# To Compare the effect of Chloroprocaine and Chloroprocaine with Fentanyl for Spinal Anaesthesia: A Prospective Randomised Double Blind Study.

**Sarada Devi Vankayalapati, Manjula V Ramsali, P Surender, Dilip Kumar Kulkarni, A Swathi,**

Dept of Anaesthesia, MRMCW, Hyderabad, Telangana, India.

## Abstract

**Background:** Usually for lower abdomen and lower limb short surgical procedures, spinal anaesthesia is a reliable and safe anaesthesia technique.2-chloroprocaine (2-CP) is an amino-ester local anaesthetic with a very short half-life. Adjuvants are required with short acting local anaesthetic for spinal anaesthesia to prolong analgesia.

**Aims and Objectives:** The present study was conducted to analyse the effect of 2-CP alone and with fentanyl combination in spinal anaesthesia for short surgical procedures in terms of onset of block, adequacy of anaesthesia, analgesia and recovery.

**Materials and Methods: T**he study was conducted in our hospital in 60 patients undergoing lower abdomen and lower limb short surgical procedures under spinal anaesthesia with either 2-CP or 2-CP and fentanyl (group I or group II) after randomisation into two groups. Spinal anaesthesia characteristics of sensory and motor block, duration of analgesia were noted and appropriate statistical analysis was performed.

**Results: T**he onset of sensory and motor block was faster in group II[5.00 ± 3.19 vs 7.156 ± 3.38 min. (p= 0.0138) and 8.03 ± 5.65 vs 11.03 ± 3.97 min. (p= 0.021)] than in group I, and duration of effective analgesia was prolonged in group II (147.63 ± 40.71 vs 130.40 ± 50.85 min with p value of 0.0002)as compared to group I. Eleven patients in group I required analgesic supplementation in the intraoperative period.

**Conclusion:** The patients undergoing short surgical procedures of lower abdomen and lower limb under spinal anaesthesia with short acting local anaesthetic 2-CP with fentanyl as an additive provides rapid onset of sensory and motor block and prolonged duration of analgesia.

**Key words:** 2-chloroprocaine (2-CP), fentanyl, spinal anaesthesia, analgesia.

### Introduction

Spinal anaesthesia is considered the most favourable technique because of ease in administration, rapid onset of action and low cost. But, some of the characteristics such as delayed ambulation, urinary retention and pain after block regression may limit its usage for short surgical procedures. The commonly used spinal anaesthetic drug bupivacaine causes unpredictable duration of block even with smaller doses and lead to delay in discharge[1,2]. Preservative free 2-chloroprocaine has re-emerged as an alternative for daycare spinal anaesthesia. It is an amino-ester local anaesthetic with short half-life and so produces faster recovery from anaesthesia and considered ideal for short surgical procedures but early recovery from pain may be unwarranted. Slow onset of sensory block is not liked by the surgeons so small additives to the neuraxial local anaesthetics prolong the intra and postoperative analgesia[3,4]. Very few studies are available with fentanyl as an additive to 2-chlorprocaine (2-CP) for spinal anaesthesia[5].

This study aims to evaluate the effect of 1% 2-CP and 1% 2-CP with fentanyl mixture in spinal anaesthesia for short surgical procedures of lower abdomen and lower limb and compare in terms of providing a satisfactory surgical block while permitting an earlier discharge from hospital with good analgesia.

**Address for Correspondence:**

**Dr Sarada Devi Vankayalapati**

Associate Professor, Dept of Anaesthesia,
MRMCW, Hyderabad, Telangana.
E- mail: drsarada_devi@yahoo.com

**Materials and Methods:**

After the approval of the institutional ethics committee and the written informed consent, randomised study was conducted in our hospital in patients coming for short surgical procedures (<40 min duration) under spinal anaesthesia scheduled for lower abdomen, perineal and lower limb surgeries between the age group of 20 and 50 yr., weighting between 50 and 70 kg, height ranging from 140 to 170 cm of either sex and of ASA I/II. The exclusion criteria included patients with contraindications to spinal anaesthesia, surgery lasting for more the 40 min or requiring level above T10 dermatome, patients' refusal, infection at the site of injection, hypovolemia, allergy, increased ICP, coagulopathy, sepsis, severe cardiopulmonary diseases, thyroid diseases or other neuropathies, as well as patients receiving opioids for chronic analgesic therapy. A prospective double-blind study was done in 60 patients and randomly divided into two groups of 30 each. Randomisation was done as per the PASS version 13 power analysis and sample size software generated list. Patients in group I received 4ml of 2-CP and diluted with CSF up to 4.25 ml. and patients in group II to receive 4 ml of 2-CP and 25 µg fentanyl with total of 4.25 ml.

The anaesthesia technique was standardised for all the patients. All the patients had undergone pre-anaesthetic check-up a day before surgery and they were kept fasting overnight. They received premedication with tab. pantoprazole 40mg and tab. alprazolam 0.5mg orally at night before surgery and at 6 am with sip of water in the morning on the day of surgery. On the day of surgery in the operation room, they were monitored for ECG, Non Invasive Blood Pressure (NIBP), and SpO2 and the baseline values were recorded. Intravenous access was secured with 18G cannula and were preloaded with 10ml/kg ringer lactate solution over 15 min time.

Spinal anaesthesia procedure was performed under aseptic precautions in sitting position. Lumbar puncture was done with 25 gauge quincke needle at L3-L4 space, and with free flow of CSF, the drug either 2-CP or 2-CP with fentanyl was injected as per the randomisation list and turned the patient to supine position after one minute. The person administered spinal analgesia was not involved in recording the data. An independent observer not involved in drug preparation measured the subsequent parameters. The time of intrathecal injection was considered as 0 and the parameters Heart Rate (HR), Mean Arterial Blood pressure (MAP) were recorded at every minute for 10 min, every 05 min for 20 min,every 10 min till 40 and then at 60, 90 and 120 min. Hypotension was considered when the fall in MAP of > 10 % of the baseline values.

Sensory level of the block was assessed by using pinprick method and loss of sensation at T10 level was considered onset of sensory blockade. Time to highest level of sensory blockade, time for regression of two segment, quality of sensory blockade (good, satisfactory or poor) and the time for rescue analgesia [pain at the surgical site (VAS > 3)] were the other sensory characteristics that were recorded. Time from the onset of sensory blockade to the demand for the first rescue analgesia is considered as the total duration of analgesia and was treated with paracetamol 15mg/kg.

Quality of sensory blockade was appreciated as good, satisfactory, poor. Good is defined as when the sensory blockade is adequate for surgical procedure without any analgesia supplement. Satisfactory is sensory blockade with some requirement of analgesia. Poor is inadequate analgesia requirement of general anaesthesia.

The motor blockade was assessed by modified Bromage scale. Time to reach modified Bromage scale of 3 or 4 was taken as the onset of motor block and modified Bromage score of zero as complete recovery. Time to ambulation and time to voiding were also recorded in the postoperative period. Duration of motor blockade was defined as time taken for patient to lift the extended leg after the blockade.

Modified Bromage scale:

1. Free movement of legs and feet
2. Just able to flex knees with free movement of feet
3. Unable to flex knees with free movement of feet
4. Unable to move knees and feet

Taking the mean and standard deviation of the duration of spinal anaesthesia from the previous study[6]. the effect size calculated was 1. The sample size was calculated with effect size=1, α error probability =0.05 and Power (1-β error of probability) =0.95 in G*Power 3.1.9 software (Olshausenstr, Kiel, Germany)[7]. and was total of 54 i.e 27 in each group. However taking into consideration of the dropout of cases, we have taken 30 cases in each group with total of 60 patients.

**Statistical Analysis:** Kolmogorov -Smirnov test was performed to confirm the normal distribution of the data. Numerical data was presented as Mean ± SD and Students 't' test was used to compare numerical continuous data. Haemodynamic data of the two groups was compared by ANOVA repeated measures. The categorical data analysed by Chi-square test. Demographic data (age, height and weight) and intra-operative fentanyl, time to rescue analgesic and

post-operative diclofenac requirement were analyzed using students 't' test and gender of the patients by Chi-square test. P values of <0.05 was considered as statistically significant. The analysis was performed by NCSS 10 statistical software.

**Results**

The demographic variables of patients were comparable between the groups in terms of age, height, weight, sex ratio and ASA grade (Table 1).

**Table 1: Demographic variables**

| Variables | Group I (2-CP) | Group II (2-CP + F) | P. VALUE |
|---|---|---|---|
| AGE (Mean ± SD) | 34.10 ± 13.30 | 38.33 ± 11.09 | 0.1859 |
| WEIGHT (Mean ± SD) | 59.37 ± 13.51 | 61.53 ± 12.92 | 0.5279 |
| HEIGHT (Mean ± SD) | 159.67 ± 8.43 | 160.43 ± 7.30 | 0.7081 |
| SEX (M/F) | 17/13 | 14/16 | 0.6054 |
| ASA -PS (Gr I/II) | 14/16 | 12/18 | 0.7945 |

ASA -PS (American Society of Anaesthesiologist of physical status grade I/II.)

*p <0.05 is statistically significant

Characteristic features of the spinal block are ummarised in Table 2.

**Table 2: Characteristic features of spinal block**

| Observations | Group I (2-CP) | Group II (2-CP + F) | P. VALUE |
|---|---|---|---|
| Time of onset of sensory blockade (Mean ± SD) | 7.156 ± 3.38 | 5.00 ± 3.19 | 0.0138* |
| Peak level of sensory block (number of patients) | | | |
| T4 | 2 (6.66%) | 8 (26.67%) | 0.0010* |
| T5 | 3(10%) | 1 (3.33%) | |
| T6 | 8 (26.67%) | 8 (26.67 %) | |
| T8 | 13 (43.33%) | 9 (30%) | |
| T10 | 4 (13.33%) | 4 (13.33%) | |
| Time of onset of motor blockade (Mean ± SD) | 11.03 ± 3.97 | 8.03 ± 5.65 | 0.0210* |
| Time taken for two segment regression of sensory level (Mean ± SD) | 46.97 ± 10.97 | 57.50 ± 24.99 | 0.0380* |
| Complete motor recovery (Mean ± SD) | 68.33 ± 29.943 | 93.037 ± 47.784 | 0.0190* |
| Time taken for ambulation (Mean ± SD) | 100.43 ± 44.96 | 144.90 ± 50.05 | 0.0006* |
| Time taken for voiding of urine (Mean ± SD) | 147.63 ± 40.71 | 153.53 ± 45.13 | 0.5970 |
| Duration of effective analgesia (Mean ± SD) | 82.63 ± 41.82 | 130.40 ± 50.85 | 0.0002* |

Onset of sensory block was 7.156 ± 3.38 min in group I and 5.00 ± 3.19 min in group II with p value of 0.0138. Time of onset of motor blockade in group I was 11.03 ± 3.97 min and in group II was 8.03 ± 5.65 min which is statistically significant (p 0.021). The peak sensory blockade (T4) achieved was in 8 (26.67%) patients in the group I and 2 (6.67%) in group II. Time taken for two segment regression of sensory level was 46.97 ± 10.97 and 57.50 ± 24.99 min in group I and group II respectively, with significantly shorter duration (P 0.038)in group I. Complete motor recovery was considered when modified Bromage score was 0 and time required was 68.33 ± 29.943 min in group I as against 93.037 ± 47.784 min in group II. The difference is significant with slightly longer duration in group II patients with additive fentanyl to 2-CP in spinal anaesthesia. The time to ambulate was longer in group II (144.90 ± 50.05 min) as compared to group I (100.43 ± 44.96 min) with statistically significant difference (p value of 0.019). Whereas, insignificant difference was observed for voiding time between the two groups (group I vs group II was 147.63 ± 40.71 vs 153.53 ± 45.13 min). The duration of effective analgesia was longer in group II (130.40 ± 50.85 min) as against group I (82.63 ± 41.82 min) with p value of 0.0002.

**Table 3: Quality of surgical anaesthesia**

| | Group I (2-CP) Number of patients | Group II (2-CP + F) Number of patients | P value |
|---|---|---|---|
| Good | 19 | 30 | 0.001* |
| Satisfactory | 9 | 0 | |
| Bad | 2 | 0 | |

*p <0.05 is statistically significant

Quality of surgical anaesthesia (Table-3) was satisfactory and were supplemented with fentanyl in 9 patients and was poor in 2 patients that were converted to general anaesthesia of group I. All the patients of group II had good quality of surgical analgesia.

**Table 4: Adverse effects**

| Side effects | Group I (2- CP) (number of patients) | Group II (2-CP + F) (number of patients) |
|---|---|---|
| Hypotension | 2 | 0 |
| Bradycardia | 0 | 0 |
| Pruritis | 0 | 7 |
| Vomiting | 0 | 0 |

Adverse effects were observed like Hypotension in Group 1 for 2 Patients and Pruritis in Group 2 for 7 patients. No other adverse effects were observed in either group.

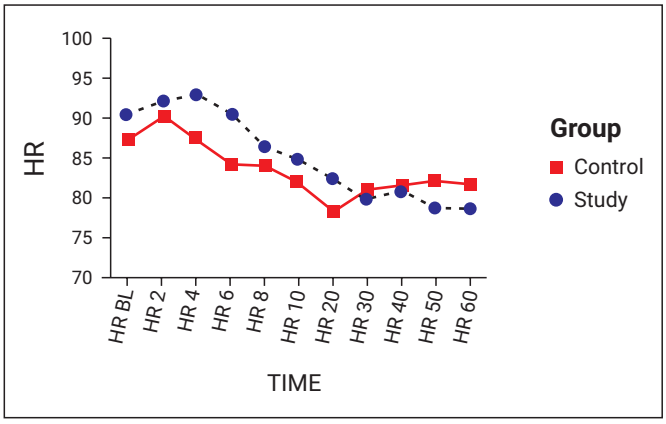


**Figure 1: Heart Rate (HR)**

at different levels when compared between the groups and within the group from baseline values were comparable.

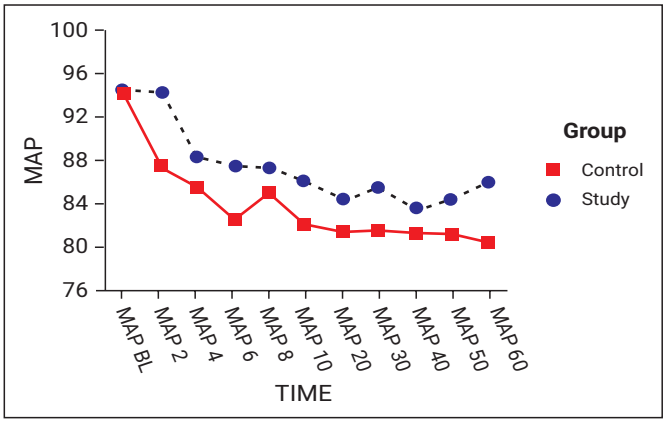


**Figure 2: Mean Arterial Blood Pressure (MAP)**

values at baseline and at different time intervals between the two groups and within the group in group II patients were comparable whereas, group I patients showed statistically significant drop in MAP from 6 min onwards when compared with the base values. Two patients of group I experienced transient hypotension that was treated with vasopressor. Seven patients in group II with fentanyl as additive experienced pruritis of mild to moderate severity that was regressed segmentally and disappeared completely with resolution of spinal block. None of them required treatment for pruritis.

## Discussion

Preservative-free formulation of 2-CP has been re-introduced recently after withdrawal (neurotoxicity concerns) and evaluated in clinical practice with a favourable profile in terms of both safety and efficacy[8]. Intrathecal 1% or 2% 2-CP constitute fascinating alternative to lignocaine or mepivacaine for short surgical procedures due to transient neurological symptoms. 2-CP also offers an alternative to general anaesthesia for short procedures[9]. Fentanyl is the most frequently used opioid which is added to local anaesthetic agent to enhance and increase the duration of sensory analgesia without intensifying the motor blockade or prolonging recovery from spinal anaesthesia[6].

The present study analysis observes the rapid onset of sensory block toT10 in group II (5.00 ± 3.19 min) with fentanyl as an additive in comparison to group I (7.156 ± 3.38 min)with only 2-CP in spinal anaesthesia. Similar finding of group II was observed by Bhaskara et al[6]. with sensory onset at 4.7 ± 0.79 min with 2-CP (3ml) and fentanyl (12.5µg). Study that was conducted in 8 volunteers with fentanyl and 2% 2- CP found to have quicker onset of sensory block in comparison to 2-CP alone[5]. Our study results of group I are in consistence with the retrospective review study of Campiglio GL et al[10]. who used 2-CP for short surgical procedures of less than 60 minutes with sensory onset at 9.6 ± 7.3min (40 mg 2-CP) and 7.9 ± 6 min (50 mg 2-CP). We observed that highest sensory block in the fentanyl and 2-CP group and similar findings were observed in an another study[5].

Two segment regression was 46.97 ± 10.97 min in group I and was prolonged with 57.50 ± 24.99 min in group II patients. Similar finding were observed with vathet al[5]. with regression time slightly longer with 2-CP and fentanyl group than the control group. Lacasse et al[11]. observed 2 segment regression in 50 ± 18 min and Yoos et al[12]. in 45± 20 min with 2-CP 40 mg in spinal anaesthesia in their comparative study with bupivacaine[9]. Whereas, Forster et al[8]. observed regression time of 60(45-75) min with 2-CP as against 60(45-75)min with articaine 60mg.Contrarary to our observations, in another study with 0.25 ml 10% dextrose added to 2-CP 40 mg, the regression time was 40±10 min as against 47 ± 8 min with the control group[13].

Previous studies indicate that, intrathecal opioids enhance the effect of the local anesthetics in spinal anaesthesia[14,15]. We observed prolonged duration of

sensory block i,e the first rescue analgesic demand in group II (130.40 ± 50.85 min)as compared to the group I (82.63 ± 41.82 min). A similar pattern of results were stated with study group in another article[5]. Camponovo et al[16]. and Forster et al[8]. observed sensory duration of 105(60-194) min with 2-CP 50 mg dose in comparison to bupivacaine and 2-CP 40mg against atricaine 40 mg respectively.

In the present investigation, significant number of patients of 2-CP group required fentanyl supplementation due to insufficient intraoperative analgesia during surgery after an otherwise successful spinal block while none in2-CP + F group. Casati et al[3]. reported the necessity of supplementation in 35 % (30 mg 2-CP), 13 % (40 mg 2-CP) and none(50 mg 2-CP) of patients and recommended the requirement of opioids with lower dose 2-CP. Others mentioned the adequate spinal anaesthesia with opioids as an adjunct to 2-CP for short surgical procedures[17]. There was rapid onset of motor block and prolonged duration of motor blockade in the group II due to the effect of fentanyl in spinal anaesthesia. Similarly, onset of motor block (5.36± 0.74min) was quick in 2-CP fentanyl group than ropivacaine fentanyl group in the study done by Bhaskara et al[6]. The duration of motor blockade with recovery to bromage-0 was shorter in control group than fentanyl group (67 ± 13 vs. 81 ± 16 min) in the study analysis of Vath et al[5]. In another study, the duration of motor block with clonidine was observed as 79 ± 19 vs 65 ±13 min as against the control group[17]. Campiglio GL et al. observed motor block for 40 min[10].

In our study, we found delayed time to ambulate in patients of 2-CP+F than the 2-CP itself. These findings are in accordance with the findings reported by Vath et al[5]. and Davis et al[17]. Insignificant difference was documented when buprenorphine was added to 2-CP in another study[6]. Previous studies demonstrated slightly increased time to void if opioid is combined with 2-CP than when compared with each drug alone without delaying the discharge of the patient[5,6,12,17]. We observed similar effects with fentanyl in spinal anaesthesia with 2-CP but the difference was statistically insignificant.

Vath et al[5]. observed significant decrease in the HR and systolic blood pressure when compared with baseline and no difference between the groups. Whereas, we observed significant drop in the MAP in the control group only. Insignificant changes were noted in study group and between the groups. HR changes were insignificant between the two groups and within the group. Pruritis was observed in seven patients of group II and was of mild type but none in group I. Our results are consistent with the findings of other studies for pruritis combining fentanyl with local anaesthetic for spinal anaesthesia[18, 19].

## Conclusion

The patients undergoing short surgical procedures of lower abdomen, perineum and lower limb under spinal anaesthesia with 2-CP, fentanyl as an additive provides faster onset of sensory and motor block. The quality of surgical anaesthesia improved and the duration of effective analgesia was prolonged with additive. Haemodynamics were better maintained.

## References


1. *Kopacz DJ. Spinal 2-chloroprocaine: minimum effective dose. Reg Anesth Pain Med. 2005; 30(1):36-42.*
2. *Hejtmanek MR, Pollock JE. Chloroprocaine for spinal anesthesia: a retrospective analysis. Acta AnaesthesiolScand 2011; 55:267-272.*
3. *Casati A, Danelli G, Berti M, Fioro A, Fanelli A, Benassi C, et al. Intrathecal 2-Chloroprocaine for Lower Limb Outpatient Surgery: A Prospective, Randomized, Double-Blind, Clinical Evaluation. AnesthAnalg [Internet]. 2006; 103(1).*
4. *Siddaiah J, Pujari VS, Madalu AS, Bevinaguddaiah Y, Parate LH. A comparative study on the effect of addition of intrathecal buprenorphine to 2-chloroprocaine spinal anesthesia in short duration surgeries. J Anaesthesiol Clin Pharmacol2019; 35:533-9.*
5. *Vath JS, Kopacz DJ. Spinal 2-Chloroprocaine: The Effect of Added Fentanyl. AnesthAnalg [Internet]. 2004; 98(1).*
6. *Bhaskara B, Prabhakar SA, Rangadhamaiah R. Intrathecal 1% 2-Chloroprocaine with Fentanyl in Comparison with Ropivacaine (0.5%) with Fentanyl in Day Care Perianal Surgery: Prospective Randomized Comparative Study. Anesth Essays Res. 2019; 13(3):471-475.*
7. *Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods. 2009; 41(4):1149-1160.*
8. *Förster JG, Rosenberg PH, Harilainen A, Sandelin A, Pitkänen A. Chloroprocaine 40 mg produces shorter spinal block than articaine 40 mg in day-case knee arthroscopy patients. ActaAnaesthesiol Scand. 2013; 57(7):911-919.*
9. *Ghisi D, Bonarelli S. Ambulatory surgery with chloroprocaine spinal anesthesia: a review. Ambulatory Anesthesia. 2015; 2:111-120.*
10. *Campiglio GL, Bufo S, De Sisto L, et al. Lineeguida per un eserciziosicurodellaChirurgiaEstetica in regime ambulatoriale [Guidelines for the safe outpatient practice of aesthetic surgery]. Minerva Chir. 2010; 65(2):145-152.*
11. *Lacasse MA, Roy JD, Forget J, Vandenbroucke F, Seal RF, Beaulieu D, et al. Comparison of bupivacaine and 2-chloroprocaine for spinal anesthesia for outpatient surgery: A double-blind randomized trial. Can J Anaesth. 2011; 58:384-91.*
12. *Yoos JR, Kopacz DJ. Spinal 2-chloroprocaine for surgery: an initial 10-month experience. AnesthAnalg 2005; 100: 553- 558.*
13. *Warren DT, Kopacz DJ. Spinal 2-chloroprocaine: the effect of added dextrose. AnesthAnalg 2004; 98: 95- 101.*
14. *Bang EC, Lee HS, Kang YI, Cho KS, Kim SY, Park H. Onset of labor epidural analgesia with ropivacaine and a varying dose of fentanyl: a randomized controlled trial. Int J ObstetAnesth. 2012; 21(1):45-50.*
15. *Kallio H, Snäll EV, Suvanto SJ, Tuomas CA, Iivonen MK, Pokki JP, et al. Spinal hyperbaric ropivacaine-fentanyl for day-surgery. Reg Anesth Pain Med. 2005; 30:48-54.*
16. *Camponovo C, Wulf H, Ghisi D, Fanelli A, Riva T, Cristina D, et al. Intrathecal 1% 2-chloroprocaine vs 0.5% bupivacaine in ambulatory surgery: A prospective, observer blinded, randomized, controlled trial. Acta AnaesthesiolScand2014; 58:560-6.*
17. *Davis BR, Kopacz DJ. Spinal 2-chloroprocaine: the effect of added clonidine. AnesthAnalg 2005; 100: 559-565.*

18. *Liu SS, Ware PD, Allen HW, Neal JM, Pollock JE. Dose-response characteristics of spinal bupivacaine in volunteers. Clinical implications for ambulatory anesthesia. Anesthesiology 1996; 85:729-736.*

19. *Ben-David B, Solomon E, Levin H, Admoni H, Goldik Z. Intrathecal fentanyl with small-dose dilute bupivacaine: Better anesthesia without prolonging recovery. AnesthAnalg. 1997; 85:560-5.*

Conflict of interest: Nil
Source of funding: Nil

Date received: Jan 23, 2022
Date accepted: Apr 28, 2022