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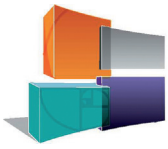

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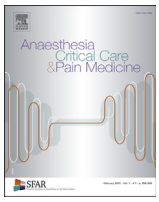

Review

Prilocaine spinal anesthesia for ambulatory surgery: A review of the available studies☆

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ABSTRACT

Transient neurologic symptoms (TNS) led to the abandonment of intrathecal lidocaine. We reviewed the published literature for information about the duration of action and side effects of intrathecal prilocaine, which has been recently reintroduced in Europe. Medline and EMBASE databases were searched for the time period from 1966 to 2015. Fourteen prospective and one retrospective study were retrieved. The duration of the surgical block can be adjusted using doses between 40 and 80 mg. Hyperbaric prilocaine in doses as low as 10 mg can be used for perianal procedures. Four cases of TNS in 486 patients were reported in prospective studies, and none in 5000 cases in a retrospective data set. Spinal prilocaine appears to be safe and reliable for day case anesthesia. However, as chloroprocaine has a shorter duration and a lower risk of TNS and urinary retention, the indications for prilocaine remain to be defined.

1. Introduction

Spinal anesthesia is a safe and reliable anesthetic modality for surgical procedures on the lower part of the body. However, because of the description of transient neurologic symptoms (TNS) following lidocaine spinal [1] with an incidence of 10% to 40% [2–5], most practitioners have abandoned the use of lidocaine for that purpose. Suggested replacements have included mepivacaine (with an incidence of TNS of up to 30% [6,7]), low-dose bupivacaine (extremely variable in the duration of the block [8]), procaine (which in one study resulted in a 15% rate of nausea, 15% failed blocks, and TNS in 6% of the cases) [9], articaine [10], 2-chloroprocaine [11] and prilocaine. The last two medications were recently approved for intrathecal use in Europe. The purpose of this article is to review the available data on the use of prilocaine for spinal anesthesia and to better define its role in the armamentarium of intrathecal medications. Given the limited amount of data, we did not undertake a formal systematic review.

2. Historical background

Prilocaine is an amide local anesthetic that has been used for over five decades for spinal anesthesia. In the liver, prilocaine is primarily metabolized by amide hydrolysis to σ-toluidine and N-propylalanine; σ-toluidine is subsequently hydroxylated to 2-amino-3-hydroxytoluene and 2-amino 5-hydroxytoluene, metabolites responsible for the occurrence of methaemoglobinemia [12]. A high dose of prilocaine (more than 6 mg/kg) is needed to cause a clinically apparent methaemoglobinemia in the healthy adult [13].

It was first introduced around 1960 and has been used for infiltration, peripheral nerve block, and epidural anesthesia. Initially, it gathered momentum slowly as a spinal anesthetic agent partially because of the popularity of lidocaine. Prilocaine is a remarkably short-acting drug and is associated with far fewer reported cases of transient neurological symptoms than lidocaine or mepivacaine [14]. A hyperbaric formulation of 5% prilocaine was used as standard medication for spinal anesthesia in England until 1978 and in France until 1998. The drug was then withdrawn from the market for commercial reasons and because of the poor

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stability of the solution during the manufacturing process [15,16]. A formulation of 2% plain solution is currently marketed in Germany (Xylonest 2% – AstraZeneca) for epidural and intrathecal administration. A hyperbaric formulation (2% with 60 mg/mL dextrose) is marketed by Sintetica as Prilocaine hyperbar in Switzerland, and by other companies as Prilotekal in the UK and Takipril in Germany, Austria and Italy.

3. Methods

The National Library of Medicine's Medline (1946–November 2015), Cochrane CENTRAL Register of Controlled Trials (2005–December 2015) and the EMBASE databases (1980–November 2015) were searched. The initial search terms with the keywords spinal anesthesia, intrathecal, prilocaine with the definition exploded were utilized. The search strategies are shown as an appendix. References of all retrieved articles were manually searched to identify any other studies not found in the electronic search. All available abstracts from major international meetings including the American Society of Regional Anesthesia (ASRA — 2005–2015), the European Society of Regional Anaesthesia (ESRA — 2007–2014), and the American Society of Anesthesiologists (ASA — 2000–2015) annual meetings were examined and published protocols on the trial registration site www.clinicaltrials.gov. Identified abstracts were screened and full-text articles meeting the selection criteria were retrieved. Sixteen articles were identified and analysed for this review.

4. Results

Studies on prilocaine have mainly sought to delineate two things: the rate of TNS compared to lidocaine, and the onset and duration of sensory and motor block in patients receiving intrathecal prilocaine in comparison to other agents.

5. Randomized controlled studies

The main clinical characteristics of the published studies are detailed in Table 1. The reported rates of TNS are shown in Table 2.

Hampl et al. [14] compared 50 mg of hyperbaric prilocaine to lidocaine and bupivacaine.

Table 2
Rate of TNS with prilocaine according to the included studies and to a retrospective data set.

Study	Cases of TNS with prilocaine
Hampl et al. [14]	1/30
Camponovo et al. [17]	0/90
Martinez-Bourio et al. [28]	1/102
Ostgaard et al. [29]	2/50
de Weert et al. [30]	0/35
Guntz et al. [22]	0/89
Kaban et al. [23]	0/25
Aguirre et al. [24]	0/65
Total of prospective studies	4/486 (0.82%)
König and Ruzicic [26] (retrospective)	0/5000
Total of published cases	4/5486 (0.07%)

Times to ambulate and to void were similar after lidocaine and prilocaine (150 vs. 165 min and 238 vs. 253 min, respectively) but prolonged after bupivacaine (200 and 299 min, respectively; $P < 0.05$). Nine of 30 patients receiving lidocaine experienced TNS, 1 of 30 patients receiving prilocaine ($P = 0.03$) had them, and none of 30 patients receiving bupivacaine had TNS.

Camponovo et al. [17] tested the effect of baricity in 90 patients randomized in three groups to receive either 2 mg/mL prilocaine (40 or 60 mg of hyperbaric prilocaine, or 60 mg of plain prilocaine). The mean time to achieve a T10 level of sensory block was comparable in the 3 groups. However, 20% of the patients in the plain prilocaine group did not reach a T10 level. The hyperbaric groups displayed a faster time to motor block onset, to maximum sensory block, to motor offset, and to first voiding. The authors concluded that while the onset time is comparable in the hyperbaric group versus the plain group, the shorter duration of the block coupled with the faster time to achieve motor block make hyperbaric prilocaine a more suitable drug for the ambulatory setting.

Black et al. [18] sought to compare the efficacy of low-dose prilocaine (20 mg) with fentanyl (20 mcg) versus bupivacaine with fentanyl. At the 2-hour mark, the block in the prilocaine group had fully resolved in 86% of the patients, compared to 27% in the bupivacaine group. Median time to regression of sensory block was

Table 1
Characteristics of clinical studies of intrathecal prilocaine.

Study	Number of subjects	Dose of prilocaine (mg)	Solution	Duration of motor block (min)	Time to void (min)
Gebhardt et al. [20]	120	10	2% H	N/A	173
		20			193
		30			211
Kaban et al. [23]	50 (25)	15	0.5% H	134	153
Black et al. [18]	48 (22)	20 (with 20 mcg fentanyl)	2% P	After 2 hours, 19/22 had Bromage score of 0	205
Reisli et al. [35]	30	40	2% P	76.8	N/A
Camponovo et al. [17]	90 (30)	40	2% H	92	195
		60	2% H	118 (H 60 mg)	218 (H 60 mg)
			2% P	157 (P 60 mg)	277 (P 60 mg)
Fisher [33] [a]	30 (12)	50	5% H	87	N/A
Hampl et al. [14]	90 (30)	50	2% H	165 ± 37 (66–235)	255 ± 55 (138–405)
Hendriks et al. [32]	72 (36)	50	2% P	184	227
Manassero et al. [21]	80	50	2% H	Operative side: 118 unilateral, 108 bilateral	220 unilateral
				Non-operative side: 64 unilateral	249 bilateral
Kreutziger et al. [19]	86	60	2% H	N/A	270
Aguirre et al. [24]	129 (64)	60	2% H	180	330
Martinez-Bourio et al. [28]	200 (100)	68.6	5% H	N/A	N/A
Ostgaard et al. [29]	50	80	2% P	197	N/A
de Weert et al. [30]	69 (34)	80	2% P	Time until onset of regression 166[b]	N/A

N/A: not available; H: hyperbaric; P: plain.
[a] Non-randomized.
[b] Measured in 17 patients only.

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