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Adverse Reactions to Midazolam and Ketamine Premedication in Children

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A previous study[1] has shown rectally administered midazolam to be an excellent form of premedication in children. The study further showed that the midazolam dosage was strongly associated with the prevalence of adverse reactions. No adverse reactions were found in the groups that received 0.25 mg/kg midazolam or saline (placebo) rectally, but, by increasing the dose of midazolam, untoward responses could be elicited. It thus seems that the incidence of adverse reactions after rectal midazolam is influenced by the dosage used.[2]

Ketamine is an attractive alternative for rectal premedication in children. It has a unique combination of sedative, amnestic, anesthetic, and analgesic properties.[3] However, undesirable dose-dependent adverse reactions may occur, which can be attenuated by administering a benzodiazepine in conjunction with the ketamine.[3]

In our study, rectally administered midazolam (0.3 mg/kg) and ketamine (5 mg/kg) were compared with each other for premedication in children undergoing oral surgical procedures. Sixty patients between the ages of 2 and 9 years were randomly allocated to 3 groups of 20 patients each in this double-blind study. Group A received 0.30 mg/kg, and groups B and C 5 mg/kg ketamine rectally, 30 min before administration of general anesthesia. In one of the two groups of patients who received ketamine, intravenous midazolam (0.05 mg/kg) was also administered immediately after induction of anesthesia.

Children were induced with the inhalational anesthetic agent halothane and evaluated for adverse reactions before and with induction of anesthesia.

The results from this trial show that 30 min after rectal administration of the two drugs, good anxiolysis, sedation, and cooperation were obtained in most patients. Twenty-six patients (43%) experienced adverse reactions at various times preoperatively after receiving premedication. Twenty of these belonged to the ketamine groups (n = 40) and 6 to the midazolam group (n = 20). No association could be shown between the preoperative adverse reactions and the type of drug administered. It appeared that patients generally experienced more nystagmus, hallucinations, and salivation in the groups receiving ketamine than those in the group receiving midazolam. One patient who had received only ketamine experienced hallucinations postoperatively. These adverse effects have often been associated with the use of ketamine.[3]

Oxygen saturation levels were monitored before premedication, 30 min after rectal administration of drugs, and during the operation. No significant differences were found in oxygen saturation levels for the groups. From the results it was evident that hypoxia was not a cause of the high incidence of adverse reactions in our study.

It is interesting to note that the ketamine groups of patients showed a slight lowering and those who had received midazolam a slight increase in arterial blood pressures after premedication. These blood pressure differences were considered to be of little clinical importance. The minimal effects of the drugs on blood pressures support their safety when administered rectally to children in the doses used in this study.

We have stated before[4] that in reviewing the literature we are left with the impression that the overall incidence of significant adverse reactions to rectal midazolam is low. However, these reactions, which largely seem to be dose dependent, are often not marked in intensity. For this reason they are not always clinically recognized, and their true incidence may be underreported.

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