Caudal administration of levobupivacaine and neostigmine for postoperative analgesia in children

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ABSTRACT

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In order to evaluate the postoperative analgesic effect of caudal administration of levobupivacaine, plain or in combination with neostigmine, 50 children who underwent medium gravity operations were studied. The children were randomly divided into two groups: Group L received 1 ml/kg of levobupivacaine 0.25% solution via caudal route, while in Group LN the same solution plus 2 μg/kg neostigmine was given. Patients were assessed for analgesia 4, 8 and 24 hours postoperatively with VAS or TPPPS scores depending on their age, and side effects (motor block, nausea-vomit, sedation, pruritus) were recorded. The overall analgesia score was better in 24 hours in LN group ($p<0.05$), although more patients in group L ($p<0.001$) received additional analgesia as needed after the first 8 hours postoperatively. Side-effects were minimal and with no difference between the two groups. Conclusively, in patients of this study the regime of caudal levobupivacaine plus neostigmine produced longer analgesia than plain levobupivacaine, and more profound mainly after the first 8 hours postoperatively.

Caudal administration of local anaesthetics is a routine classic method for post-operative analgesia in children, which lasts for several hours when using modern, long-lasting local anaesthetics[1]. Aiming at improving the quality of analgesia and prolonging its effect, various combinations of local anaesthetics with other agents such as morphine[2], clonidine[3], ketamine[4], etc. have been tried. However, these trials were accompanied by an increase in the frequency of certain undesirable side-effects (e.g. respiratory or central depression).

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Neostigmine, like all cholinesterase inhibitors, causes analgesia by preventing the breakdown of acetylcholine in the spinal cord; its use in post-operational analgesia was described as early as the 1990s, both in adults[5,6] and in children[7,8].

The aim of this study was to evaluate the effect of neostigmine on the quality and dura-

tion of postoperative analgesia, when it is administered by the caudal route in combination with levobupivacaine, a modern local anaesthetic widely used in Greece.

administered. So, at the end of the operation and before the end of anaesthesia all patients received by the caudal route 1 ml/kg levobupivacaine 0.25%, plain (Group L, n = 25) or in combination with 2 μg/kg neostigmine

Table 1: Score points of the scales used for the assessment of motor block and sedation.

BROMAGE SCALE (Assessment of motor block)	
0	Full motor strength
1	Flexion of knee and feet but weakness to raise the leg
2	Little movement of feet but weakness of knee's flexion
3	Complete motor blockade-no movement of lower limb
SEDATION SCALE	
0	Eyes open spontaneously
1	Eyes open in response to verbal stimuli
2	Eyes open only in response to physical stimuli
3	Unarousable despite verbal and physical stimuli

MATERIAL – METHODS

After the Ethical Committee approval and written inform consent was obtained by children's parents, 50 children class ASA I, who underwent scheduled operations of medium gravity under general anaesthesia, were studied during a period of six months (January-June 2005). The caudal route was used for the administration of regime for post-operative analgesia. Patients with a history of allergy to local anaesthetics, an abnormal haemostasis or pre-existing neurological syndromes were excluded from the study.

All patients received 0.5 mg/kg midazolam per os as premedication. Anaesthesia was induced by inhalation of a mixture of sevoflurane and nitrous oxide in oxygen, after 2 μg/kg iv fentanyl had been administered. In order to facilitate tracheal intubation, 0.6 mg/kg iv rocuronium was administered once the hypnosis was established. Subsequently sevoflurane and nitrous oxide in oxygen and repeated doses of fentanyl and rocuronium as needed were continued for maintenance of anaesthesia.

Patients were randomly allocated in two groups, depending on the analgesic scheme (Group LN, n = 25). Caudal injection was performed under aseptic conditions; patients were lying on their left side, with the upper thigh at 90° and the lower thigh at 45° flexion; A Tuohy needle 18G was used and sterilized adhesive bandage was applied immediately after the injection.

Patients were assessed 4, 8 and 24 hours after emergence from anaesthesia, for the intensity of pain, with two scales depending on their age: the 0-10 Visual Analog Scale (VAS) was used for children over the age of 5 years and the Toddler-Preschooler Postoperative Pain Scale (TPPPS) was used for children younger than 5 years, modified for 0-10 grading to be comparable to VAS[9]. Motor response was assessed with the modified Bromage Scale[8] and sedation with the special four point Scale, as they are shown in Table 1.

Assessment was performed by the same experienced physician of the Postoperative Analgesia Team, in order to ensure the highest possible homogeneity, since such kind of assessment is generally subjective. If the pain scale value exceeded 3, additional analgesia was provided by rectal administration of 20 mg/kg paracetamol.

The frequency with which additional analgesia was administered and signs of nausea, vomiting or itching were also recorded. Statistical evaluation was performed with respect to the kind of parameter to be analysed, using the Mann-Whitney test or Fisher's exact test at a $p < 0.05$ level of significance.

Table 2: Patients data and type of operation they underwent. The values are expressed as mean(SD) or absolute numbers.

	GROUP L (N=25)	GROUP LN (N=25)
Age (months)	28(19)	29(23)
Weight (kilograms)	13(5)	13(7)
Height (meters)	0,92(0,25)	1,00(0,18)
Levobupivacaine's dose (ml/kg)	13(4)	13(6)
TYPE OF OPERATION		
Orchidopexy	9	5
Inguinal hernia	7	10
Hypospadias repair	3	2
Circumcision	1	3
Funiculocele	0	2
Hydrocele	2	1
Colostomy Closure	1	0
V.U.R.-ureteral reimplantation	1	0
Polydactyly-resection	1	2

RESULTS

The patients of the study were demographically comparable with no significant differrences between the two groups. The relevant data as well as the type of operation performed are presented in Table 2.

During the first 4 hours after awaking no child needed any additional analgesia, since no child showed a score exceeding 3. After that and until 24 hours, several children were administered analgesics, as needed according to pain scores; most of them belonged to Group L and less in group LN (21/25 versus 7/25), but the difference between the two groups was statistically significant (p=0.001) only after the first 8 hours (Table 3, Figure 1).

Despite the administration of more additional analgesia in group L, pain scores (VAS or TPPPS) recorded over a 24 hour period were lower (p=0.012) in group LN (Table 4).

Table 3: Number of patients who received additional analgesia.

	0-4 h	4-8 h	8-24 h	Total
Group L	0	2	19	***21***
Group LN	0	1	6	*7*
Statistics	NS	NS	p=0,001	p=0,001

Table 4: Pain scale score at the 4 time points of the assessments. The values are expressed as median (minimum-maximum).

	0 h	4 h	8 h	24 h
Group L	0 (0-0)	0 (0-1)	0 (0-5)	3 (0-6)
Group LN	0 (0-0)	0 (0-1)	0 (0-3)	1 (0-5)
Statistics	NS	p=0,805	p=0,603	p=0,012

Pruritus, itching or any grade of motor block was not observed in any child. Vomiting was observed only in 2 children of Group L as well as very light sedation (grade 1 in the relevant scale) in 1 child of Group L and 2 children of Group LN. No child had any episode of bradycardia or hypotension during the first 24 post-operative hours.

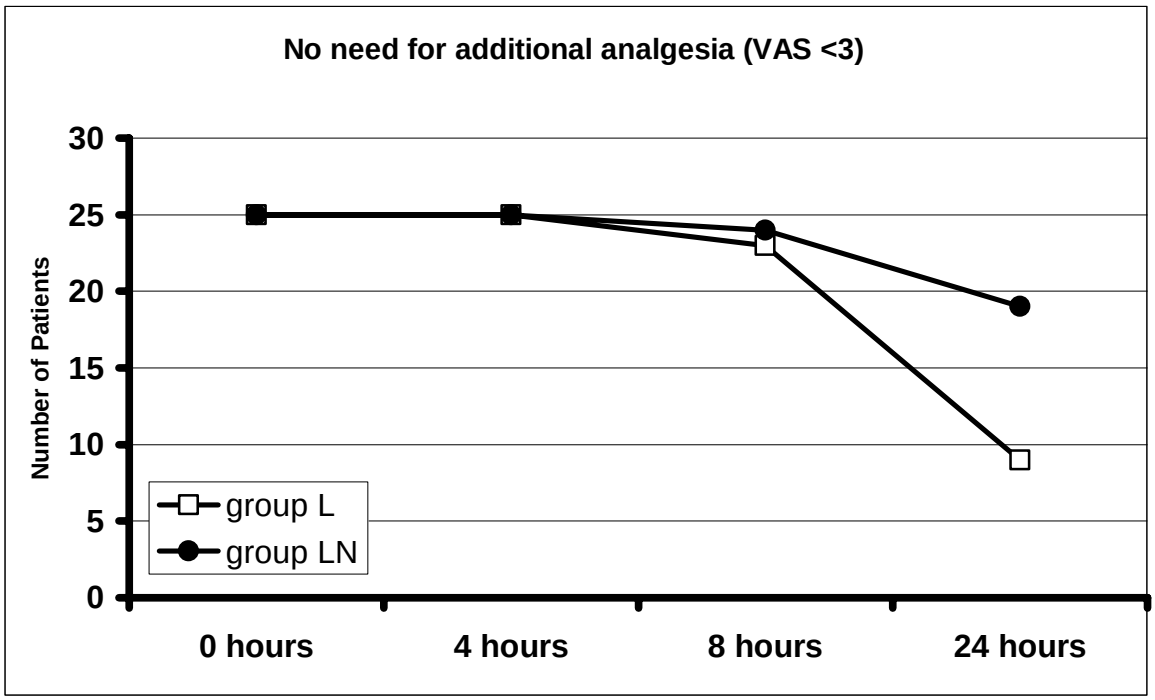
DISCUSSION

In the last 10 year period it has become clear that all children, even premature babies, perceive pain in quantitative and qualitative terms, just as adults do. This has led to the need to find effective analgesic techniques. Thus, modern paediatric anaesthesia was redirected towards intra-operative and post-operative local analgesia. The frequently used caudal block is a simple, safe and effective

method for administering local anaesthetics or other pharmaceutical agents epidurally. This study used levobupivacaine, plain or in combination with neostigmine. A solution of 0.25% levobupivacaine was preferred because

between pressure, pain and paraesthesia. Therefore their sleepy state and the lack of a specific testing technique do not constitute a disadvantage[13,14].

Figure 1: Number of patients (out of 25 in each group) who did not need (pain score ***<3)*** and did not receive additional analgesia at the 4 time points of the study: just after emergence from anaesthesia (0 hours) and 4, 8, and 24 hours later.



it is safer and less toxic in case of accidental intra-vascular injection, rarely causes some degree of motor block and is considered to have a longer analgesic effect because it is absorbed more slowly than bupivacaine. Its higher cost compared to bupivacaine is considered as disadvantage, but this can be overbalanced from the above mentioned properties of the drug[10,11,12].

The caudal approach was performed with the children under anaesthesia, and there is a debate about the probability of increased incidence in accidentally local injuries. Most paediatric anaesthesiologists argue that the technique can and should be used in children who are sedated or under anaesthesia, since it is difficult to cooperate with patients of this age. Furthermore, it is useless to perform locoregional techniques in conscious children, because they do not perceive the difference

Neostigmine decelerates the breakdown of acetylcholine by inhibiting acetylcholinesterase. The analgesic action of acetylcholine is achieved through the M1 muscarinic receptors in the posterior horn of the spinal cord as well as central M1, M2 and N receptors[8], and is also directly associated with the deceleration of pain transmission. Its advantages include the analgesic effect itself through the above mentioned mechanism, the prolonged analgesic effect of the local anaesthetic and the reduced dose, as well as sympathetic block side-effect compensation, a higher respiratory rate, and finally its low cost[7]. Neostigmine side-effects include increased frequency of nausea and vomiting, bradycardia, bronchospasm, increased mucosal secretions, a feeling of weakness in the lower limbs, night bedwetting and delirium. However, low dose neostigmine co-administration with local anaesthetics in the sub-arachnoid or epidural

space seems to prolong post-operative analgesia and reduces the need to administer additional analgesics. The 2 μg/kg dose has none of the side-effects mentioned above, with the exception of nausea and vomiting, which are nevertheless not statistically significant. There was a very low frequency of vomiting in children in this study who received 2 μg/kg neostigmine, and there was no difference between the two study groups in this respect. This dose of neostigmine administered by the caudal route has used by other authors previously in combination with other local anaesthetics, based on published adult studies and on the hypothesis of a probable mechanism of action on the spinal cord (due to diffusion into the cerebro-spinal fluid) rather than on the periphery[8,13,15].

A single epidural administration leads to a relatively short post-operative analgesic effect, comparable with the characteristics of the local anaesthetic used. That is why numerous practitioners prefer administering local anaesthetics through a catheter in continuous flow, since recent studies have proven the safety of this method[14]. However, although this is considered safe and clinically more effective, it has been found that even as many as 20% of continuous flow sacrococcygeal catheters may be colonized by bacteria, although without any clinical symptoms[14,16].

In conclusion, according to the study's results, administering a combination of levobupivacaine and neostigmine by the caudal route resulted in improved quality of post-operative analgesia and prolonged its duration, while no significant side-effects were observed.

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