Oral Ketamine. Is it safe?

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ABSTRACT

Introduction: Safety of use of ketamine by the oral route has not been verified.

Methods: Randomized controlled trial involving 30 patients in each group, comparing effects of oral ketamine and intravenous morphine on vital signs and oxygen saturation.

Results: Significant change in Systolic blood pressure was noted after administration of oral ketamine ($p < 0.05$), which normalized after 2 hours of administration of the drug but change in Diastolic blood pressure, Mean Arterial pressure and oxygen saturation was insignificant ($p>0.05$).

Conclusion: Use of Oral Ketamine can be considered a safe method for conscious sedation.

Key words: Oral Ketamine, Conscious sedation, Premedication.

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INTRODUCTION

Before subjecting children to uncomfortable and painful procedures, premedications are necessary. But use of premedication in our set up is not that encouraging. One reason that premedication is not part of the routine is that the ideal medication or combination of medications has not been found. The ideal premedication for procedures should be easy to administer, have a rapid and predictable onset, and produce both amnesia and analgesia, without significantly affecting cardiovascular and respiratory function.[1]

Ketamine, developed in 1963 as a dissociative anesthetic agent, has hypnotic, analgesic, amnestic and sedative properties.[2] It has been used intravenously with success for several years to facilitate major operative procedures in children. Use of ketamine by the oral route is also gradually gaining acceptance for conscious sedation and as premedication. Study done by the authors in the same setting demonstrated that oral ketamine provides improved sedation compared to intravenous morphine during manipulation of the wound without many clinically significant complications.[3] However its effect on cardiovascular and respiratory system of the children has not been verified yet.

Hence, this study was carried out with the aim to establish oral ketamine as a safe and convenient agent for procedural sedation and analgesia.

METHODS

This study was carried out in Tansen Mission Hospital. Sixty children of 13 years or below undergoing painful procedure like dressing change or expression of pus, etc were included in the study. Cases were randomly assigned to receive either oral ketamine (Mixture of IV preparation of the ketamine in 'Rasna' syrup is used for the oral route) at the dose of 8 mg/kg or intravenous morphine at 0.1 mg/kg with the help of an independent doctor, who will choose an envelope from an already numbered 60 opaque envelopes (30 envelopes containing paper written with oral ketamine and rest of 30 containing paper written with morphine). Vital signs and oxygen saturation were recorded manually by the same instruments by a single observer. The randomization codes were not broken to observers until all of the data were analyzed. Approval letter for the study was obtained from Nepal Health Research Council.

RESULTS

The study was carried out from the month of November 2005 to February 2006. Sixty two patients undergoing painful procedures were referred by the surgeons for the purpose of the study, hence was eligible for the study. Two of them was excluded and sixty procedures were enrolled, 30 in each group.

	Before drug administration (a)	Before procedure (b)	After procedure (c)	2 hours after procedure (d)	p value between		
					a & b	a & c	a & d
Oral Ketamine group (Mean +/- SD)	92.66 +/- 10.48	96.66+/- 11.54	97.83+/- 10.80	94.16+/- 10.00	0.063	0.016	0.300
Morphine group (Mean +/- SD)	94.59+/-9.83	94.66+/- 9.35	96.86+/- 10.66	92.86+/- 10.35	0.688	0.195	0.509
p value	0.578	0.464	0.729	0.623			

Table # 1: Comparison of mean Systolic Blood Pressure (SBP) before drug administration (baseline) with SBP before procedure, after procedure and 2 hours after procedure

	Before drug administration (a)	Before procedure (b)	After procedure (c)	2 hours after procedure (d)	p value		
					a & b	a & c	a & d
Oral Ketamine group (Mean +/- SD)	58.46+/-12.32	60.33+/- 13.25	62.00+/- 12.7	61.00+/-11.84	0.303	0.054	0.054
Morphine group (Mean +/- SD)	58.20+/-9.5	59.33+/- 11.83	57.66+/- 13.19	60.33+/-8.89	0.485	0.808	0.190
p value	0.926	0.759	0.200	0.806			

Table # 2: Comparison of mean Diastolic Blood Pressure (DBP) before drug administration (baseline) with DBP before procedure, after procedure and 2 hours after procedure

	Before drug administration (a)	Before procedure (b)	After procedure (c)	2 hours after procedure (d)	P value Between		
					a & b	a & c	a & d
Oral Ketamine group (Mean +/- SD)	70.82 +/- 11.06	72.33 +/- 12.07	72.83 +/- 11.22	71.83 +/- 10.30	0.423	0.303	0.440
Morphine group (Mean +/- SD)	69.16 +/- 8.66	71.32 +/- 9.8	70.88 +/- 11.80	71.16 +/- 8.66	0.033	0.334	0.186
P value	0.520	0.725	0.516	0.787			

Table # 3: Comparison of Mean Arterial Pressure (MAP) before drug administration with MAP before procedure, after procedure and 2 hours after procedure

	Before drug administration (a)	Before procedure (b)	After procedure (c)	2 hours after procedure (d)	p value between		
					a & b	a & c	a & d
Oral Ketamine group (Mean +/- SD)	97.86 +/- 1.77	97.73 +/- 1.92	97.96 +/- 1.69	97.23 +/- 1.43	0.717	0.789	0.154
Morphine group (Mean +/- SD)	98.4 +/- 1.9	97.63 +/- 2.73	97.36 +/- 1.97	97.63 +/- 1.37	0.201	0.031	0.031
p value	0.267	0.871	0.211	0.274			

Table # 4 : Comparison of mean SPO2 before drug administration (baseline) with mean SPO2 before procedure, after procedure and 2 hours after procedure.

(N.B. None of the patients required supplemental oxygen)

Changes in Vitals	*In oral ketamine group N = 30*		*In IV morphine group N = 30*		P value
	After procedure (%)	2 hours after procedure(%)	After procedure(%)	2 hours after procedure(%)	
No. of patients with >10% increase in SBP	15(50)	8(26.66)	12(40)	7(23.33)	0.92
No. of patients with >20% increase in SBP	3(10)	2(6.66)	5(16.66)	2(6.66)	0.33
No. of patients with >10% increase in PR	17(56.66)	10(33.33)	15(50)	13(43.33)	0.47
No. of patients with >20% increase in PR	6(20)	4(13.33)	11(36.66)	5(16.66)	0.61

Table # 5: Change in vitals from baseline before procedure, after procedure and 2 hours after the procedure:

N.B. Vitals taken before the procedure were taken as the baseline.

	Oral Ketamine Group N = 30 a	*Intravenous Morphine Group N = 30 b*	
Vomiting	0	0	-
Nausea	0	0	-
Irrelevant talk	8	0	0.005
Excessive Salivation	0	1	1
Crying	6	18	0.002
Lacrimation	2	0	0.492
None	15	12	0.436
Total	31	30	

Table # 6: Adverse effects after the administration of the drug:

Discussions

The most prominent side effect of ketamine is emergence phenomena of a psychological nature, which have been described as lively dream activity, sensory distortions or hallucinations. The incidence of hallucinatory phenomena has been reported in from 0% to 50% of adults and from 0% to 10% of children.[4] These symptoms are less frequent in children of less than 10 years old and seen commonly in elderly patients of fourth of fifth decades of life.[5]

Beyond emergent reactions, ketamine produces a number of side effects that influence major body systems. The drug stimulates the cardiovascular system, producing increases in heart rate and blood pressure by 20%, immediately after injection and this effect may persist throughout the period of anaesthesia. [5, 6] These effects are indirect and are most likely mediated by inhibition of both central and peripheral catecholamine reuptake. Ketamine has direct negative inotropic and vasodilating activity, but these effects usually are overwhelmed by the indirect sympathomimetic action.[7]

In this study, there has been no considerable change in Heart rate, SBP, DBP and MAP in between oral Ketamine and IV Morphine group but significant change in SBP was observed within the oral Ketamine group. However, SBP seems to normalize after 2 hours of administration of the drug. Since this statistical change is not observed when

DBP and MAP between the two groups was compared (see Table # 3), clinical implication of this statistical change in SBP is probably not significant.

In Oral Ketamine group, only 10 and 6.66 percent of total patients had more than 20% rises in SBP from baseline soon after procedure and 2 hours after the procedure respectively (see Table#5). These figures are quite low as anticipated by Sage and Laird [5] while Ketamine is administered intravenously.

Adverse effects related to intravenous Ketamine were relatively uncommon when ketamine is given orally. This finding is consistent with study done by Toblas et al.[8] The most frequent and significant side effects in oral ketamine group were irrelevant talking (p=0.005) and lacrimation (p=0.492). Excessive Salivation was the commonest side effects noted after IV Ketamine use.[9] Eight (26.66%) patients had irrelevant talk during procedure, which was quite high compared to the study by Toblas et al, where only 9% showed variable emergence phenomena. [8] However, the number of patients who had no side effects were similar in two groups in this study; 23 vs 24 (p=0.754) and 15 vs 12 (p=0.436) after drug administration and during procedure respectively.

In this study, clinically significant oxygen desaturation was not noted in either group and oxygen supplementation was not given to any of the cases, which is inconsistent to a similar study [10] with intravenous ketamine in which oxygen was supplemented to 46% of the total cases. The oral route of drug administration is the reasonable cause for the less incidences of oxygen desaturation in this study. In a study done to assess the effect of oral Ketamine to alleviate procedure related distress in 35 pediatric oncology patients, no patient developed oxygen saturation less than 95% while breathing room air. Oral use of ketamine having less side effects as compared to intravenous use has been stated by other authors too. [11] Still, we recommend close monitoring by personnel competent in paediatric airway management for all patients receiving oral ketamine sedation.

In conclusion, SBP (but not DBP and MAP) was significantly elevated in the Oral Ketamine group along with some minor complications like irrelevant talking and lacrimation whereas SPO2 dropped significantly in the IV Morphine group. But there were no clinically significant changes in the vitals in both the groups. Hence, use of Oral Ketamine can be considered a safe method for conscious sedation.

From the experience gained from this study, we recommend use of oral ketamine at the dose of 8 mg/kg for the painful procedures as premedication. As it is safe and causes only minor cardiovascular changes, we recommend promotion of oral ketamine at the level of district hospital where the monitoring facilities are minimal. Oral ketamine has shown to provide conscious sedation in the majority of the patients which may not require all the airway precautions as an unconscious patient. Still, we recommend the procedure to be performed in NPO (nil per oral) status in the presence of a skilled person who can manage the basic airway problems and all the rescuscitaion facilities should be present at the site of the procedure.

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