

# Prevention of post-tonsillectomy pain with analgesic doses of ketamine

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## Summary

The prevention of postoperative pain in children who had undergone tonsillectomy was investigated in a double-blind trial. Ketamine (Ketalar; Parke-Davis) 0,5 mg/kg was given intravenously before the operation to 20 children and saline to a control group of 20 children. Premedication consisted of oral trimeprazine 4 mg/kg given 2 hours pre-operatively. The anaesthetic technique was standardised. There were no significant differences between the groups pre-or intra-operatively. Postoperatively there were significant differences in the measurement of pain but not in that of sedation. No hallucinations were encountered in those receiving ketamine. It is concluded that analgesic doses of ketamine are safe and effective.

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Tonsillectomy is a traumatic event for a child for a variety of reasons. Pain should not be one of them. Pain in the immediate postoperative period should be prevented in order to smooth extubation, awakening and the recovery period.<sup>1</sup> A safe analgesic, which could be used routinely, should have little or no potential for respiratory depression, should be readily available in the operating theatre and should not require any countersignatures.<sup>1</sup> Ketamine (Ketalar; Parke-Davis) in a dose of 0,5 mg/kg fulfils these requirements.

A search of the literature provided only one publication<sup>2</sup> where ketamine had been used for the treatment of post-tonsillectomy pain. The present study investigates various aspects of pain relief and the safety of ketamine when used as an analgesic in the postoperative period.

## Patients and methods

A double-blind trial was conducted with two groups of 20 children over the age of 4 years and of both sexes. Premedication consisted of oral trimeprazine 4 mg/kg for the younger children. For the older children droperidol 0,1 mg/kg was added. For children weighing over 25 kg, diazepam 5 mg was used as the sole premedication.

The anaesthetic technique included a 'gas induction' with nitrous oxide, oxygen and halothane or thiopentone 4 - 6 mg/kg in the

older children. Suxamethonium 1 mg/kg was used to facilitate oral intubation. Anaesthesia was maintained with N<sub>2</sub>O, O<sub>2</sub> and halothane with assisted spontaneous respiration.

An assistant prepared a 5 ml syringe with either normal saline or a diluted ketamine mixture (5 mg/ml) (according to a randomised list). Each child received ketamine 0,5 mg/kg body weight or saline as soon as an intravenous line was established and the time at which this occurred was noted. The same surgeon (S.Y.) performed all the tonsillectomies in a standardised manner using a Mollison semi-sharp enucleator. The duration of surgery was noted and the surgeon assessed bleeding on a two-point scale: normal or excessive. Secretions were assessed by the anaesthetist as being normal or excessive. None of the personnel (anaesthetist, surgeon or recovery-room staff) were aware of the contents of the ketamine/saline syringe administered pre-operatively.

The following times were noted in the immediate postoperative period to assess speed of recovery: (i) time halothane switched off; (ii) time of extubation; (iii) time of opening eyes on command; (iv) time of opening eyes spontaneously; (v) time the child could 'protect the airway' (this was defined as a movement of the head within four breaths when the mouth and nose were occluded); and (vi) awakening time (this was defined as the time when an experienced recovery room sister would consider the child to be awake).

The children were observed in the recovery room for 90 minutes. Assessments of various indicators of pain (Table I) were made every 30 minutes. The state of sedation of the child was noted on a 5-point scale (Table I). Tilidine (Valoron; Warner) drops (1 drop per year of age) were given to provide analgesia when required. The times at which they were required were noted. Children who received analgesics were excluded from further analysis but were still observed for any complications or untoward effects, which were noted. These assessments were made by two experienced nursing sisters.

The results were analysed using an unpaired Student's *t*-test for parametric data, chi-square test for nominal data and Fisher's exact probability tables for nominal data with cells less than 5. The study was approved by the Ethical Committee of Tygerberg Hospital and the University of Stellenbosch.

## Results

**Pre-operative status and premedication.** The ages in the whole trial group ranged from 4 years to 13 years and the weight range was from 16 kg to 35 kg (Table II). There were 8 boys and 12 girls in each group. There were no significant differences between the groups in respect of age, weight, height, sex, type of premedication, dose of premedication, time from premedication to induction of anaesthesia, pre-operative haemoglobin concentration or effects of the premedication.

**Anaesthetic and surgical technique.** There were no significant differences between the two groups with regard to anaesthetic technique, duration of anaesthesia or surgery, bleeding during surgery or secretions during surgery and the extubation period. The following were noted: site of endotracheal tube (oral/nasal), duration of surgery, duration of anaesthesia, bleeding during surgery, secretions during surgery and awakening time.

**Recovery and extubation period.** There were no significant differences between the groups regarding awakening times as measured the five times set out in 'Patients and Methods' (Table III).

**The first 30-minute postoperative period.** For the analysis of the results, the categories numbered 1 and 2 in Table I were combined and the other measurements 3, 4, 5 and 6 (where

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TABLE I. RECOVERY-ROOM ASSESSMENTS

	Score					
	1	2	3	4	5	6
<b>Indicators of pain</b>						
Child's expression of pain when left alone	Sleeping	Awake, pain-free	Crying	Crying due to pain	Spontaneous complaint of pain	Asking for pain relief
Verbal expression of pain when asked	No pain	Mild	Moderate	Severe	Unbearable	
Nurse's general impression of child's pain	Sleeping peacefully	Sleeping restlessly	Awake, pain-free	Moaning about pain	Requires analgesia immediately	
Restlessness	Asleep	Awake and quiet	Moaning	Crying	Thrashing about	
Crying	Sleeping	Awake, not crying	Sighing, moaning	Sobbing softly	Crying	Screaming
Sedation score	Sleeping, cannot rouse	Rouse with difficulty	Can be woken but sleeping in between	Awake	Screaming	

TABLE II. PRE-OPERATIVE AND OPERATIVE DATA

	Ketamine group			Control group		
	No. of patients assessed	Mean $\pm$ SD	Range	No. of patients assessed	Mean $\pm$ SD	Range
Age (yrs)	20	7,4 $\pm$ 1,8	4 - 10	20	8,3 $\pm$ 3,1	4 - 13
Weight (kg)	20	23,9 $\pm$ 5,6	16 - 35	20	26,4 $\pm$ 10,8	14 - 56
Length (m)	19	1,23 $\pm$ 0,13	0,96 - 1,48	19	1,1 $\pm$ 0,2	0,94 - 1,5
Haemoglobin (g/dl)	20	12,0 $\pm$ 0,8	10,5 - 13	19	11,6 $\pm$ 0,9	10,5 - 14
Dose trimeprazine (ml)	19	12,1 $\pm$ 1,7	8 - 12,5	15	11,5 $\pm$ 1,9	7 - 12,5
Time from pre-med. to induction (min)	20	112 $\pm$ 42	50 - 329	20	129,0 $\pm$ 32,0	120 - 300
Duration of surgery (min)	20	12,9 $\pm$ 2,7	8 - 18	20	14,2 $\pm$ 5,0	8 - 30
Time from bolus to end of surgery (min)	20	21,2 $\pm$ 6,5	9 - 39	20	27,8 $\pm$ 10,7	14 - 51

TABLE III. RECOVERY TIMES (min)

	Ketamine			Control		
	No. of patients	Mean $\pm$ SD	Range	No. of patients	Mean $\pm$ SD	Range
<b>Halothane off to</b>						
<b>Extubation</b>	20	6,0 $\pm$ 5,8	1 - 22	20	6,2 $\pm$ 4,8	2 - 13
<b>Open eyes on command</b>	17	23,1 $\pm$ 16,3	2 - 63	17	25,2 $\pm$ 14,3	7 - 60
<b>Open eyes spontaneously</b>	19	21,4 $\pm$ 10,6	3 - 46	19	23,8 $\pm$ 12,5	10 - 60
<b>Protect airway 'Awake'</b>	19	16,5 $\pm$ 8,8	3 - 35	20	13,5 $\pm$ 8,1	7 - 35
0 - 5 min	0			1		
5 - 10 min	7			12		
10 - 15 min	6			2		
15 - 20 min	2			2		
>20 min	5			3		

TABLE IV. PAIN MEASUREMENTS AND ANALGESIC REQUIREMENTS IN THE FIRST 30-MINUTE PERIOD

Category*	Ketamine	Control	Significance
<b>Restlessness</b>			
Scores 1+2	14	6	$P < 0,02$
Scores 3+4+5	6	14	
<b>Crying</b>			
Scores 1+2	14	6	$P < 0,02$
Scores 3+4+5+6	6	14	
<b>Child's expression of pain</b>			
Scores 1+2	13	5	$P < 0,02$
Scores 3+4+5+6	7	15	
<b>Child's verbal assessment of pain</b>			
Scores 1+2	4	1	
Scores 3+4+5	2	2	
<b>Nurse's impression</b>			
Scores 1+2	13	8	
Scores 3+4+5	7	12	
<b>Analgesics</b>			
Required	8	14	$P = 0,055$
Not required	12	6	

\*The scores in each category are combined figures from Table I.

appropriate) were also combined. There were significant differences between the groups as shown in Table IV, with the ketamine group scoring better with regard to restlessness, crying and the child's expression of pain ( $P < 0,02$ ). The degree of sedation was similar in both groups (Fig. 1). The number of control patients requiring analgesia was not significantly higher ( $P = 0,055$ ) than in the ketamine group (Table IV).

**The second 30-minute postoperative period.** The ketamine group scored significantly better, with less restlessness and crying. The two groups did not differ significantly in the other measurements or in sedation scores (Fig. 2).

**The third 30-minute postoperative period.** There were no significant differences between the patients in the two groups.

**Side-effects and complications.** No hallucinations were noted. No other complications were encountered.

## Discussion

The need for better postoperative analgesia has been stated repeatedly.<sup>3</sup> A recent report<sup>4</sup> cites 14 references and concludes that almost 40% of patients consider their postoperative anal-

gesia insufficient or even poor. The psychological trauma of pain in children is even more far-reaching than in adults. The reasons for the lack of proper postoperative analgesia are mainly fear of respiratory depression and addiction, both of which are unfounded in a normal recovery period with short-term postoperative pain. Another problem is the shortage of registered staff to unlock and check narcotic (schedule 7) drugs.

An ideal analgesic drug would be one that is readily available to the anaesthetist in the operating theatre, does not require paper-work, is not a respiratory depressant and has low addictive potential.<sup>1</sup> Ketamine has been used by one of the authors for this purpose for many years but the clinical impression needed scientific investigation and validation.

The duration of action of ketamine as an anaesthetic agent is quite short, but its analgesic effect is of much longer duration.<sup>5</sup> The reason for this dual action lies in the pharmacokinetics of the drug. The intravenous drug initially decays fast, with an  $\alpha$ -half-life of 11 - 17 minutes and a  $\beta$ -half-life of 150 - 186 minutes.<sup>5-7</sup> The analgesic action is also thought to be due to a long-acting metabolite, nor-ketamine,<sup>8</sup> which is excreted in the

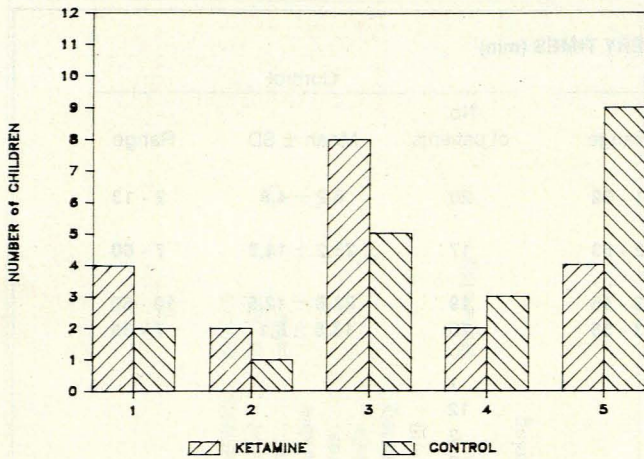


Fig. 1. Distribution of sedation scores for the first 30-minute period. For key see Table I.

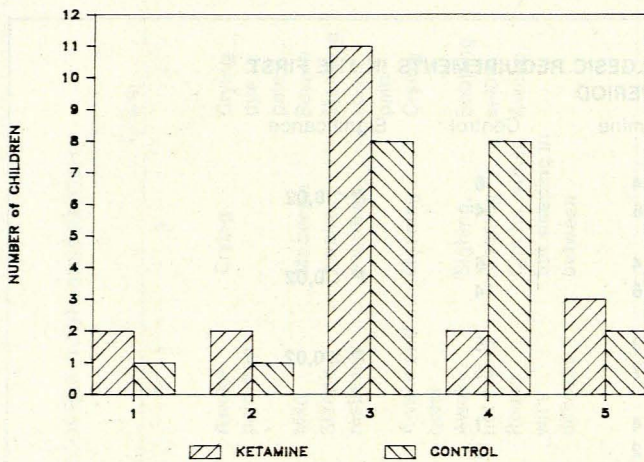


Fig. 2. Distribution of sedation scores for the second 30-minute period. For key see Table I.

urine for up to 24 hours.<sup>7</sup> The intravenous bolus dose at the beginning of a short procedure such as a tonsillectomy should, therefore, maintain an analgesic action throughout the early postoperative period. A longer lasting effect could be obtained by giving the dose intramuscularly. Sadove *et al.*<sup>9</sup> in a study using intramuscular ketamine in a dose of 0,44 mg/kg for postoperative pain in adults, showed a significant analgesic effect lasting at least 60 minutes (which was the duration of their observations). Nimmo and Clements<sup>8</sup> state: '... of particular clinical importance is the fact that in small intramuscular doses ketamine may produce prolonged periods of analgesia after operation'. Other methods of prolonging the analgesic effect of ketamine would be to give a larger initial intravenous dose or a top-up dose towards the end of the anaesthetic. Oral ketamine has also been used for analgesia.<sup>10</sup>

Ketamine does not prolong the awakening time or the recovery phase (Table IV). A dose of ketamine smaller than 2 mg/kg is also unlikely to produce hallucinations.

The first 30-minute period showed significant differences between the two groups in four of the measurements of pain and pain relief. These differences decreased during the successive two periods. This is possibly due to the decreasing blood levels of ketamine, and the fact that a large percentage of the control group had to receive an analgesic in this period. Could the 'pain scores' have been due to a sedative effect of ketamine rather than an analgesic effect? There are two reasons why this is probably not so. The first is that patients in pain who are given sedatives become unmanageable and restless.<sup>11</sup> The second reason is that a larger number of patients who had received ketamine did not require any analgesic at all in the observation period ( $P = 0,055$ ). This supports the concept of decreased intensity of postoperative pain if the patient awakes free of pain. A small percentage of the control group (15%) did not receive any analgesic at all in the study period. Although these patients did not receive any analgesics, they still had a certain amount of pain which could have been safely relieved.

### Conclusion

Although the measurement of pain is notoriously difficult, especially in children, and the variables measured are often indirect measurements of behaviour, we feel that this study shows that the stressful and painful postoperative period after tonsillectomy can be improved significantly and safely with a small dose of ketamine.

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### REFERENCES

- Hannington-Kiff JG. The need for analgesic cover after ENT surgery: comparison of nefopam and papaveretum. *Anaesthesia* 1985; **40**: 76-78.
- Sheffer LA, Dean HN, Stefferson JL. Recovery room analgesia: a comparative study of drug effects. *Anesth Analg* 1973; **52**: 853-860.
- Sriwatanakul K, Weiss OF, Alloza JL *et al.* Analysis of narcotic analgesic usage in the treatment of postoperative pain. *JAMA* 1983; **250**: 926-929.
- Dick W, Knoche E, Gundlach G. Postoperative infusion analgesia. In: Vickers MD, Lunn JN, eds. *Mortality in Anaesthesia* European Academy of Anaesthesiology Proceedings. 1982. Berlin: Springer-Verlag, 1983: 190-195.
- White PF, Way WL, Trevor AJ. Ketamine: its pharmacology and therapeutic uses. *Anesthesiology* 1982; **56**: 119-136.
- Clements JA, Nimmo WS. Pharmacokinetics and analgesic effect of ketamine in man. *Br J Anaesth* 1981; **53**: 27-30.
- Wieber J, Gugler R, Hengstman JH, Dengler HJ. Pharmacokinetics of ketamine in man. *Anaesthesist* 1975; **24**: 260-263.
- Nimmo WS, Clements JA. Pharmacokinetics of ketamine: Anaesthetic Research Society abstracts. *Br J Anaesth* 1981; **53**: 186.
- Sadove MS, Shulman M, Hatano S, Fevold N. Analgesic effects of ketamine administered in dissociative doses. *Anesth Analg* 1971; **50**: 452-457.
- Morgan AJ, Dutkiewicz T. Oral ketamine. *Anaesthesia* 1983; **38**: 293.
- Galloway PA, Braude BM, Clinton CW, Klopper E. Combination analgesic-antihistamine drugs. *S Afr Med J* 1984; **66**: 125-126.