and bleeding diathesis, and pregnancy, on systemic steroids or anticoagulants, and with history of drug abuse were excluded from the study.

Well-informed written consent was obtained from all the patients. Subjects were blinded by sealed envelope technique and the observer anesthesiologist was kept unaware of which drug was being infiltrated to which patient, thus avoiding observer's bias. The anesthesiologist who performed the general anesthesia (GA) took no further part in the study.

All the patients were randomly allocated into one of the three groups according to the different drugs infiltrated. Group I (n = 32) received local infiltration at the incision site of 20 mL of 0.5% levobupivacaine HCl preemptively before skin incision. Group II (n = 32) received local infiltration at the incision site of 20 mL of 0.5% ropivacaine HCl preemptively before skin incision. Similarly, group III (n = 32) incisional site was infiltrated with 20 mL of 0.9% normal saline.

Patients were premedicated with inj. glycopyrrolate 0.2 mg intramuscularly 30 minutes preoperatively.

In the operation room, each patient was monitored for continuous noninvasive blood pressure, pulse oximetry (Spo2), and electrocardiography. In the operation room, injection midazolam 0.03 mg/kg intravenously was given 3 minutes before induction. A standard anesthetic protocol was used to induce GA (2–2.5 mg/kg propofol, 1–1.5 mg/kg fentanyl, 1.5 mg/kg succinyl choline). The anesthesia was maintained with 1% isoflurane with oxygen and nitrous (40:60). And sufficient muscle relaxation was achieved throughout the operation with intermittent doses of inj. atracurium.

Perioperative data, i.e., demographic characteristics (age, gender, weight, ASA), and duration of operation were recorded. The following vital parameter data were recorded: Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and pulse rate (PR) at induction, 5, 10, 30, 60, and 120 minute intervals intraoperatively.

After extubation, the postoperative vital parameter data were recorded at 0, 1, 4, 16, 20, and 24 hours after the operation. Additionally, an 11-point visual analog scale (VAS) was used to assess pain intensity at 2, 4, 12, and 24 hours and overall VAS score at 24 hours postoperatively. A VAS score of 0 indicates no pain, whereas a score of 10 indicates most severe pain imaginable.

The time of first rescue analgesic, i.e., analgesic given when first postoperatively patient complains of pain, was recorded. A rescue analgesic, inj. tramadol 3 mg/kg, was given intravenously to the patients (VAS score > 5).

Total dose of analgesic consumption postoperatively in 24 hours was observed. Adverse effects, such as postoperative nausea vomiting (PONV), hypotension/hypertension, bradycardia, headache, dizziness, constipation, and cardiovascular instability, were recorded.

Hypotension and hypertension are defined as fall or rise in SBP > 20% from the baseline value respectively. Similarly bradycardia and tachycardia are defined as fall or rise in PR > 20% from the baseline value.

Statistical Analysis

Assuming that the pain scored would be compared using VAS with two-sided 10% level of statistical significance and 90% power, at least 96 patients were need to be included in the study. The observation recorded in all the groups was tabulated using Student's t-test and paired t-test (demographic data, and comparison of total tramadol requirement, time to first analgesic administration, and VAS among the group respectively). Statistical analysis was carried out using Statistical Package for the Social Sciences software (version 17). $p < 0.05$ was considered statistically significant.

Power analysis was performed, which estimated that there was a probability of 0.85 in standard deviation.

DISCUSSION

This study demonstrated that the preemptive local infiltration of 0.5% levobupivacaine HCl over the incision site in lumbar laminectomy patients effectively reduces postoperative pain, decreases VAS, and delays time for rescue analgesics and total analgesic consumption as compared with 0.5% ropivacaine and control group. Efficacious postoperative analgesia is necessary to speed up postoperative recovery and reduce morbidity and hospital stay.

Since lumbar laminectomies are the most common surgeries performed by superspecialty neurosurgeon and are on the rising trend recently in accordance with the sedentary lifestyle, there is a prevailing upsurge in the incidence of lumbar disk ailments. Many patients with lumbar surgeries experience severe postoperative pain. Pain intensity usually peaks during the first hour and over the following 24 hours postoperatively. Most often, opioids or nonsteroidal anti-inflammatory drugs are used, leading to adverse effects related to their use, such as respiratory depression, pruritus, sedation, and bleeding diathesis.[10]

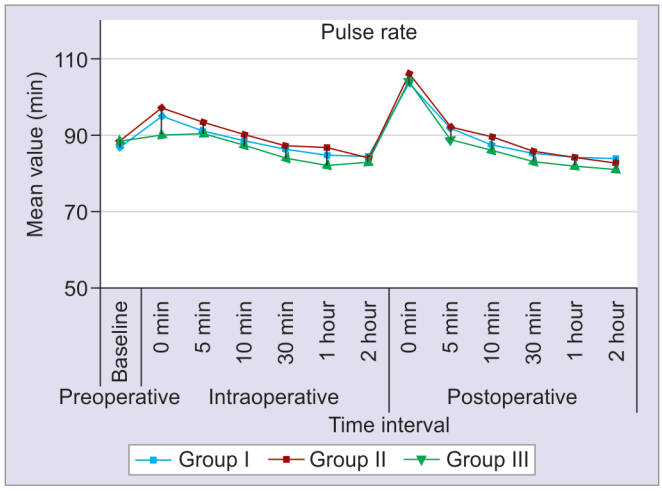
The role of LA infiltration as "preemptive analgesia" (refers to previously administered medication that modulates the arousal of nociception action in postoperative period) in reducing postoperative pain by preventing the central sensitization to painful stimuli by decreasing response from pain sensation has been emphasized by Karaaslan et al.[11]

The reduction in postoperative pain using infiltration with LA over wound edges was reported by Capelle.[12] And the interest in the use of this technique has been recently revived.[13] The main advantages of this technique are its simplicity, safety, and cost-effectiveness.[5]

The preoperative infiltration of LA provides a greater reduction in postoperative pain than peri or postoperative infiltration, the mechanism being that the local infiltration and the resulting nerve impulse block prevent the nociceptive impulses from reaching the CNS and suppress the sustained state of hyperexcitability responsible for intense postoperative pain.[14,15]

Levobupivacaine is an LA with long duration of action. Various doses of levobupivacaine have been studied for infiltration anesthesia. The dose of 150 mg (1.35 mg/kg) levobupivacaine recommended for incisional analgesia is well below the toxic dose (277 ± 51 mg).[5,16] To avoid local and systemic toxicity we used 100 mg of levobupivacaine for preemptive tissue infiltration.

In the present study, pain was evaluated by VAS. As pain is a subjective experience and objective judgment seems to be difficult, VAS score assessed by the patients might be subjected to variability depending upon literacy and socioeconomic status of the patients.



Graph 1: Comparison of mean pulse rate among three groups

Statistical comparison of VAS score among the three groups demonstrated statistically significant lower score in groups I and II as compared with group III in overall 24 hours postoperatively as shown in Graph 1. The findings of our study correlate well with the literature of Papagiamnopaulou et al[17] who observed that levobupivacaine group experienced significantly less pain than placebo and ropivacaine group postoperatively.

Other studies supporting our findings with significantly greater VAS score in the placebo than the levobupivacaine and bupivacaine groups are Callesen et al,[18] Dreher et al,[19] Vinson-Bonnet et al,[20] Kim et al,[21] and Gurbet et al.[22] Contradictory to our study was the study of Bay-Nielson et al,[23] who observed that there was a significant difference in VAS score at any time interval between 0.25% levobupivacaine and 0.25% bupivacaine. Milligen et al[24] and Cherian et al[25] also concluded in their studies that bupivacaine is beneficial and has a better VAS score.

Rescue analgesic consumption is also one of the most important parameters to evaluate the influence of preemptive analgesia. Best results were seen with levobupivacaine infiltration as compared with ropivacaine and saline groups. The study by Papagiamnopaulou et al[17] showed that consumption of rescue analgesic was significantly lower in the levobupivacaine group than in the ropivacaine group ($p < 0.01$) and placebo group ($p < 0.001$).[17] On comparing the three groups in our study, we observed results in accordance with the provided literature. The total consumption in group I was 253.1 ± 50.70 mg, group II 312.50 ± 33.60 mg, and group III 396.8 ± 40 mg as shown in Table 1.

Thus, preemptive surgical wound infiltration with LA is effective to control acute postoperative pain in different procedures as it decreases pain as well as analgesic consumption.[26-28]

Time to first rescue analgesia was also observed in our present study to evaluate postoperative pain and

Table 1: Postoperative data

	Group I (n = 32)	*Group II (n = 32)*	*Group III (n = 32)*
Time for first rescue analgesia (min)	208.8 ± 27.02	155 ± 39.53	8.72 ± 6.19
Total analgesic consumption at 24 hours (mg)	253.1 ± 50.78	312.50 ± 33.60	396.8 ± 40

Data are given as mean ± SD; $p < 0.05$ is significant

Table 2: Demographic characteristics

Parameters	*Group I (n = 32)*	*Group II (n = 32)*	*Group III (n = 2)*
Age (years)	41.563 ± 11.6	40.44 ± 11.74	39.44 ± 12.37
Sex (male/female)	20/12	22/10	9/23
Weight (kg)	58.3 ± 6.37	60.28 ± 6.69	57.72 ± 7.13
ASA (I/II)	14/18	6/26	12/20
Duration of surgery (min)	115 ± 15.8	115 ± 16.28	108.28 ± 13.8

Data are given as mean ± SD

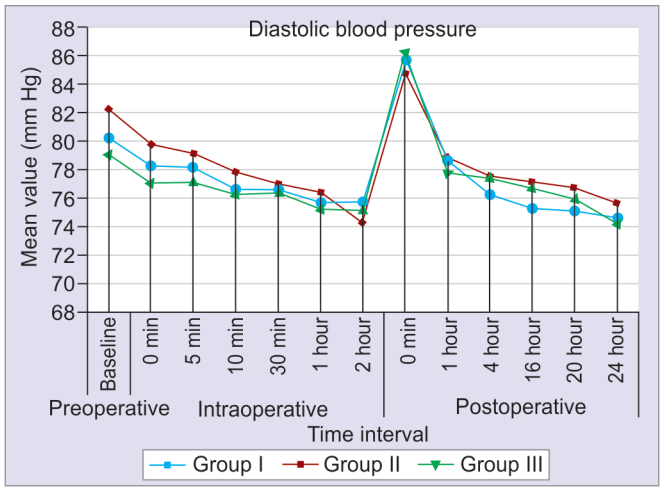
the data were appreciative for receiving levobupivacaine infiltration as compared with bupivacaine and saline groups as shown in Table 1. Various literatures support our studies.[5,14,16] Only nausea and vomiting were present in all three groups, with more in groups I and II as compared with group III. Moreover, side effects like hypotension, bradycardia, dyspnea, chest pain, and dysarrythmia were not present in either group. Absence of these adverse effects could be well explained assuming a lower autonomic system response to surgery in groups I and II because of better pain control. Absence of these in group III may be due to release of placebo-induced endorphins. None of our patients displayed symptoms of toxicity due to LA.[29]

RESULTS

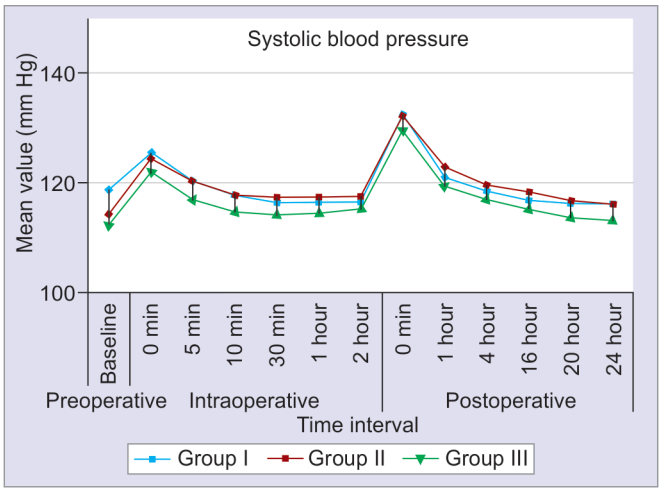
A total of 96 patients were enrolled in the present study. There was no significant difference when groups were compared based on demographic data with respect to mean age, sex distribution, mean weight, proportion of ASA classification, and mean duration of operation time, as shown in Table 2.

There were also no significant differences among the groups with respect to PR, SBP, DBP, and MAP during induction, during operation, and in the first 24 hours postoperatively, as shown in Graphs 1 to 4 ($p < 0.05$).

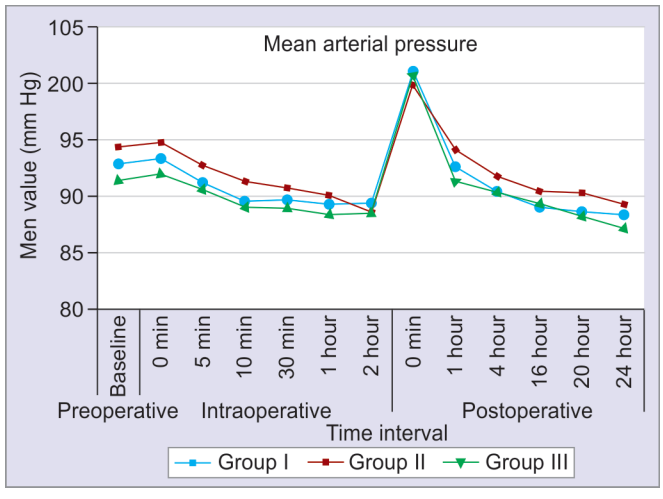
The results of the postoperative data are represented in Table 1. Time to first request of rescue analgesia was longest in group I (208 ± 27.02 minutes) as compared with group II (155 ± 39.53 minutes) and group III (8.72 ± 6.19 minutes). Groups I and II had significantly longer mean time than group III ($p < 0.05$). On comparison, the total analgesic consumption at 24 hours postoperatively among the three groups was found to be statistically significant, i.e., total tramadol consumption was lowest in group I (253.1 ± 50.78 mg), than groups II (312.50 ± 33.60 mg) and III (396.8 ± 40 mg). The overall



Graph 2: Comparison of diastolic blood pressure among the groups



Graph 3: Comparison of systolic blood pressure among the groups



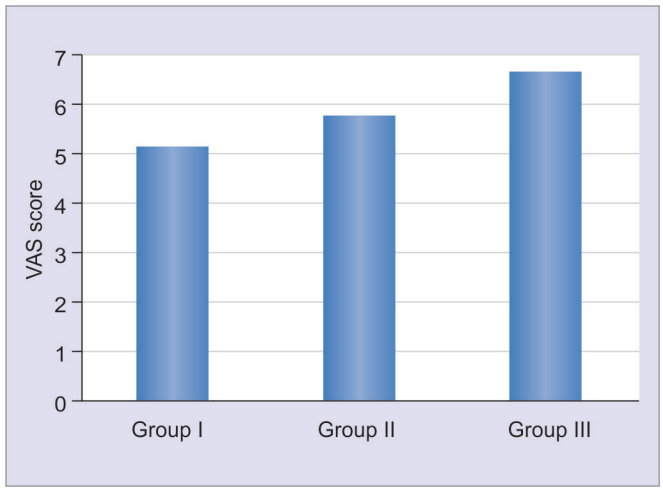
Graph 4: Comparison of mean arterial pressure among the groups

Table 3: Postoperative adverse effects among the three groups

	Group I (n = 32) (%)	*Group II (n = 32) (%)*	*Group III (n = 32) (%)*
PONV	5 (15.62%)	2 (6.25%)	3 (9.35%)
Hypotension	0	0	0
Bradycardia	0	0	0
Dyspnea	0	0	0
LA toxicity	0	0	0

VAS score over 24 hours was statistically lower in group I as compared with groups II and III as shown in Graph 5.

The adverse effect observed in this study was mainly PONV. Within 24 hours, 5% of patients in group I, 2% in group II, and 3% in group III experienced PONV as shown in Table 3. Neither were there any side effects related to LA drug toxicity nor any incidences of hypotension, bradycardia, dyspnea, chest pain, and dysarrythmia observed. Overall analysis showed that adverse effects were not statistically significant among all the three groups.



Graph 5: Overall visual analog scale score (VAS) over 24 hour postoperatively

CONCLUSION

Preemptive administration of levobupivacaine at the incision site in patients undergoing lumbar laminectomy provides effective analgesia.

Wound infiltration with levobupivacaine was effective in controlling pain, with better results when done before surgical incision. It has significantly decreased pan intensity and tramadol consumption and has delayed rescue analgesic request, promoting a more comfortable postoperative period.

When potential complications related to different modes of postoperative pain management and potential side effects related to drugs were taken into consideration, wound infiltration remains the safest, comfortable, and efficacious method to provide analgesia.

REFERENCES

1. Johansson B, Glise H, Hallerback B, Dalmn P, Kristoffersson A. Preoperative local infiltration with ropivacaine for postoperative pain relief after cholecystectomy. Anesth Analg 1994 Feb;78(2):210-214.
2. Garcia RM, Cassinelli EH, Messerschmitt PJ, Furey CG, Bohlman HH. A multimodal approach for postoperative pain management after lumbar decompression surgery: a prospective randomized study. J Spinal Disord Tech 2013 Aug;26(6):291-297.
3. Glasser RS, Knego RS, Delashaw JB, Fessler RG. The perioperative use of corticosteroids and bupivacaine in the management of lumbar disc disease. J Neurosurg 1993 Mar;78(3):383-387.
4. Guilfoyle MR, Mannion RJ, Mitchell P, Thomson S. Epidural fentanyl for postoperative analgesia after lumbar canal decompression. A randomized control trial. Spine J 2012 Aug;12(8):646-651.
5. Gurbet A, Bekar A, Bilgin H, Korfali G, Yilmazlar S, Tercan M. Preemptive infiltration of levobupivacaine is superior to at-closure administration in lumbar laminectomy patients. Eur Spine J 2008 Sep;17(9):1237-1241.
6. Hernández-Palazón J , Tortosa Serrano JA, Burguillos López S, Molero Molero E. Infiltration of surgical wound with local anesthetic for postoperative analgesia in patients operated on for lumbar disc herniation. Comparative study of ropivacaine and bupivacaine. Rev Esp Anestesiol Reanim 2001 Jan;48(1):17-20.
7. Bamigboye AA, Justus HG. Ropivacaine abdominal wound infiltration and peritoneal spraying at cesarean delivery for preemptive analgesia. Int J Gynaecol Obstet 2008 Aug;102(2): 160-164.
8. Glaser C, Marhofer P, Zimpfer G, Heinz MT, Sitzwohl C, Kapral S, Schindler I. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. Anesth Analg 2002 Jan;94(1):194-198.
9. Foster RH, Markham A. Levobupivacaine. A review of its pharmacology and use as a local anesthetic. Drugs 2000 Mar;59(3):551-579.
10. Yorukoglu D, Ates Y, Temiz H, Keciky Y, Yamali H. Comparison of low dose intrathecal and epidural morphine and bupivacaine infiltration for postoperative pain control after surgery of lumbar disc disease. J Neurosurg Anesthesiol 2005 Jul;17(3):129-133.
11. Karaaslan D, Sivali RG, Akbulut G, Dilek ON. Preemptive analgesia in laparoscopic cholecystectomy. A randomized control study. Pain Pract 2006 Dec;6(4):237-241.
12. Capelle W. The importance of wound pain and its elimination forth flow of respiration in Laparotomierten. German Ztschr F Chir 1936;246:466-485.
13. Lewis DL, Thombson WAL. Reduction of postoperative pain. Br Med J 1953 May;1(4817):973-974.
14. Johansson B, Hallerback B, StubberodA, Janbu T, Edwin B, Glise H, Solhaug JH. Preoperative local infiltration with ropivacaine for postoperative pain relief after inguinal hernia repair. A randomized control trial. Eur J Surg 1997 May;163(5):371-378.
15. Woolf CJ. Recent advances in the pathophysiology of acute pain. Br J Anesth 1989 Aug;63(2):139-146.
16. Mcleod GA, Burke D. Levobupivacaine. Anesthesia 2001 Apr;56(4):331-341.
17. Papagiamnopaulou P, Argiriadou H, Georgiou M, Papaziogas B, Sfyra E, Kanakoudis F. Preincissional local infiltration of levobupivacaine *vs* ropivacaine for pain

control after laparoscopic cholecystectomy. Surg Endosc 2003 Dec;17(12):1961-1964.

18. Callesen T, Hjort D, Mogonsen T, Schouenborg L, Nielsen D, Revetlid H, Kehlet H. Combined field block and for instillation of ropivacaine for pain management after laparoscopic sterilization. Br J Anesth 1992 Nov;82(4):586-590.
19. Dreher JK, Nemeth D, Limb R. Pain relief following day care laparoscopic tubal ligation with intraperitoneal ropivacaine. A randomized double blind control study. Aus NZ J Obstet Gynaecol 2000 Nov;40(4):434-437.
20. Vinson-Bonnet B, Coltat JC, Fingherhut A, Bonnet F. Local infiltration with ropivacaine improve immediate postoperative pain control and haemorrhoidal surgery. Dis Colon Rectum 2002 Jan;45(1):104-108.
21. Kim TH, Kang H, Park JS, Chang IT, Perk SG. Intraperitoneal ropivacaine instillation for postoperative pain relieve after laparoscopic cholecystectomy. J Korean Surg Soc 2010 May;79(2):130-136.
22. Gurbet A, Bekar A, Bilgin H, Ozdemir N, Kuytu T. Preemptive wound infiltration in lumbar laminectomy for postoperative pain. Comparison of bupivacaine and levobupivacaine. Turk Neurosurg 2014 Feb;24(1):48-53.
23. Bay-Nielson M, Klarskov B, Bech K, Andersen J, Kehlet H. Levobupivacaine versus bupivacaine as infiltration anesthesia in inguinal herniorraphy. Br J Anesth 1999 Feb;82(2):280-282.
24. Milligen KR, Macafee AL, Fogarty DJ, Wallace RG, Ramsey P, Wallace RG. Intraoperative bupivacaine diminishes pain after lumbar laminectomy. A randomized double blind study. J Bone Joint Surg Br 1993 Sep;75(5):769-771.
25. Cherian MN, Mathews MP, Chandy MJ. Local wound infiltration with bupivacaine in lumbar laminectomy. Surg Neurol 1997 Feb;47(2):120-122.
26. Moiniche S, Kehlet H, Dahi JB. A qualitative and quantitative systematic review of preemptive analgesia for post operative pain relief. The role of time of analgesia. Anesthesiology 2002 Mar;96(3):725-741.
27. Bianconi M, Ferrarol L, Ricci R, Zanoli G, Antonelli T, Giulia B, Guberti A, Massari L. The pharmacokinetics and efficacy of ropivacaine continuous wound instillation after spine fusion surgery. Anesth Analg 2004 Jan;98(1):166-172.
28. Pavlides TE, Afmatzidis KS, Papaziogas BT, Makris JG, Lazaridis CN, Papaziogas TB. The effect of preincisional periportal infiltration with ropivacaine in pain relief after laparoscopic procedure. A prospective randomized control trial. JSLS 2003 Oct-Dec;7(4):305-310.
29. Pasqualucci A, De Angelis V, Contardo R, Colo F, Terrosu G, Donini A, Bresadola F, Pasetto A, Bresadola F. Preemptive analgesia; intraperitoneal local anesthetic in laparoscopic cholecystectomy. A randomized double blind, placebo-controlled study. Anesthesiology 1996 Jul;85(1):11-20.