Research Article

Comparative evaluation of addition of polygeline to bupivacaine in ilioinguinal-iliohypogastric nerve blocks in patients undergoing hernioraphy—a randomized, double-blind, controlled trial

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Abstract

Background: Postoperative pain care is an essential component of the anesthesia armamentarium. Nerve blocks with local anesthetic drugs do an important role in that care. Many drugs have been added to prolong the duration of action of local anesthetics. We wished to add polygeline to look into the prolongation possibly because of its physical effects. **Aims and Objective:** To evaluate the addition of polygeline to bupivacaine in ilioinguinal and iliohypogastric nerve blocks in patients undergoing hernioraphy. **Materials and Methods:** Sixty patients undergoing hernioraphy under spinal anesthesia were randomly divided into three groups of 20 each. End operatively, they received saline (group C), bupivacaine with saline (group B), or bupivacaine with polygeline (hemaccel) (group BH) as the drug for ilioinguinal and iliohypogastric blocks. Postoperatively, 0–10 pain scores numerical rating scale (NRS), sedation scores, time to first analgesia, and narcotic requirements were noted. The narcotic was in the form of intravenous pentazocine (12 mg). Any side effects including 3-month follow-up for any neurological symptoms were noted. One way ANOVA with SPSS software, version 16.0 was used. **Result:** The age, sex, and the duration of surgery were similar in all the three groups. The NRS and the sedation scores were significantly high in 0 h in group C than the other groups. Later, they were similar and comparable between groups. The narcotic requirement was significantly higher in group C than other groups. In a comparison between groups, the pentazocine requirement was higher in group B than group BH but was not statistically significant. The time to first analgesia was significantly higher in group BH, which was higher than group C. There were no undue side effects in any group. A 3-month follow-up did not report any neurological symptom in patients of any group. **Conclusion:** Addition of polygeline to bupivacaine in nerve blocks provides early postoperative pain relief by possibly prolonging the duration of action of bupivacaine. Even though the narcotic requirements are less with addition of polygeline in the first postoperative 12 h, it is not statistically significant. There were no untoward side effects.

KEY WORDS: Nerve Blocks; Local Anesthetics; Adjuvant; Polygeline

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Introduction

Postoperative pain relief is an essential component of perioperative anesthetic care. Suitable peripheral nerve blocks form the main stay of such a care.[1] Long-acting local anesthetics such as bupivacaine when used in nerve blocks after surgery can effectively abolish pain. A lot of additives have been used, which include adrenaline, alpha-2 agonists,

and opioids.[2] Whichever the additive used, the prolongation is not proved to be more than 50%. Colloids such as dextran have been used to enhance the duration of action of local anesthetics.[3] Polygeline is available as a 3.5% solution in 500 mL plastic bottles (hemaccel), and, in addition to polygeline, the other contents are sodium, potassium, calcium, and chloride ions. We tried to add colloid in order to prolong the duration of local anesthetics possibly more than the available additives to attract clinical attention. Hence, in this study, we combined bupivacaine with polygeline in ilioinguinal-iliohypogastric nerve (ILIH) block in patients undergoing hernioraphy under spinal anesthesia. Any immediate obvious side effect along with a follow-up for 3 months for any nerve dysfunction was noted.

Materials and Methods

In this prospective, randomized, double-blind, controlled trial, successive 60 patients of American Society of Anesthesiology I and II admitted to a peripheral hospital near Puducherry undergoing inguinal hernioraphy with spinal anesthesia within a period of 3 months were included for the study. The inclusion criteria comprised patients undergoing repair of inguinal hernia under spinal anesthesia. Patients who were not willing, mentally disturbed patients, and children were excluded from the study. After approval of the institutional research committee, all these 60 patients were randomized by a sealed envelope technique to be in any of the three groups. Informed consent was taken from all the patients. The sample size was calculated with an expected prolongation of more than 50% with a type 2 error of 20%. With this, a sample size of 42 was arrived at. We increased to 60 to overcome dropouts. Of these 60 samples, group B received 8 mL of 0.25% bupivacaine with normal saline, group BH received 8 mL of 0.25% bupivacaine with hemaccel, and group C received 8 mL of normal saline for ILIH block [Figure 1]. The mixture was prepared by a blinded anesthesiologist. All the 60 patients were entered into the trial. All the 60 patients were subjected to an appropriate preanesthetic checkup overnight. The (0–10) 11-point numerical rating scale (NRS) was explained to all the patients. The safety profile of polygeline in nerves and the safe use of other colloids such as dextran with local anesthetics in previous studies were explained in detail to the patients. On the day of surgery, 1 mg of intravenous midazolam was administered. 500 mL of Ringer's lactate solution was preloaded. A subarachnoid block with 2.8–3 mL of 0.5% hyperbaric bupivacaine was administered to achieve a level of around T8–T10 in all cases. The conduct of anesthesia was according to traditionally accepted guidelines by the concerned anesthesiologist. At the end of surgery, according to randomization, they were administered ILIH block. Group C was administered with 8 mL of normal saline; group B, 4 mL of 0.5% bupivacaine + 4 mL of normal saline; and group BH, 4 mL of 0.5% bupivacaine + 4 mL of 3.5% polygeline (hemaccel). The ILIH block was administered at the end of surgery according to the classical teaching of hitting the bone, withdraw, and administer. Postoperatively, the receding of level to T12 was taken as "0" h. The sedation scores were monitored as follows—1. asleep and comfortable, 2. awake and comfortable, and 3. awake with pain. The sedation scores used above is being routinely used by us for more than a decade with needed precision. The pain and the sedation scores were noted down every 3 h. Pulse and blood pressure were measured every half-an-hour, and any other side effects were monitored by a blinded staff nurse. When the patient complained of pain or when the NRS score was 4 or more, pentazocine (12 mg) intravenous was used. The blinded staff nurse who administered analgesic noted down the time of administration from 0 h. The data were entered in a pro forma and subjected to statistical analysis using SPSS software, version 16 using one way ANOVA with post hoc tests after decoding. The

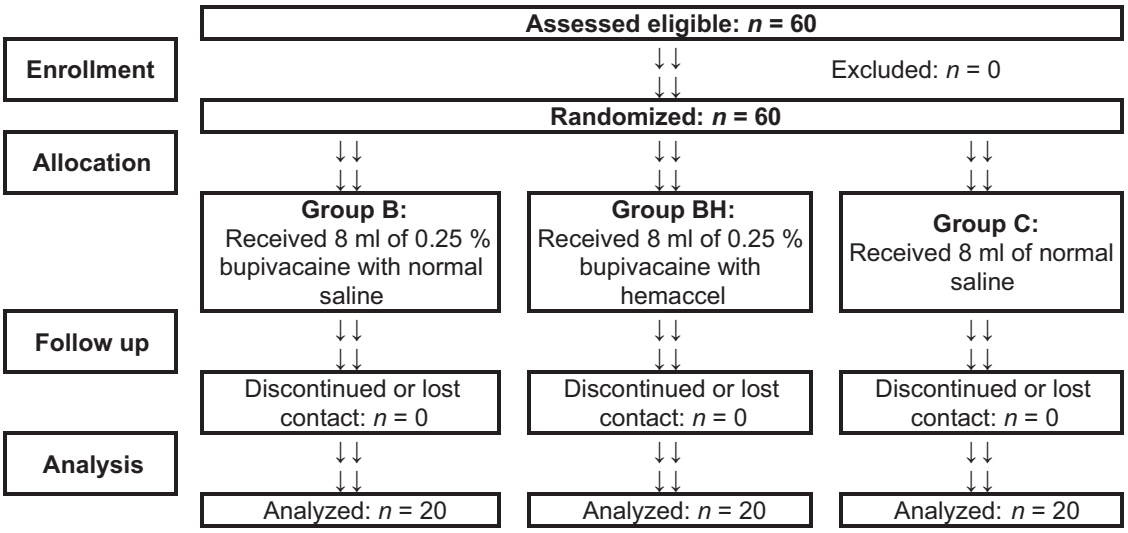

Figure 1: Consort flow diagram.

Table 1: Similar demographic variables

	Age (years), mean ± SD	weight (kg), mean ± SD	Duration (min)
Group C	32.15 ± 11.38	55.85 ± 4.82	42.24 ± 5.63
Group B	38.05 ± 13.65	53.05 ± 4.69	45.35 ± 6.32
Group BH	37.30 ± 13.94	54.25 ± 5.56	48.36 ± 4.59

hemodynamics was noted. All patients were asked to report after 3 months for any evidence of neurological dysfunction. The time to first analgesia (TFA), pain scores, and the requirement of narcotics form the primary outcome measures. Any other side effects including sedation and neurological dysfunction were the secondary outcome measures.

Result

All the patients completed the study, and there were no drop outs. There was no new recruitment either. Patients of all the groups were comparable with regard to age, sex, and duration of surgery [Table 1].

The sedation scores were similar in all the groups except in 0 h when patients of group C were less sedated (p = 0.05). On all the rest of the study period, they were comparable between the groups. The NRS scores were significantly high at 0 h (p = 0.000) but similar and comparable in rest of 3, 6, 9, and 12 h. Pain scores and sedation scores were similar between groups B and BH [Figures 2 and 3].

There was an increased requirement of analgesic to maintain the pain scores in group C (p = 0.000.) Even though the narcotic requirement was less in Group BH than group B, it was not significant [Figure 4, Table 3].

The mean and SD of TFA are shown in Table 2.

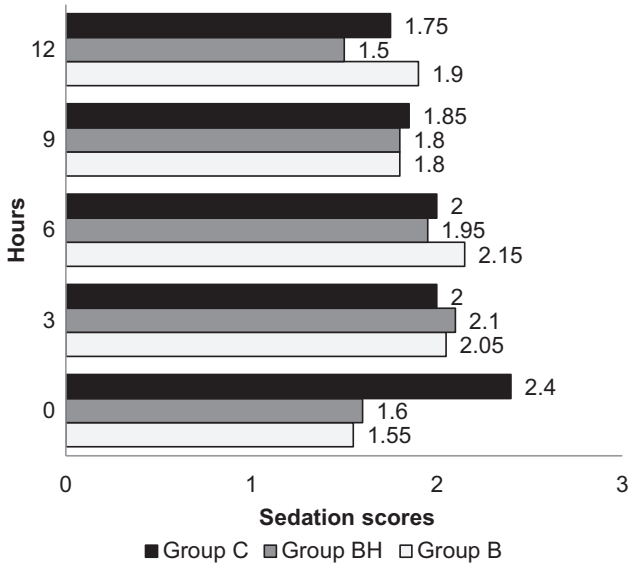

Figure 2: Sedation scores—0, 3, 6, 9, and 12 h for various groups "0" h.

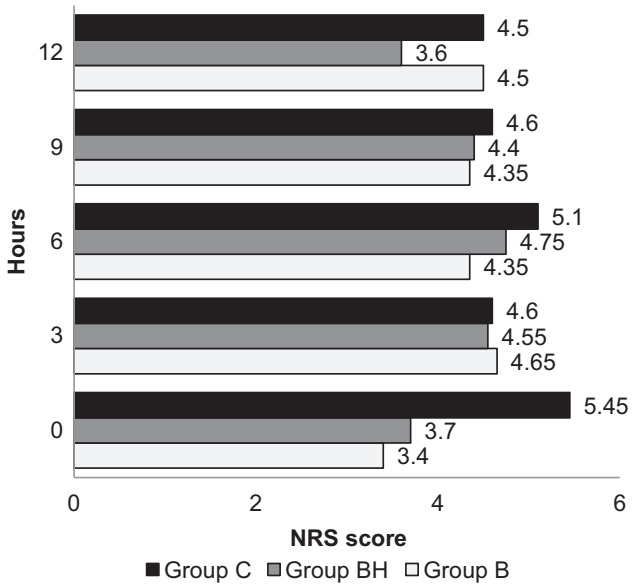

Figure 3: NRS scores—0, 3, 6, 9, and 12 h for various groups "0" h.

TFA was significantly more in group BH than group B. In both the groups that received bupivacaine in either form, the TFA was significantly higher than control group, which did not receive any local anesthetic drug. There were no significant hemodynamic or gastric side effects. The 3-month follow-up of all the cases did not reveal any neurological finding in any of the cases.

Discussion

Adjuvants to local anesthetics to prolong either the duration or to improve the quality of neural blockade had been on the anvil since the invention of regional anesthesia. Three types of drugs

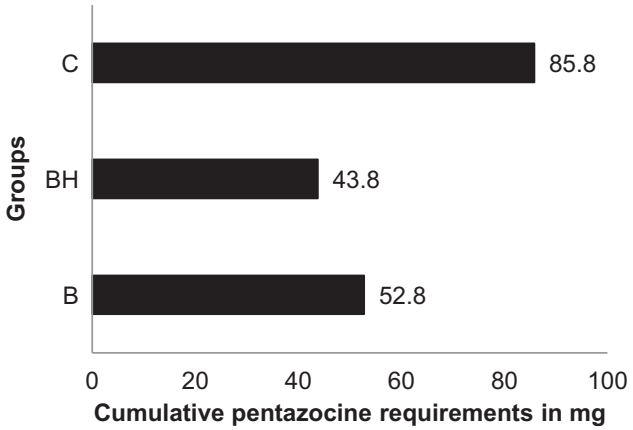

Figure 4: Cumulative pentazocine (fortwin) requirements of various groups in 12 h.

Table 2: The mean and SD of time to first analgesia

TFA	Mean in minutes	SD
Group C	11.75	6.645
Group B	*124.00	77.64
Group BH	**209.75	172.142

*Group B vs. group C—statistical significance.
**Group B vs. group BH—statistical significance.

have been used commonly to effectively do the abovesaid action. The first being adrenaline, which when added in one in two lakh concentration, prolongs the duration by decreasing vascular absorption of the drug and alpha agonistic action. The effect is prolongation of the blockade by as much as 50% and a decrease in the systemic absorption of local anesthetic drugs. These effects may vary significantly among different types of local anesthetics and individual nerve blocks. The addition of adrenaline to lignocaine (a natural vasodilator) may prove more useful than bupivacaine.[4] As lignocaine is slowly giving way for bupivacaine and ropivacaine in nerve blocks, the drug adrenaline as an additive is slowly losing significance. But, addition of polygeline may act at a physical level to cause prolongation, which may not be influenced by the type of local anesthetic. It is established that, in centrineuraxial blocks, addition of opioids may be significantly useful to prolong blockade or improve quality. But, in peripheral nerves, similar receptors are less or the effects of opiates may be less than the effects seen after using it along with local anesthetics in centrineuraxial blocks.[5] For this reason, opiates may not have a significant clinical role in peripheral nerve blockade even though a few studies have shown the effectiveness of opioids in peripheral nerve blockade.[6,7] Alpha-2 agonists and dexamethasone have been added to drugs in neural blockade with useful results.[8,9] Colloids as such are rarely combined with local anesthetics to prolong blockade, of which, dextran has been shown to prolong the duration. The mechanism of action may be difference in pH or the formation of macromolecules. In a study by Simpson et al.,[3] significant prolongation of local analgesia was achieved with high-molecular weight dextran, and this was most consistently obtained when the solution used contained adrenaline.[10] In our study, we did achieve prolongation by 3.5% polygeline, which is a polymer of urea and polypeptides derived from degraded gelatin. The TFA values were significantly higher in our study, which depicted the effectiveness of combining with polygeline. In our cases, we noticed a reduction of narcotic requirement by the addition of polygeline, but it was statistically not significant. There is enough evidence in a study by Chanimov et al.[11] to clear polygeline for nerve blocks as it has got no neurotoxic effects. We did not encounter any significant side effects in the immediate postoperative period. Side effects, especially sedation, orthostatic hypotension, and fainting should be considered when using clonidine.[12] The latter two effects can interfere with postoperative mobilization. Such problems are not with the use of polygeline. The narcotic requirement is found to be less in bupivacaine hemaccel group, which specifies a possible decrease side effect profile also. In our case, it was not significantly less. The limitations of the study were that there was neither a chemical analysis nor a pH study done, as it was simply considered as a clinical trial. Larger studies with different percentages of polygeline with chemical and pH analysis may be done to confirm the efficacy of the drug in prolongation of local anesthetic action.

Conclusion

Adding polygeline in a 3.5% solution to bupivacaine in ILIH nerve block gives significant early postoperative pain relief without any major noticeable side effects.

Table 3: Multiple comparisons with *p* value and confidence intervals

Dependent variable	(I) group	(J) group	Mean difference (I–J)	Std. error	Sig.	95% Confidence interval	
						Lower bound	Upper bound
Fortwin	Bupivacaine	Bupivacaine hemaccel	9.000	5.504	0.108	-2.02	20.02
		Control	-33.000*	5.504	0.000	-44.02	-21.98
	Bupivacaine hemaccel	Bupivacaine	-9.000	5.504	0.108	-20.02	2.02
		Control	-42.000*	5.504	0.000	-53.02	-30.98
	Control	Bupivacaine	33.000*	5.504	0.000	21.98	44.02
		Bupivacaine hemaccel	42.000*	5.504	0.000	30.98	53.02
Time–dose	Bupivacaine	Bupivacaine hemaccel	-112.250*	34.611	0.002	-181.56	-42.94
		Control	-198.000*	34.611	0.000	-267.31	-128.69
	Bupivacaine hemaccel	Bupivacaine	112.250*	34.611	0.002	42.94	181.56
		Control	-85.750*	34.611	0.016	-155.06	-16.44
	Control	Bupivacaine	198.000*	34.611	0.000	128.69	267.31
		Bupivacaine hemaccel	85.750*	34.611	0.016	16.44	155.06

*The mean difference is significant at the 0.05 level.

References

1. Murauski JD, Gonzalez KR. Peripheral nerve blocks for post-operative analgesia AORN J. 2002;75(1):136–47. quiz 148–54.
2. Brummett CM, Williams BA. Additives to local anesthetics for peripheral nerve blockade. Int Anesthesiol Clin. 2011;49(4):104–16.
3. Simpson PJ, Hughes DR, Long DH. Prolonged local analgesia for inguinal herniorrhaphy with bupivacaine and dextran. Ann R Coll Surg Engl. 1982;64(4):243–6.
4. Lagan G, McClure HA. Review of local anaesthetic agents. Curr Anaesth Crit Care. 2004;15(4–5):247–54.
5. Durieux ME. Peripheral analgesic receptor systems. Br J Anaesth. 2006;97(3):273–4.
6. Candido KD, Hennes J, Gonzalez S, Mikat-Stevens M, Pinzur M, Vasic V, et al. Buprenorphine enhances and prolongs the postoperative analgesic effect of bupivacaine in patients receiving infragluteal sciatic nerve block. Anesthesiology. 2010;113:1419–1426.
7. Nishikawa K, Kanaya N, Nakayama M, Igarashi M, Tsunoda K, Namiki A. Fentanyl improves analgesia but prolongs the onset of axillary brachial plexus block by peripheral mechanism. Anesth Analg. 2000;91(2):384–7.
8. Pöpping DM, Elia N, Marret E, Wenk M, Tramèr MR. Clonidine as an adjuvant to local anesthetics for peripheral nerve and plexus blocks: a meta-analysis of randomized trials. Anesthesiology. 2009;111(2):406–15.
9. Parrington SJ, O'Donnell D, Chan VW, Brown-Shreves D, Subramanyam R, Qu M, et al. Dexamethasone added to mepivacaine prolongs the duration of analgesia after supraclavicular brachial plexus blockade. Reg Anesth Pain Med. 2010;35(5):422–6.
10. Rosenblatt Richard, Fung Dennis. Optimal ratio of bupivacaine and dextran for regional anesthesia. Reg Anesth. 1979;4(4):2–3.
11. Chanimov M, Berman S, Cohen ML, Friedland M, Weissgarten J, Averbukh Z, et al. Dextran 40 (Rheomacrodex) or Polygeline (Haemaccel) as an epidural patch for post dural puncture headache: a neurotoxicity study in a rat model of Dextran 40 and Polygeline injected intrathecally. Eur J Anaesthesiol. 2006;23 (9):776–80.
12. Pöpping DM, Elia N, Marret E, Wenk M, Tramèr MR. Clonidine as an adjuvant to local anesthetics for peripheral nerve and plexus blocks: a meta-analysis of randomized trials. Anesthesiology. 2009;111(2):406–15.

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