

Annotations

Sedation for invasive procedures in paediatrics

It is inappropriate to subject children to distressing procedures if this can be avoided. Moreover, many procedures may be difficult or unsafe in the uncooperative child. The number of valuable but invasive techniques in use has increased steadily over the years, and to facilitate these, sedative agents are often given. Such use of sedation is generally supervised by non-anaesthetists. Despite the obvious benefits associated with this practice, there are unresolved concerns about its efficacy and safety.

The ideal sedative regimen would act predictably and rapidly and would induce a level and duration of sedation appropriate to the procedure being performed. In practice, few regimens are truly satisfactory in these terms. General anaesthesia may therefore be preferred, but for many procedures (for example, liver biopsy) this might seem inappropriate. Widespread use of general anaesthesia for these purposes would also have substantial resource implications for paediatric departments.

The use of sedation in our hospital is probably comparable with that in many similar institutions.^{1–3} Many children undergo cardiac catheterisation and other radiological procedures under sedation. Protocols vary, but often include high dose chloral hydrate, or a combination of temazepam and droperidol, and in many cases it is necessary to induce quite deep levels of sedation. As an indication of the volume and importance of this activity, magnetic resonance imaging alone accounts for more than 1100 procedures in our radiology department each year. We also perform about 800 gastrointestinal endoscopic procedures annually in infants and children, and for most of these we employ intravenous sedation using a combination of midazolam and pethidine.

Gastrointestinal endoscopy became part of paediatric practice about 20 years ago, and from the beginning this invasive technology posed great challenges with regard to sedation.³ In this article I shall discuss the difficulties and controversies surrounding endoscopic sedation in order to provide a focus on the issues of efficacy and safety with paediatric sedation in general.

Principles and definitions

The level of central nervous system (CNS) depression induced during sedation depends on the agents employed, the dose, the rate of administration, and the individual response. Thus the effects can vary along a continuum from minimal depression to general anaesthesia. Moreover, it is difficult to characterise the level of sedation precisely using clinical criteria. In general two apparently distinct states are commonly recognised, and these are referred to as 'conscious sedation' and 'deep sedation'. The distinction between these states is central to the debate about safety and efficacy.

Conscious sedation is *a medically induced state of CNS depression in which communication is maintained so that the patient can respond to verbal command*. By implication conscious sedation is associated with preservation of the protective reflexes, and the patient is able to maintain a patent airway independently.

Deep sedation is *a medically induced state of CNS depression in which the patient is essentially unconscious, and so does not respond to verbal command*. The subject is expected to

continue breathing spontaneously, but the protective reflexes may sometimes be impaired or lost, and the patient's ability to maintain a patent airway is not assured.

General anaesthesia is *a medically controlled state of CNS depression in which the patient is unconscious, and in which the protective reflexes and the ability to independently maintain a patent airway are lost*.

Three important issues arise from these definitions. Firstly, although there is a difference between conscious and deep sedation, patients may unexpectedly pass from one level to the other. Secondly, there are varying levels of deep sedation. Thirdly, there is an obvious overlap between deep sedation and general anaesthesia, and consequently some authorities do not accept that a distinction should be made between these states.

In the United Kingdom, recommendations and guidelines on the use of sedation have been produced by several professional bodies.^{4–7} These were formulated from a perspective largely informed by the needs of adult clinical practice, and all oppose the use of deep sedation by non-anaesthetists. Acceptance of this view would pose enormous difficulties in paediatric practice.

Sedation for gastrointestinal endoscopy

A skilled endoscopist can complete a thorough diagnostic upper gastrointestinal endoscopy (UGIE) in less than 10 minutes. Unfortunately, because UGIE elicits powerful protective reflexes it is a distressing experience for children unless they receive adequate sedation. Colonoscopy differs in that, although it is less acutely distressing, it often takes up to 40 minutes and it may cause transient discomfort or pain. There is no consensus with regard to the ideal approach to sedation for these procedures.³ The strategies currently employed mainly evolved from adult practice, but although similar intravenous sedatives (benzodiazepines and opiates) are employed, a much deeper level of sedation is usually induced.

ADULT ENDOSCOPY

In adult patients the serious complication and mortality rates associated with UGIE have been reported at 1/1000 and 5–30/100 000 examinations respectively.^{8–9} Many of these adverse outcomes have resulted from cardiorespiratory complications, and sedation has been a contributory factor.^{10–12} Surveys in the United Kingdom and the United States in the late 1980s indicated that 90% of adult endoscopists used intravenous sedation for UGIE.^{11–14} A benzodiazepine was usually employed, often in combination with an opiate. Although the populations are of course quite different, the mortality with UGIE must be compared with an overall mortality of only 1/185 000 for general anaesthesia.¹⁵ It was recently suggested that, even though adult patients have a clear preference for receiving sedation, consideration should be given to abandoning its routine use in the interests of safety.¹⁶

PAEDIATRIC ENDOSCOPY

Paediatric gastroenterologists who have received training in adult endoscopy units are aware that older patients often need relatively little sedation. Unfortunately, with conscious sedation young children usually become distressed

and agitated, and endoscopic procedures cannot be carried out without significant physical restraint. There is usually complete amnesia, and so some may consider this a tolerable situation. Many, however, would disagree. If endoscopic examinations are unduly hurried, their reliability may be compromised. Moreover, in such circumstances there may be dangers both to the patient and to the endoscopic equipment. If young children are to undergo gastrointestinal endoscopic examinations without general anaesthesia, then deep sedation is usually necessary. The true morbidity and mortality rates associated with sedation for paediatric endoscopy are quite unknown.¹⁷

There are no detailed protocols available for endoscopic sedation that have gained widespread acceptance. Published articles focusing on the practical aspects of paediatric endoscopy avoid precise recommendations with regard to sedation. In published medical reports, studies designed to compare sedative regimens have often involved relatively small numbers of subjects, and the sedative doses have been surprisingly low.¹⁸⁻²⁰ Although some have expressed satisfaction with particular regimens, close scrutiny of the results often suggests significant problems with efficacy.¹⁹ In reality, local practice varies, and the details are not readily accessible for public scrutiny. Personal experience suggests that the sedative doses employed in many centres are actually much higher than the manufacturers' recommendations, and that deep sedation is the intended or actual endpoint. In a recent personal survey of practice in nine United Kingdom centres, six relied on intravenous sedation rather than general anaesthesia and all used midazolam/pethidine combinations. The dosage regimens described varied widely, but four centres generally gave more than 5 mg of midazolam with 1-2 mg/kg of pethidine. Regimens such as this would induce deep sedation in many children.

OUR EXPERIENCE WITH ENDOSCOPIC SEDATION

Several years ago, in collaboration with our department of anaesthesia, we established a detailed written protocol for intravenous sedation, using a pethidine/midazolam combination (table 1). The intended sedation endpoint was one in which careful and unhurried endoscopic examinations could be carried out without persistent patient distress, and without the need for strenuous or prolonged physical restraint. It was accepted that transient episodes of agitation might occur, for example during the initial process of intubation, and that modest restraint might occasionally be necessary. The aim was to give the minimum quantity of sedation necessary to achieve this endpoint. Maximum permitted doses of midazolam and pethidine were specified. A designated trained nurse was given the sole task of monitoring the patient and of ensuring airway patency. Pulse oximetry was employed routinely, and oxygen was given if the saturation fell below 94%; if oxygen was required no further sedation was permitted.

We subsequently reviewed the outcome with this protocol in 100 children undergoing UGIE or colonoscopy, or both.²¹ The doses of intravenous sedation given are shown

Table 1 Protocol for endoscopic sedation

| | |
|--|--|
| <i>Oral premedication</i> | |
| UGIE | Midazolam (<2 years, 2 mg; >2 years, 4 mg) |
| Colonoscopy | Chloral hydrate (50 mg/kg, max 2000 mg) and chlorpromazine (1 mg/kg, max 25 mg) |
| <i>IV sedation (for both UGIE and colonoscopy)</i> | |
| Pethidine | Initial dose 1 mg/kg 0.5-1 mg/kg boluses; maximum permitted dose 2.5 mg/kg |
| Midazolam | 0.05-0.1 mg/kg boluses; maximum permitted dose 0.75 mg/kg (but never more than 15 mg total dose) |

UGIE = upper gastrointestinal endoscopy.

Table 2 Doses of sedation required for gastrointestinal endoscopy in our unit

| Procedure | Midazolam (median, range) | Pethidine (median, range) |
|-----------------------|-----------------------------|---------------------------|
| UGIE | 0.5 mg/kg (0.02-0.75 mg/kg) | 1.5 mg/kg (0-2 mg/kg) |
| Colonoscopy | 0.3 mg/kg (0-0.6 mg/kg) | 1.5 mg/kg (0-2.5 mg/kg) |
| UGIE plus colonoscopy | 0.3 mg/kg (0-0.6 mg/kg) | 0.5 mg/kg (0-2.5 mg/kg) |

UGIE = upper gastrointestinal endoscopy.

in table 2. It proved impossible to perform the endoscopy because of unsatisfactory sedation in just three cases. In 70% the outcome was considered highly satisfactory in that the intended sedation endpoint was achieved. In the remaining children sedation was less satisfactory, but the examination was nevertheless completed. In 14% oxygen was required for mild hypoxia, but all responded promptly and there were no episodes of severe or sustained hypoventilation. There was no correlation between the sedative doses (per kg) given and the occurrence of hypoventilation. This study showed that endoscopy could be performed reasonably satisfactorily in many children using a midazolam/pethidine regimen, but that as we had anticipated the sedative doses required were much greater than those recommended by the drug manufacturers and by other authorities.^{22 23}

One of the problems with this sedative regimen was that the duration of action was often inappropriate. Even though all were fit for discharge within six hours, close monitoring was often necessary for up to an hour after the procedure. This has both safety and resource implications. Consequently, we are currently performing a prospective comparison of the pethidine/midazolam regimen with a low dose intravenous ketamine regimen.

Our use of deep sedation is in principle consistent with practice in many paediatric institutions, both in the United Kingdom and elsewhere.^{1 2 24-26} It also is in keeping with the published recommendations of the American Academy of Pediatrics.^{27 28} However, it is at odds with recent United Kingdom recommendations and guidelines.⁴⁻⁷

Published recommendations and guidelines on sedation

In 1990 the General Dental Council's standing advisory committee addressed the use of general anaesthesia and sedation in dentistry.⁴ This committee held the view that deep sedation and general anaesthesia were to be considered as indistinguishable, and so should be supervised by an accredited anaesthetist. Conscious sedation was acceptable, and could be supervised by a dentist trained in the technique. It was advised that intravenous sedation should not be given to children because the effects were considered 'unpredictable'.

Since then several other professional bodies in the United Kingdom have produced recommendations on safe sedation, and all have expressed a similar view with regard to the use of deep sedation. In addition, they have given advice on other matters including the need for adequate facilities, equipment, personnel, and training. These recommendations appear to have been compiled without advice from paediatricians, and they reflect the needs of adult practice.

In 1991 the endoscopy committee of the British Society of Gastroenterology published recommendations on safe sedation for endoscopy.⁵ Conscious sedation was considered an acceptable endpoint, but deep sedation was not. It was stated that 'the manufacturer's recommended dose for any sedative should seldom be exceeded'. Benzodiazepine/opiate combinations were said to increase the risk of

adverse events, and were discouraged.²⁹ If an opiate was required for analgesia, drug doses were to be markedly reduced.

In 1992 a joint working party of the Royal Colleges of Anaesthetists and Radiologists produced a report on sedation and anaesthesia in radiology.⁶ This report restated the views of those preceding it regarding conscious and deep sedation. Importantly, it did acknowledge that some procedures, particularly in children, could not be performed under conscious sedation. However, it concluded that deep sedation required supervision by an anaesthetist.

In 1993 a set of guidelines for sedation by non-anaesthetists was produced by a working party of the Royal College of Surgeons of England.⁷ Again the view was expressed that any technique in which verbal contact with the patient was lost should be 'regarded as general anaesthesia.' This report addressed the pharmacological aspects of sedation in some detail. Benzodiazepines, carefully titrated, were considered to provide an adequate safety margin between conscious sedation and anaesthesia. Benzodiazepine/opiate combinations were again considered potentially hazardous, and if given, reduced doses were to be used. In many cases sedation would probably be administered by the individual performing the procedure, and so monitoring was to be the responsibility of a trained assistant. Appropriate training objectives for the individual supervising the process of sedation, and for the assistant monitoring the patient, were outlined. Basic life support (BLS) training was regarded as essential, and it was suggested that medical staff involved in supervising sedation should undergo advanced life support (ALS) training. The only available training courses for sedation were those introduced for dentists, and it was recommended that such courses should be established for others. Importantly, these guidelines included the following statement: 'Intravenous sedation is hazardous in children as the therapeutic margin between sedation and anaesthesia is very narrow. In view of this, [it] should be administered only under very special circumstances.' The evidence in support of this assertion was not cited.

In contrast to these various bodies, the American Academy of Pediatrics, recognising the realities of paediatric practice in the United States, has taken a different viewpoint.^{27, 28} In 1985 it issued a set of guidelines (revised in 1992) regarding the safe use of sedation. These differ from the various United Kingdom recommendations in one fundamentally important respect. The distinction between conscious and deep sedation was recognised, but both were considered acceptable endpoints, depending on the clinical requirements. Conscious and deep sedation required different levels of monitoring, and because any patient might unexpectedly become deeply sedated, it followed that one had to be prepared to upgrade the level of monitoring when necessary. The need to apply the same standards of monitoring in deep sedation as in general anaesthesia was recently emphasised in a publication from the Association of Anaesthetists of Great Britain and Ireland.³⁰ The recommendations from the American Academy of Pediatrics are in line with that view, but considered that *it was not mandatory that deep sedation should be supervised by an anaesthetist*. The responsible practitioner had to be trained in basic paediatric life support (BPLS), and advanced paediatric life support (APLS) training was strongly advocated.²⁸ A designated trained individual, was to monitor the patient's condition, and in the case of deep sedation this was to be their sole task. Many other safety issues were addressed in these recommendations. Continuous monitoring of heart rate and oxygen saturation was advised, and an anaesthetic type time based record of the patient's condition was to be

maintained. Emphasis was also placed on the need for continued monitoring and observation in an appropriately equipped recovery facility after the procedure, until various defined discharge criteria were met. These guidelines were designed to address the general principles of safe paediatric sedation. They did not therefore address specific issues such as the choice and administration of sedative agents.

Conclusion

In the United Kingdom, the General Dental Council, the Royal Colleges of Anaesthetists and Radiologists, the Royal College of Surgeons of England, and the British Society of Gastroenterology have each produced sets of guidelines regarding the safe use of sedation. All have refused to recognise a distinction between deep sedation and general anaesthesia. These guidelines have been written largely from the perspective of those involved in the care of adult patients.

Conscious sedation is quite inadequate for many procedures in young children, and in reality paediatricians routinely employ deep sedation to facilitate a wide range of investigations and treatments. No individual practitioner can take comfort from their own safety record in the use of sedation in children, because serious complications are likely to be rare.¹⁷ On the other hand, the view that deep sedation is inherently unsafe unless supervised by an anaesthetist is opinion based rather than evidence based. Paediatricians routinely work in neonatal intensive care units, and many become highly proficient at carrying out a range of activities that in other circumstances might be considered as appropriate responsibilities for an anaesthetist. Some have expressed the view that general anaesthesia should replace sedation, at least for certain specific procedures.^{31, 32} Others have cogently argued that in some circumstances deep sedation may actually be safer than general anaesthesia.²² The total abandonment of deep sedation as a technique for use by non-anaesthetists would have enormous logistic consequences for paediatric practice. Indeed it is possible that such a policy might imperil patient safety by delaying or preventing the use of various investigative and therapeutic techniques. On the other hand, careful consideration should be given to the appropriateness or otherwise of deep sedation for specific procedures. Recognising these realities, the American Academy of Pediatrics produced guidelines on the safe use of deep sedation in children. We in the United Kingdom should address this important subject.

M STEPHEN MURPHY

*Institute of Child Health,
The Nuffield Building,
Francis Road, Birmingham B16 8ET*

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Asthma treatment and growth

It is generally acknowledged that asthma may have an effect on children's growth independent of any treatment they may be receiving. The many studies showing this have been reviewed recently by Russell in this journal.¹ In summary, children with moderate to severe asthma may have a characteristic pattern of slowing of prepubertal growth, delayed puberty, and a late pubertal growth spurt, with catch up to an adult height within the expected target range. It is because of this effect that difficulties can arise in trying to separate the effects of asthma from the effects of any treatment in studies of growth in children with asthma.

Oral corticosteroids

There is little doubt that oral corticosteroids such as prednisolone can have a detrimental effect on growth. Martin *et al.*,² in a prospective survey over 14 years, showed that children who had received oral steroids were significantly shorter than either asthmatic children who had not received steroids or non-asthmatic controls. However, this difference in height was only seen at age 14 years, and no difference was apparent by 21 years, indicating that the main effect of oral corticosteroids was to cause growth delay and affect the timing of puberty. The degree of growth retardation has been clearly linked to the frequency of oral corticosteroid use.³ However, there is also evidence that adult height can be permanently reduced in some children who have received long term oral corticosteroids for asthma.⁴

Inhaled corticosteroids

These were initially introduced in the 1970s and have revolutionised the management of asthma. Earlier work on the possible effects of inhaled corticosteroids on growth was contradictory and was often based on retrospective studies. Littlewood *et al.*,⁵ in a report on 346 children, 81 of whom were receiving inhaled beclomethasone in doses ranging from 200 to 800 µg daily, showed that those on inhaled corticosteroids had significantly lower height standard deviation scores than those not on steroids. However, there was also a difference in age between the two groups, so they may have been demonstrating the natural pattern of prepubertal growth deceleration seen in the older corticosteroid treated patients. Although Balfour-

Lynn showed a high prevalence of delayed puberty in his study,⁶ there were no apparent adverse growth effects with beclomethasone doses of up to 600 µg daily. Similarly Ninan and Russell,⁷ in a study of 58 prepubertal children receiving budesonide or beclomethasone in doses ranging from 200 to 1600 µg daily, did not detect a relation between height standard deviation score and corticosteroid use. There was, however, a clear relation with asthma severity.

Despite these reassuring studies it has become apparent to some paediatricians, particularly those running growth clinics, that certain children on inhaled corticosteroids can grow extremely slowly, with growth rates far below those expected for delayed puberty alone. Wales *et al* reported six children with marked suppression of height velocity while receiving 400 to 1000 µg/day of beclomethasone,⁸ four of whom showed catch up growth on dose reduction. A similar observation was reported by Thomas *et al.*⁹

Additional information has come from the studies of Pedersen's group in Denmark, studying children with mild asthma to eliminate the potential effect of asthma severity on growth. They have used the technique of knemometry, which accurately measures changes in lower leg length velocity as an index of short term growth. An initial placebo controlled double blind study¹⁰ of eight weeks' treatment with budesonide showed a significant reduction in lower leg length growth velocity in children receiving 800 µg daily, whereas no difference from placebo was seen with doses of 200 or 400 µg daily. A further study¹¹ showed marked reductions in lower leg length growth velocity with beclomethasone when given in doses of 400 or 800 µg daily. The degree of suppression of growth rate was similar to that seen when they studied children receiving oral prednisolone in a dose of 2.5 mg/day.¹²

Although these studies have been criticised on the basis that short term changes in lower leg length velocity are not predictive of long term growth, their findings have been supported by three intermediate term studies. Crowley *et al* studied 56 prepubertal children with asthma over a 12 month period.¹³ They were divided into four groups: those children receiving no steroids, those receiving budesonide in a mean dose of 762 µg/m², those receiving beclomethasone in a mean dose of 560 µg/m², and a group of children