

KETAMINE (Commentary)**Love it or hate it – conflicting views on the use of ketamine**

Views on the appropriateness of using ketamine for sedation, analgesia and anaesthesia in children vary widely, and are also often held quite strongly. Those who looked to the *British National Formulary for Children* for advice in 2005 were told that “Ketamine is rarely used now. ... There is a high incidence of extraneous muscle movement; also cardiovascular stimulation and arterial pressure may rise with tachycardia. The main disadvantage of ketamine is the high incidence of hallucinations, nightmares and other transient psychotic sequelae, although these may be much less significant in children under 16. The incidence of psychotic effects can be reduced when drugs such as diazepam are also used.” In contrast, an article in *Pediatric Anesthesia* written in the same year held ketamine to be “an excellent choice for procedural sedation in children, as its profound anaesthesia is associated with few respiratory and haemodynamic side effects.” (Lin and Durieux, 2005).

By 2007 the *British National Formulary* was rather less dismissive. It was saying that ketamine “has good analgesic properties at sub-anaesthetic dosage”, but it was still saying that the drug’s many “transient psychotic effects ... can be reduced by drugs such as diazepam” when, in fact, the use of a benzodiazepine does little to reduce the number of children troubled by ‘emergence phenomena’ (restlessness, hallucinations or nightmares). While minor problems of this nature are seen in up to a quarter of all children, real distress was only seen one in fifteen of all the children studied by Wathen *et al.* in 2000, and the use of midazolam in this randomised controlled trial did nothing to reduce the incidence of serious, if transient, distress during recovery (although it did make brief nausea and vomiting rather less common). In fact the Scottish Intercollegiate Guidelines (see below) strongly discourage the use of sedative cocktails, saying that “Sedative drug combinations should be avoided in children as they are often associated with deeper levels of sedation and with more adverse effects.”

A 2 mg/kg IV dose of ketamine administered over at least one minute is known to provide about 10 minutes of surgical anaesthesia after about 30 seconds, while a 1 mg/kg IV dose seems to be enough for any procedure that is not going to last more than 5 minutes, and seems to provide significant analgesia for twice this time (Herd and Anderson, 2007). The many different ways in which the drug can be given provide the clinician with useful added flexibility, because it has been given subcutaneously, transcutaneously, intranasally and intravenously, as well orally, rectally and by intramuscular injection (Kronenberg, 2002). In addition, because the onset of sedation by some of these routes is too slow to be of use when providing pain relief for emergency treatment, a ‘jet-injector’ technique was also developed some few years ago (Zsigmond *et al.*, 1996). Giving a simultaneous dose of atropine or glycopyrronium may reduce the risk of nausea and vomiting during recovery, and *does* reduce the incidence of troublesome salivation (Heinz *et al.*, 2006), but salivation is seldom a problem in very young children.

Potential hazards of use in the first year of life

Several large scale retrospective studies have recently been conducted into the use of ketamine in children (see below). Some have reviewed use in more than a thousand children. All have concluded that, in experienced hands, ketamine provides an extremely valuable and safe means of alleviated the stress and fear that young children frequently experience when admitted to an accident and emergency unit. The only commonly reported adverse reactions were emesis, ataxia, subclinical cyanosis, brief short-lasting behaviour abreaction, and agitation. However, very few of the children in these studies were less than a year old. The only reports yet traced report the use of IV or intranasal ketamine to provide analgesia without, if possible the need for intubation or general anaesthesia, in babies requiring retinal cryotherapy for retinopathy for prematurity (Tashiro *et al.*, 1991; Louon *et al.*, 1993). While there is no reason to suppose that ketamine is any less effective when used in a child as young as this, such use needs to be studied with equal rigour before it becomes yet another untested routine.

The small study undertaken by Sarrenmaa (2001) was, therefore, particularly welcome. It was designed to see if a 2 mg/kg IV bolus of ketamine would blunt or abolish the changes in heart rate and blood pressure caused by regular routine endotracheal suction. It did not. Whether it controlled the child’s conscious distress could not, of course, be determined. Perhaps the study should be repeated in some older children to see if it does. Since the babies on a continuous morphine infusion did not respond to routine tracheal suction differently from those on a placebo infusion in the recent, large, double-blind NEOPAIN trial either, we also need to accept that many of the behavioural responses seen during suctioning are not necessarily caused by pain. Some procedures are annoying rather than painful, and resistance is sometimes mostly reflex in nature. Responses of this nature are not going to be abolished by light anaesthesia, and this may not matter as long as the patient has no memory of it on waking.

Judging the efficacy of ketamine sedation in pre-verbal children is never, therefore, going to be easy. Realistically, any such study will probably have to assume that a dose that is effective in an older child is

going to be equally effective in the pre-verbal child, and then establish that such use is safe. Such studies are going to have to be as large as those that have now established the safety of ketamine use in older children. It also remains important to stress that ketamine should only be given to a patient of any age by an experienced intensivist, and to acknowledge that a range of other anaesthetic options will often be open to any clinician who has those skills (as summarised in the authoritative overview that Krauss and Green published in the *Lancet* in 2006).. Mild respiratory depression, cyanosis, and apnoea may well require attention during two per cent of all procedures. Such problems are not usually difficult to deal with. Acute laryngospasm is much less common, occurring perhaps once in every five hundred procedures (Morton, 2008), but a much more challenging one – nobody should be administering ketamine who is not confident that they know how to manage such a sudden complication.

The guidelines that SIGN, the Scottish Intercollegiate Guideline Network, issued in 2004 on providing safe sedation in children undergoing diagnostic and therapeutic procedures (www.sign.ac.uk/pdf/sign58.pdf) have been widely endorsed. They can be accessed from this web page by clicking [here](#).

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