

# Distress at induction: prevention and consequences

Andrew Davidson<sup>a,b,c</sup> and Ian McKenzie<sup>a</sup>

<sup>a</sup>Department of Anaesthesia, Royal Children's Hospital,  
<sup>b</sup>Anaesthesia Research Group, Murdoch Childrens  
Research Institute and <sup>c</sup>Department of Paediatrics,  
University of Melbourne, Melbourne Australia

Correspondence to A/Professor Andrew Davidson,  
Department of Anaesthesia, Royal Children's Hospital,  
Flemington Road, Parkville, 3052 VIC, Australia  
Tel: +61 3 9345 5522; fax: +61 3 9345 6003;  
e-mail: andrew.davidson@rch.org.au

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## Purpose of review

Distress in children during hospitalization is increasingly seen as unacceptable and preventable. Surgery and anaesthesia are distressing events for children with maximum stress at induction of anaesthesia. This review aims to report the recent research relevant to reducing this distress in children with a focus on the preoperative period and the impact of this on behaviour at induction and long-term postoperatively.

## Recent findings

The development of new measures of anxiety in children, which are specifically designed to measure anxiety in the perioperative period has allowed better assessment of the efficacy of interventions. Studies continue to demonstrate that a variety of nonpharmacological interventions have a modest effect in reducing anxiety and that sedative premedication is more effective. Clinical indications for preoperative sedative/ anxiolytic medication across institutions are very variable. Clonidine and dexmedetomidine ( $\alpha$ 2-adrenergic agonists) produce satisfactory sedation in children but have long onset times. Recent focus on the importance of minimizing children's distress in clinical areas outside the operating suite is creating pressure on anaesthetists to reassess what is considered 'acceptable' in relation to distress at induction of anaesthesia. The ChildKind Initiative summarizes pain minimization strategies, which should be applied to children. It is logical to extend this concept to minimization of distress unrelated to pain.

## Summary

New measures of anxiety will facilitate better evaluation of children clinically and better future research. The role of  $\alpha$ 2-adrenergic agonists in premedication remains unclear. There is still little research, which examines outcomes for techniques for minimizing distress, which are based on specific assessment of the child and family.

## Keywords

anxiety, behavioural change, paediatric anaesthesia, premedication

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## Introduction

It is increasingly recognized that hospitalization should not be regarded as inevitably distressing for children. In the 21st Century, we should be striving to ensure that all children are managed in ways that minimize distress. This is not only an ethical imperative but it also improves compliance and prevents long-term behavioural issues. There are many ways in which children are distressed by their experience in hospital and there are many ways we can reduce that distress.

This review focuses on the perianaesthetic period in children. Managing procedural pain and distress in children separate to anaesthesia episodes is crucial for the child's outcome but is outside the scope of this review. Behavioural issues relating to emergence from anaesthesia such as emergence agitation or delirium are also not

addressed. This update summarizes significant papers published in the latter part of 2009 and 2010.

## Perioperative anxiety in children: measures, predictors and consequences

It has long been recognized that anaesthetic induction is an anxiety provoking time for children and that preoperative anxiety is associated with postoperative behavioural changes. Risk factors for anxiety at induction have been well described, although they vary somewhat from study to study depending on the population and tools used to measure anxiety.

Recently, Chorney and Kain [1•] examined in detail the behaviour of 293 children during induction of anaesthesia. They confirmed that a high proportion of children are distressed at anaesthesia induction; 40% of children

showed some signs of distress, with 17% having significant distress, whereas 30% resisted efforts to induce anaesthesia. Acute distress was seen particularly in younger children, whereas anticipatory distress was seen across all ages. There was a strong association between behaviours exhibited while walking to the operating room and those exhibited during induction. In another study, Fortier *et al.* [2] examined predictors of anxiety in the preoperative period. Unlike many earlier studies, Fortier *et al.* measured anxiety in the postoperative period as well. They found that anxiety peaked at induction and steadily declined postoperatively. Low sociability in the child and high anxiety in the parents were factors associated with child anxiety. These two studies highlight the growing understanding of the importance of assessing the entire perioperative experience in detail, as well as closely examining the nature of the distress.

The Spielberger State-trait Anxiety Inventory (STAI) and the modified Yale Preoperative Anxiety Scale (m-YPAS) are tools used to measure anxiety. The STAI is lengthy and difficult to administer in the clinical setting, whereas the m-YPAS is specifically designed to assess anxiety at the point of induction. Bringuier *et al.* [3\*\*] evaluated a visual analogue anxiety scale, which might be used throughout the perioperative period. They found the scale to be valid and easy to use. The Perioperative Adult Child Behaviour Interaction Scale (PACBIS) has also been developed to provide a more robust measure of child distress in the perioperative period. It was recently evaluated by Sadhasivam *et al.* [4\*\*] and found to be reliable and easy to use. Clinically, these tools can provide standardized ways to assess distress, which can focus the individual clinician's attention and allow charting of a validated measure. This can facilitate improvement in assessment of distress and the efficacy of interventions for that patient. For research purposes, improved assessment tools should improve the quality and comparability of the data in this important area.

### Postoperative behaviour

Postoperative behaviour change is a recognized measure of the consequences of perioperative distress. To examine the predictors of behaviour change, Fortier *et al.* [5] reanalysed the data in a previously published study but this time controlled for pain. There was a high incidence of behaviour change with pre-existing somatic and anxious/depressed children more likely to exhibit postoperative general anxiety. Younger children were more likely to develop separation anxiety and children with inhibited temperament were more likely to have sleep disturbance. This study used the Post Hospitalisation Behaviour Questionnaire (PHBQ) as the outcome measure. This behaviour assessment tool was developed

### Key points

- Distress is common in children in the perioperative period.
- Nonpharmacological interventions have a modest impact.
- Sedative premedication is effective.
- Clonidine and dexmedetomidine are effective but have slow onset times.

in the 1960s and has been widely used in research in this area for decades. Lopez and Habre [6\*\*] have written a thought-provoking editorial in which they argue the tool is inherently flawed and has never been tested for validity and reliability. There is a striking lack of consistency between studies using this tool with frequency and duration of behaviour disturbances varying considerably.

One criticism of the PHBQ is that there is no consistency in how to construct a summary score. There is also no consistency in accounting for situations in which behaviour actually improves. Howard *et al.* [7\*] looked at a cohort of children after otolaryngological surgery using the PHBQ and the Pediatric Quality of Life Inventory Core Scales (the PedsQL). The PedsQL has been very carefully validated and is used in many fields of child health research to assess function and quality of life. In the study by Howard *et al.*, the PedsQL demonstrated that, at day 7, physical functioning was worse than that preoperatively, whereas social functioning was unchanged, but, at day 30, both physical and social functioning were better than that preoperatively. A similar result was seen with the PHBQ if both deterioration and improvement in behaviour were considered. The preoperative PedsQL values were lower than normal for the general population at that age. This last finding is very interesting and implies that children have poor functioning and are distressed in the period before surgery. This means that preoperative assessments of children are made at a time when a child (and family) is more distressed than 'usual'. Children's PedsQL values tend to return to normal (i.e. better than the lower than normal preoperative values) in delayed fashion after surgery. It is unclear whether this improvement from preprocedure relates to improvement in the underlying surgical condition or relief of the preprocedure anticipatory stress. If anticipatory stress is a significant contributor, this adds weight to the argument for providing better support and preparation well before surgery is scheduled.

One possible consequence of a stressful perioperative experience is poor compliance with future medical therapy, including anaesthesia. This suggestion is supported by data from Proczkowska-Bjorklund *et al.* [8] who found that children who were younger or reluctant

to take their premedication were more likely to avoid playing with anaesthetic equipment 14 days after a procedure.

### Managing the distressed resisting child

The management of the resisting combative child or one who is assessed as at high risk for this behaviour is controversial. A recent survey of members of the Association of Paediatric Anaesthetists of Great Britain and Ireland found a wide range of opinions. Oral premedication, intramuscular ketamine and distraction were often used for these high-risk children. A flexible approach tailored to the circumstances was considered important in areas such as induction technique as was the ability to reschedule with a different preparation and plan. Intramuscular ketamine is sometimes used. Physical restraint for induction of anaesthesia was confirmed as a controversial area with respect to what constituted physical restraint, what degree of restraint was acceptable and in what circumstances. The majority of respondents rarely or never let a child be wholly restrained by staff members, especially in older children. Restraint by parents and partial restraint were commonly used, especially for younger children. Physical restraint was more frequently used if the surgery was urgent or if the child had 'special needs' [9<sup>•</sup>]. There are no studies examining the behaviour of children postoperatively when they have had physical restraint for induction.

Many formal studies examining anxiety and premedication have exclusively studied children without neurobehavioural problems. These data cannot be simply extrapolated to children with neurobehavioural problems, yet the children with behavioural problems are at high risk of distress and provide a significant clinical challenge. Children with neurobehavioural problems are more likely to require anaesthesia and the cognitive problems and anxiety that these children have make preparation and management more difficult. Failure to address the issues may result in distressing procedures, which are likely to exacerbate the anxiety and behavioural issues for subsequent procedures. Tait *et al.* [10<sup>•</sup>] compared induction and postoperative behaviour in children with attention deficit hyperactivity disorder (ADHD) and normal children. They found that children with ADHD were less cooperative at induction and had a greater risk of maladaptive behaviours postoperatively. This result, along with findings described by Homer and Bass [9<sup>•</sup>], suggests that children with neurobehavioural problems are a high-risk group and should be the focus of future research into perioperative distress in children. There are no studies examining what is the best premedication for these children.

### What is new in nonpharmacological management of anxiety at induction of anaesthesia?

Apart from sedative premedication, a variety of other techniques are used to reduce distress and increase compliance in children at induction of anaesthesia. The most important recent publication is a Cochrane review. This review included 17 trials of nonpharmacological interventions. Eight studies examined parental presence with none finding any improvement in child anxiety with parental presence. Effective interventions included using computer packages, hand-held video games, clowns and a low sensory environment. No evidence for effect was seen with music and hypnosis [11<sup>••</sup>].

An evidence-based review specifically examining parental presence has also been published. The investigators found no evidence that parental presence reduces child or parental anxiety at induction of anaesthesia [12]. Recently, Wright *et al.* [13] argued that benefits of parental presence have been masked in previous studies including older children wherein parental presence is less likely to be helpful. They studied 3–6-year-old children and found that the parental presence did decrease anxiety at separation, but there was no evidence for a difference at induction of anaesthesia. Maintaining parental presence remains common practice, with the majority of paediatric anaesthetists polled at a recent meeting indicating that they had one parent present for the majority of the inductions and a substantial number included both parents. It is clear that parental presence *per se* does not decrease distress at induction. The role, confidence and engagement of the parent are key issues that are not assessed by studies of 'presence' of parents. The effect of parental presence on the child's long-term perception of the event and stress levels in relation to further medical interventions are also worthy of examination and may reveal benefits not apparent in the acute phase (see 'Recovery' below). A key difference in process in different parts of the world is whether the person administering the anaesthesia has had a chance to consult and create a personal connection with the child and family prior to the induction of anaesthesia. Chorney and Kain [14<sup>••</sup>] have written an excellent review on family-centred care in paediatric perioperative care. In this, they argue that parental presence at induction is an integral part of respecting the parent's wishes and engaging the parents in decision-making processes. The review also outlines the importance of providing information not only to the children but also to the parents as part of preparing the entire family in the preoperative period. Information should be procedural and sensory (what will happen and what the child will feel), sufficiently detailed and delivered in a developmentally appropriate manner. The child should also be taught coping mechanisms. This

approach has the potential to decrease distress relating to anticipation of the procedure, distress relating to associated interventions such as pathology or imaging separate to anaesthesia induction, as well as distress in the posthospital phase. Assessment of the efficacy of this approach should examine these broader areas and not just the immediate perioperative period.

Vagnoli *et al.* [15] studied a population of children aged 5–12 years of age who were all accompanied by a parent. One group had a parent and a clown, another a parent and midazolam premedication and a third group had the parent alone (control). They found evidence for a reduction in anxiety in the parent and clown group compared to the other two groups. There was no evidence for a difference between the premedication and parent group and the parent only control.

Maternal voice has also been shown to reduce anxiety. Kim *et al.* [16] randomly assigned children having cardiac catheter studies under ketamine anaesthesia to a group wherein a recording of their mother's voice was played continuously from the preoperative holding area to the postanaesthesia care unit (PACU), or a control group. Both anxiety at induction and emergence agitation were decreased in the mother's voice group.

### What is new in sedative premedication?

Sedative premedication is widely used to reduce preoperative anxiety and facilitate anaesthesia induction in children. Although it has been shown to be more effective in reducing anxiety than most other preparation programmes, its use is still debated. The use of sedative premedication varies from routine use for all children to some that use it very rarely. A provocative pro-con debate has recently highlighted the issues [17<sup>••</sup>]. Most paediatric anaesthetists use sedative premedication selectively and many see it as a supplement rather than alternative to other strategies to reduce anxiety such as parental presence, family preparation and psychological techniques. It remains a challenge to identify those children and circumstances wherein premedication will be most effective. The results of studies that enrol all children are not directly applicable to the many practices in which premedication is only prescribed to selected patients. Similarly, the overall management of the child and family may mean that there are major differences in outcome in different institutions separate to the effect of premedication.

Midazolam is still used widely for sedative/anxiolytic premedication. A recent study by Kazak *et al.* [18] found similar levels of anxiety comparing midazolam 0.5 mg/kg without parental presence to midazolam 0.25 mg/kg with parental presence, whereas parental presence without

any midazolam resulted in greater anxiety. This study confirms the efficacy of midazolam compared with parental presence alone. It raises questions about the possibility of an effective lower dose of midazolam and whether the efficacy of the lower dose was dependent on parental presence.

The potential for adverse effects relating to midazolam in some children [17<sup>••</sup>] has increased interest in alternative sedative premedication. The  $\alpha$ 2-adrenergic agonists clonidine and dexmedetomidine have sedative and analgesic properties and have been increasingly investigated. The  $\alpha$ 2-adrenergic agonists are essentially tasteless and nonirritant. This contrasts with the unpleasant taste associated with midazolam, which creates issues with compliance and a need for special preparations to mask the flavour if given orally (as is usual). If administered topically via the nasal mucosa, midazolam stings.

Dahmani *et al.* [19<sup>•</sup>] performed a meta-analysis of trials comparing clonidine 2–4  $\mu$ g/kg and midazolam or diazepam 0.2–0.5 mg/kg. Ten trials were included and outcomes of interest were sedation at induction, emergence agitation and postoperative pain and vomiting. Analysis of two studies that compared midazolam and clonidine for preoperative sedation found clonidine to be superior. Analysis of three studies that compared diazepam to clonidine found no evidence for a difference in preoperative sedation. These results must be treated with caution given the small numbers and considerable heterogeneity between studies. The meta-analysis also found evidence that clonidine was superior to benzodiazepines in preventing emergence agitation and postoperative pain. The use of clonidine is limited by its long duration of action and slow onset of effect.

Dexmedetomidine is a highly selective  $\alpha$ 2-adrenergic agonist. It produces sleep or drowsiness, but the child remains easy to arouse and cooperative once aroused. The sedation is dose-dependent and there is minimal respiratory depression, even at large doses. Dexmedetomidine has a shorter duration of action than clonidine so may be more suitable as premedication. Yuen [20] recently reviewed dexmedetomidine's role in paediatric anaesthesia, including its use as premedication. Dexmedetomidine has a low bioavailability when given orally (15%) but may be more effective when given intranasally. In an earlier study, 1  $\mu$ g/kg of intranasal dexmedetomidine was more effective as a sedative than 0.5 mg/kg oral midazolam [21]. Like clonidine, dexmedetomidine has a slow onset and with an onset time of 30–45 min. Yuen *et al.* [22<sup>•</sup>] also studied the optimal time for administering intranasal dexmedetomidine. The median onset of sedation after 1  $\mu$ g/kg of intranasal dexmedetomidine was 25 min, though the authors recommend the dexmedetomidine be given at least

30 and preferably 45 min prior to the procedure. The duration of sedation was 85 min.

Transmucosal administration of dexmedetomidine via the buccal rather than nasal route has also been studied. Sakurai *et al.* [23] compared 3–4 µg/kg of buccal dexmedetomidine to 0.7 mg/kg of oral diazepam, both given 60 min before induction. The dexmedetomidine group displayed greater sedation at induction compared to the diazepam group. Limitations with this study include that participants were not randomized and the observer was not blinded. The recovery times were also not reported and the 60-min period between premedication and induction may not be practical clinically.

Dexmedetomidine and clonidine have similar efficacy to midazolam in producing sedation, but the  $\alpha_2$ -adrenergic agonists may have some advantages in providing analgesia, fewer paradoxical reactions and less agitation on arousal. The long onset time could remain a problem for their use clinically. As with many other interventions, there is a need for more data about the role of  $\alpha_2$ -adrenergic agonists in a population of ‘higher risk’ children in institutions where premedication is selectively prescribed.

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## Recovery

Emergence agitation and delirium are important issues that have been the subject of a large volume of recent research, which would require a separate review for satisfactory analysis. There are substantial issues with defining and measuring agitation versus delirium or pain, and in assessing the influence of preoperative state, premedication, distress at induction, quality of analgesia and anaesthesia and other drugs on emergence.

Despite the focus on the role of parental presence at induction of anaesthesia, there have been few studies examining parental presence on emergence or in the PACU. Lardner *et al.* [24<sup>\*</sup>] performed a randomized controlled trial comparing parental presence and no parental presence in the PACU. They found no evidence for a difference in crying in the PACU, but children allocated to the parent present group had less behavioural regression 2 weeks after going home. This is a fascinating observation that has many ramifications for the assessment of the importance of ‘family-centred care’. If similar results apply to parental presence at induction, it may be the important delayed effects, which show the benefit rather than the actual response to induction that is usually studied.

Similarly, there has been little study on the impact of music on recovery from anaesthesia in children. In a randomized trial, Nilsson *et al.* [25] found that playing

proprietary calming music in the postanesthetic care unit reduced distress and morphine consumption in children aged 7–16 having day surgery.

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## A global approach

The ChildKind Initiative and associated ‘Bellagio Declaration’ summarizes pain minimization strategies that should be applied to children. The initiative is supported by many organizations, including the World Federation of Societies of Anesthesiology (WFSA) ([http://www.iasp-pain.org/PainSummit/ChildKind\\_Initiative2010.pdf](http://www.iasp-pain.org/PainSummit/ChildKind_Initiative2010.pdf)). Pain is almost universally distressing, but many children suffer significant distress in hospital unrelated to pain. It is logical to extend this concept to minimization of distress unrelated to pain.

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## Conclusion

Recent review and research has highlighted the importance of reducing distress in children in the perioperative period. Important advances have been made in better understanding the nature of this distress and in generating validated measures that are more applicable to the perioperative period. These improved measures will lead to both easier and more accurate assessment clinically and to better quality future research.

Recent studies show that a variety of nonpharmacological interventions have modest effects on reducing distress. Sedative premedication is more effective, but there is continued debate over the extent to which it should replace or supplement nonpharmacological interventions. There is increasing interest in the  $\alpha_2$ -adrenergic agonists, clonidine and dexmedetomidine. The  $\alpha_2$ -adrenergic agonists produce sedation as effectively, or more effectively, than midazolam but have slow onset and recovery times.

Translating research to practice is difficult. Most studies of premedication recruit from all healthy children, including many ‘low-risk’ children and often excluding children with neurobehavioural issues. Only one study specifically examines children with neurobehavioural issues. Clinical practice frequently directs interventions selectively to those who are perceived most at risk of distress. Assessing the value of the role of parents during induction of anaesthesia is also difficult. The data are limited in that most studies examine only ‘parental presence’ (and not the parent’s role, confidence and engagement in the process) and do not look at potential late benefits in the child’s behaviour, confining observations to the induction or immediate perioperative period.

The anaesthesia community should continue its efforts to minimize distress in the perioperative period. There is

growing evidence that when seen from the child's and family's perspective, these efforts may be of minor impact unless integrated with programmes aimed to minimize distress from the time of booking and at all other points of intervention (e.g. preoperative tests). Engagement of the family in the child's care may have beneficial late outcomes that are missed if only induction and PACU distress is assessed.

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## References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 357–358).

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