Original Article

The effect of dexmedetomidine on postoperative behaviour change in children: a randomised controlled trial

P. F. Lee-Archer,[1,2] B. S. von Ungern-Sternberg,[3,4] M. Reade,[5] M. Betts,[6] D. Haenke,[6] A. Keys,[6] T. Rance,[6] K. Gibbons[7] and D. Long[8]

1 Consultant, 6 Fellow, Department of Anaesthesia, Queensland Children's Hospital, Brisbane, Australia

2 PhD candidate, 5 Professor of Military Surgery and Medicine, Royal Brisbane Clinical Unit, 7 Associate Professor, Senior Epidemiologist, 8 Associate Professor, Paediatric Critical Care Research Group, Child Health Research Centre, Faculty of Medicine, University of Queensland, Brisbane, Australia

3 Consultant, Department of Anaesthesia and Pain Management, Perth Children's Hospital, Perth, Australia

4 Professor, Medical School, University of Western Australia, Perth, Australia

Correspondence to: P.F. Lee-Archer

Email: Paul.Lee-Archer@health.qld.gov.au

Twitter:

Key words: dexmedetomidine; paediatrics; children; emergence delirium; behaviour changes

Accepted: 2 May 2020

This article is accompanied by an editorial by Bailey CR. Dexmedetomidine in children: when should we be giving it?

Summary

Children may develop changes in their behaviour following general anaesthesia. Some examples of negative behaviour include temper tantrums, nightmares, as well as sleep and eating disorders. The aim of this study was to determine whether dexmedetomidine reduces the incidence of negative behaviour change after anaesthesia for day case surgery in children aged two to seven years. Children were randomly allocated to one of three groups: the premedication group received 2 μg.kg-

[1] intranasal dexmedetomidine; the intra-operative group received 1 μg.kg^{-1} intravenous dexmedetomidine; and a control group. The primary outcome was the incidence of negative behaviour on postoperative day 3 using the Post-Hospitalisation Behaviour Questionnaire for Ambulatory Surgery and the Strength and Difficulties Questionnaire. Secondary outcomes included: the incidence of negative behaviour on postoperative days 14 and 28; anxiety at induction; emergence delirium; pain; length of recovery and hospital stay; and any adverse events. Of the 249 children randomised, two did not undergo surgery and data for 247 patients were analysed. Negative behaviour change on postoperative day 3 was similar between all three groups when measured with the Post-Hospitalisation Behaviour Questionnaire for Ambulatory Surgery (47%, 44% and 51% respectively; adjusted p=0.99) and the Strength and Difficulties Questionnaire (median scores 7.5, 6.0 and 8.0 respectively; adjusted p=0.99). The incidence of negative behaviour in the group who received dexmedetomidine intra-operatively was less at postoperative day 28 (15% compared with 36% in the dexmedetomidine premedication group and 41% in the control group, p<0.001). Median time to discharge was longer in children who received dexmedetomidine (173 minutes in the dexmedetomidine premedication group, 169 minutes in the dexmedetomidine intra-operative group and 139 minutes in the control group, p<0.001). Children who received dexmedetomidine had less pain and less emergence delirium. There were no serious adverse events related to dexmedetomidine. We conclude that dexmedetomidine does not reduce the incidence of negative behaviour on postoperative day 3 in children aged two to seven having day case procedures; however, the administration of an intra-operative dose resulted in a lower incidence of negative behaviour a month after discharge.

Introduction

Children requiring surgery under general anaesthesia may subsequently develop changes in their behaviour. These changes can occur during early recovery from anaesthesia or may be delayed until days and weeks after surgery. Acute behavioural changes are characterised by an alteration in a child's awareness of their surroundings and disorientation [1]. Delayed behaviour change (known as post-hospitalisation behaviour change) is characterised by sleep and eating disorders, temper tantrums, nightmares and anxiety. Post-hospitalisation behaviour change has been reported as occuring in more than 50% of children having a general anaesthetic and have some risk factors in common with emergence delirium, such as pre-school age and underlying anxiety [2,3]. These changes may lead to increased general practitioner visits, parental time off work and reduced compliance with future episodes of healthcare [4]. Dexmedetomidine is a highly selective alpha-2 adrenergic agonist that has been shown to be effective at reducing the incidence of emergence delirium in children; however, its effect on postoperative behaviour change has not been evaluated [5]. Dexmedetomidine has been reported to reduce peri-operative anxiety and, as a result, may be an effective therapy for post-hospitalisation behaviour change when given as a premedication. It also has anti-inflammatory, analgesic and neuroprotective effects which may make it effective when given pre-operatively or intra-operatively. The aim of this study was to determine whether dexmedetomidine is effective at reducing post-hospitalisation behaviour change in children aged between 2 and 7 y following day case procedures. A secondary aim was to ascertain whether there is a greater benefit to administering it as a premedication, or whether the same effect can be achieved by giving it intra-operatively.

Methods

We recruited children aged 2-7 y, booked for elective day case procedures. Exclusion criteria were: significant comorbidities (ASA physical status 3 or above); allergy to dexmedetomidine; anti-hypertensive medication, ; existing behavioural problems (defined as being under the care of a paediatrician for behavioural problems or currently taking medications for behavioural issues or attention deficit hyperactivity disorder); procedure was predicted to take < 10 min; or if the child was assessed as requiring premedication by the attending anaesthetist on the day of surgery.

After obtaining written informed consent from parents, and before surgery, a researcher collected baseline data from the family. This included: child's age; sex; number of siblings; number of previous surgical procedures; parent's level of education; ethnicity; type of surgery; the child's temperament (measured using the Emotionality, Activity, Sociability Temperament Survey); the parent's baseline anxiety (measured using the State-Trait Anxiety Inventory; and the child's baseline score on the Strengths and Difficulties Questionnaire (SDQ). A score on the Modified Yale Preoperative Anxiety Scale was obtained at two time-points by a researcher: before the intervention whilst the child was in the holding bay; and at the time of induction. We randomly allocated children to one of three groups in a 1:1:1 ratio in permutated blocks using an online randomisation system (Griffith University, Brisbane, Australia). Forty minutes prior to the procedure children received a nasal spray. Children in the dexmedetomidine premedication group received 2 $\mu g.kg^{-1}$ intranasal dexmedetomidine (dexmedetomidine HCl, Precedex; Hospira, Lake Forest, IL, USA) via a mucosal atomisation device (MAD^{TM}, Teleflex, San Diego, CA, USA). Children in the other two groups received a nasal spray of the same volume of saline prepared by an intensive care nurse that appeared identical to the study drug. The researcher, parents, children, treating anaesthetist and those assessing outcomes were all blinded as to group allocation. Only two intensive care nurses who prepared the medications for each child were made aware of the allocation of participants and were not otherwise involved in the study. Children were then accompanied by a parent to the operating theatre where an anaesthetist, blinded to group allocation, induced general anaesthesia using an inhalational or intravenous method at their discretion. After induction, the anaesthetist administered the study intravenous solution over 10 min. Children in the intra-operative dexmedetomidine group received 1 $\mu g.kg^{-1}$ of dexmedetomidine made up in a solution of saline to a concentration of 1 $\mu g.ml^{-1}$. Children in the intra-operative or placebo groups received the same volume of saline made up by an intensive care nurse to appear identical to the study drug. The intranasal and intravenous doses were chosen based on the bioavailability of dexmedetomidine reported in pharmacokinetic studies of dexmedetomidine [6,7]. After the procedure, each child was taken to the recovery area where a researcher recorded adverse events; intra-operative analgesia

administered; the initial pain score in recovery; analgesic requirements in recovery; incidence of emergence delirium; time to discharge from recovery; and time to discharge home.

On day 3 following the procedure, parents were contacted by telephone and the presence of any negative behaviour change was assessed using the Post-Hospitalisation Behaviour Questionnaire for Ambulatory Surgery (PHBQ-AS) and the SDQ. The child's pain score and parental satisfaction with the anaesthetic were also recorded. Parental time off work and general practitioner visits were also recorded. The same assessments were repeated on postoperative days 14 and 28.

The PHBQ-AS is an 11-item parental report measure used to assess negative behaviour change after hospitalisation. It is a revised and updated version of the original PHBQ which contained 27 items [8]. The PHBQ-AS was developed by examining the California Irvine School of Medicine database of children who had been assessed using the original PHBQ in 17 studies over 15 years (n=1064, mean age= 5.88, SD 2.32, range 1.97–12.00) [9]. The authors suggest that the revised, shortened questionnaire may be more relevant for day case procedures as well as being more efficient and valid [9]. Each item had a 'not applicable' option to avoid problems with missing data. A summed score was obtained by allocating a score of 1–5 for each item with any 'not applicable' responses scoring 3, indicating no behaviour change. A score above 3 indicated the presence of negative behaviour change, a score of 3 indicated no change in behaviour and a score less than 3 indicated an improvement in behaviour. We dichotomised the results into the presence or absence of negative behaviour change and also calculated it as a continuous variable.

The SDQ is a validated behaviour screening tool for children aged 2–16 y, consisting of 25 items on 5 scales. We used the follow-up versions for children aged 2–4 y and 4–10 y. These versions are designed for use after an intervention [10]. Reliability, construct and criterion validity and measurement invariance have been established for preschool aged children [11].

Child temperament was measured using the Emotionality Activity Sociability Temperament Survey; parental anxiety was measured using the State Trait Anxiety Inventory; child anxiety was measured at baseline and at induction using the Modified Yale Preoperative Anxiety Scale; emergence delirium was measured using the Cornell Assessment of Paediatric Delirium; a numeric rating scale was used when asking parents to rate their child's pain; and the Face, Legs, Activity, Cry, Consolability Scale was used when assessing pain in the recovery unit. For a full description of the outcome measurement tools used, please refer to the published study protocol [12].

The primary outcome was the prevalence of negative behaviour change measured at day 3 after surgery. The prevalence and severity of negative behaviour change was recorded using the PHBQ-AS

and the SDQ. Secondary outcomes were: anxiety at induction; emergence delirium; pain; length of stay in recovery and in hospital; parental satisfaction; and adverse events.

Based on published data of trials that have used the same diagnostic criteria as the present study, negative behaviour on postoperative day 3 was conservatively estimated to be 50% [2-4]. We defined a clinically significant reduction in negative behaviour as a 50% reduction to an overall rate of 25%. The effect size was calculated by determining the difference in proportions between two of the three groups and pooling the data from the two comparison groups. Therefore, 78 patients per group were required to detect a 50% reduction in negative behaviour change on day 3 after surgery, assuming a power of 90% and an alpha error of 5%. Due to the possibility of loss to follow-up, we continued recruitment until there were 234 complete day 3 follow-ups.

Data were collected and managed using REDCap electronic data capture tools hosted at Griffith University, Queensland, Australia. Data were analysed using StataSE version 14 (StataCorp Pty Ltd, College Station, TX, USA). Normally distributed variables were compared using analysis of variance. Non-parametric data were compared using the Kruskal Wallis test. Categorical variables were analysed using Fisher's exact test. In the event of a statistically significant difference, post-hoc comparisons were undertaken to determine which groups were different; appropriate adjustment for multiple comparisons were made. The p values for primary outcome measures (PHBQ-AS and SDQ at day 3) were also adjusted for multiple comparisons with Bonferroni's correction; further corrections were not undertaken for secondary outcomes. A p value <0.05 was considered statistically significant.

Results

We enrolled 249 children in the study; however, two were excluded and so data from 247 children were analysed. A CONSORT flow diagram of recruitment is shown in Figure 1. Baseline characteristics of the patients and intra-operative data are shown in Table 1.

The incidence of negative behaviour changes on postoperative day 3 was similar in all three groups when measured using the PHBQ-AS and is shown in Table 2 (dexmedetomidine premedication group = 47%, dexmedetomidine intra-operative group = 44% and control group = 51%, adjusted p=0.99). Improvement in behaviour was also similar across the three groups (8%, 17% and 10% respectively, p=0.22). The incidence remained similar on postoperative day 14 in all three groups. At postoperative day 28 there was a significant reduction in the incidence of negative behaviour change in the dexmedetomidine intra-operative group (Table 3). The mean (SD) PHBQ-AS scores on postoperative day 3 were 3.12 (0.29) in the dexmedetomidine premedication group, 3.12 (0.24) in the dexmedetomidine intra-operative group and 3.12 (0.27) in the control group, p=0.99. On postoperative day 14 the mean (SD) PHBQ-AS scores were 3.07 (0.35), 3.07 (0.25) and 3.09 (0.26) respectively, p=0.91. On postoperative day 28 they were 3.05 (0.24), 3.02 (0.18) and 3.06 (0.33) respectively (p=0.73.

When using the SDQ as the outcome measure, the median scores on day 3 were similar in all three groups and remained similar throughout the follow-up period (Tables 2 and 3). The incidence of children considered at high risk for negative behaviour, defined as an SDQ score above 13, was 31% in the premedication group, 20% in the intra-operative group and 21% in the control group at baseline (p=0.24) and by day 28 they were 13%, 13% and 20%, respectively (p=0.45).

There were no significant differences between groups in terms of anxiety, either pre-operatively or at induction. The rates of high anxiety at induction were similar in all three groups (Table 3).

The incidence of pain reported in recovery, was 5% in the dexmedetomidine premedication group, 6% in the dexmedetomidine intra-operative group and 16% in the control group, p=0.04.

Emergence delirium was recorded in seven patients (3%). Of these, five were in the control group and one was in each of the treatment groups (p=0.22). Two of the seven cases were hypoactive in nature (i.e. detected by the hypoactive items of the Cornell Assessment of Paediatric Delirium but not the hyperactive items).

The median (IQR [range]) length of stay in recovery for dexmedetomidine premedication, dexmedetomidine intra-operative and control groups were 45 (37-60 [25-125]), 49 (40-65 [23-130])

and 36 (30-45 [19-85]) min, respectively (p<0.001). The median (IQR [range]) hospital lengths of stay were 173 (145-230 [80-326]), 169 (140-197 [100-890]) and 139 (105-177 [70-460]) min, respectively (p<0.001).

One adverse event (hypertension requiring admission to intensive care) was reported to the Drug Safety Monitoring Board, however it determined that it was unlikely to be related to dexmedetomidine. There were three minor adverse events related to low heart rate, one in the dexmedetomidine premedication group and two in the dexmedetomidine intra-operative group. Seven patients received treatment for a low heart rate or low blood pressure, three in each of the treatment groups and one in the control group. The mean (SD) difference between admission heart rate and the lowest heart rate recorded in the dexmedetomidine premedication group, the dexmedetomidine intra-operative group and the control group was 11.6 (16.9), 7.5 (17.6) and 3.4 (18.5) beats per min, respectively, p=0.02. There was no statistically significant difference between the systolic blood pressure on admission and the lowest recording in any of the three groups.

There was no difference between the groups in terms of parental satisfaction (dexmedetomidine premedication group = 9.1, dexmedetomidine intra-operative group = 9.2, control group = 9.3).

Discussion

This study showed that there was no difference in the prevalence of behaviour change three days after simple day case procedures in healthy children aged 2–7 y when dexmedetomidine was administered either before or during surgery. The overall prevalence of negative behaviour change on day 3 in our trial was similar to that reported in previous studies (49%). It should be noted that the average PHBQ-AS score was only 3.12 at day 3 which equates to an average of 1.3 out of the 11 behaviours on the questionnaire being scored as worse than baseline. Using the SDQ to measure the primary outcome yielded similar results. The median scores were similar in all three groups across each of the time-points. However, over time, there did appear to be a trend towards some improvement in SDQ scores in the children who received dexmedetomidine, whereas in the control group the incidence of children at high risk of behaviour problems remained the same.

There was a significant reduction in the incidence of negative behaviour in the intra-operative dexmedetomidine group from 44% on day 3 to 15% on day 28. However, the actual scores on the PHBQ-AS were similar in all three groups at each of the time-points and no such difference was detected when using the SDQ. A possible reason why there was no difference in behaviour detected on day 3 is that the cohort consisted of otherwise healthy children having simple day case procedures. The average length of surgery was 37 min and the average length of hospital stay following the procedure was 160 min. Furthermore, the majority of children had no pain after their procedure. It is possible that there may be a benefit using dexmedetomidine for longer, more painful procedures or in children who have well-documented anxiety or behaviour problems. This provides an opportunity for future research.

Dexmedetomidine used as a premedication and as an intra-operative intravenous bolus appears to be safe. In our study there were seven patients who required treatment for low heart rate or low blood pressure, but there was no difference between the groups. Those who received dexmedetomidine had longer stays in both recovery and in hospital. Children who had dexmedetomidine stayed on average 11 min longer in recovery and 33 min longer in hospital. It is possible that the increased length of stay is related to the fact that these children were not anxious, had minor procedures and that the sedative effect of dexmedetomidine was enhanced. The increased time spent in hospital is clinically and economically insignificant.

The incidence of emergence delirium was very low overall (3%) and it is difficult to make any definitive conclusions regarding this. In the control group, the prevalence was 6% whereas in each of the two dexmedetomidine groups the prevalence was 1%; however this difference was not statistically significant. One possible reason for the low incidence of emergence delirium observed

may have been due to the introduction of a new measurement tool into the recovery unit. The staff were trained in its use, but a lack of familiarity may have led to some underreporting. This tool, the Cornell Assessment of Paediatric Delirium, was developed as a rapid observational screening tool for use in intensive care and it is not currently used in the recovery setting [13]. It is designed to detect hyperactive, hypoactive and mixed delirium and consists of the five PAED scale items plus three additional items specific to hypoactive delirium. In this study, of the seven total cases of emergence delirium detected, two were hypoactive in nature. Whilst the numbers are small, our study suggests that a significant number of emergence delirium cases are hypoactive in nature. If this is true, then this is an area that warrants further investigation.

The majority of children in all three groups had no pain in recovery, however the incidence of pain in the control group was 16% compared with only 5.5% for the children who received dexmedetomidine. This result is consistent with the results of other studies demonstrating an analgesic effect of dexmedetomidine [14].

Overall, there was no difference in parental satisfaction with the anaesthetic treatment received. This suggests that there is no need to change our current practice of anaesthesia for otherwise healthy children having day case procedures. The low scores in the PHBQ-AS and SDQ in all three groups in this patient population implies that our current standard of care is appropriate. Improvements in the physical environment, patient and family preparation and staff training may all have contributed to making the hospital visit less threatening for children and subsequently reduced the incidence and severity of post-hospitalisation negative behaviour change.

A strength of this study is that it is an appropriately powered, double-blind, randomised controlled trial. However, it also has a number of limitations. It is a single-centre study and so the results may not be generalisable to other paediatric populations. In addition, our study included only healthy children aged 2–7 y having simple day case procedures and may have excluded children who would benefit most from the addition of dexmedetomidine. This type of research is also hampered by the lack of a well-validated, easy-to-use measurement tool for assessing behaviour change after anaesthesia. In our study we found that the scores from the PHBQ-AS and the SDQ provided similar results. We plan to perform a more detailed comparison and analysis of these outcome measures in the future.

Dexmedetomidine can be a useful adjunct to general anaesthesia in children as it is well-tolerated, provides analgesia and reduces emergence delirium. Our study showed that an intra-operative dose

may also reduce negative behaviours 28 days following surgery. Careful selection of patients is recommended as the greatest benefit from dexmedetomidine is likely to be in children who are anxious or having major surgery, although further research is required to confirm this.

Acknowledgements

Approval for this study was granted by the Children's Health Queensland Human Research Ethics Committee and the University of Queensland Human Research Ethics Committee (HREC/15/QRCH/248 and 2016001715). The trial was registered with the Australian and New Zealand Clinical Trial Register (Clinical Trial Registration number: ACTRN12616000096459). The authors acknowledge T. Williams, R. Doyle and K. Pearson for their contribution to the conduct of this study in terms of advice, patient recruitment, drug administration, data collection and management. This work was carried out with the support of a grant from the Australian and New Zealand College of Anaesthetists (ANZCA Grant 17/038). BvUS is partly funded by the Perth Children's Hospital Foundation, the Stan Perron Charitable Trust and the Frank Callaghan Estate. No other competing interests declared.

References

1. Mason KP. Paediatric emergence delirium: a comprehensive review and interpretation of the literature. *British Journal of Anaesthesia* 2017; **118**: 335-343.
2. Fortier MA, Kain ZN. Treating perioperative anxiety and pain in children: a tailored and innovative approach. *Paediatric Anaesthesia* 2015; **25**: 27-35.
3. Kain ZN, Mayes LC, O'Connor TZ, Cicchetti DV. Preoperative anxiety in children: Predictors and outcomes. *Archives of Pediatric and Adolescent Medicine* 1996; **150**: 1238-45.

4. Power NM, Howard RF, Wade AM, Franck LS. Pain and behaviour changes in children following surgery. *Archives of Diseases in Childhood* 2012; **97**: 879-884.
5. Pickard A, Davies P, Birnie K, Beringer R. Systematic review and meta-analysis of the effect of intraoperative alpha(2)-adrenergic agonists on postoperative behaviour in children. *British Journal of Anaesthesia* 2014; **112**: 982-90.
6. Li A, Yuen VM, Goulay-Dufaÿ S, Sheng Y, et al. Pharmacokinetic and pharmacodynamic study of intranasal and intravenous dexmedetomidine. *British Journal of Anaesthesia* 2018; **120**: 960-8.
7. Mahmoud M, Mason KP. Dexmedetomidine: review, update, and future considerations of paediatric perioperative and periprocedural applications and limitations. *British Journal of Anaesthesia* 2015; **115**: 171-82.
8. Vernon DT, Schulman JL, Foley JM. Changes in children's behavior after hospitalization. *American Journal of Diseases in Children* 1966; **111**: 581–93.
9. Jenkins BN, Fortier MA, Kaplan SH, Mayes LC, Kain ZN. Development of a short version of the modified Yale Preoperative Anxiety Scale. *Anesthesia and Analgesia* 2014; **119**: 643-50.
10. Goodman R. The strengths and difficulties questionnaire: a research note. *Journal of Child Psychology and Psychiatry* 1997; **38**: 581-6.
11. Stone L, Janssens J, Vermulst A, Van Der Maten M, Rutger C, Otten R. The Strength and Difficulties Questionnaire: psychometric properties of the parent and teacher version in children aged 4-7. *BMC Psychology* 2015; **3**: 4.
12. Lee-Archer P, McBride C, Paterson R, Reade M, Regli-von Ungern-Sternberg B, Long D. Does dexmedetomidine given as a premedication or intraoperatively reduce post-hospitalisation behaviour change in children? A study protocol for a randomised controlled trial in a tertiary paediatric hospital. *British Medical Journal Open* 2018; **8**: e019915.
13. Traube C, Silver G, Kearney J, et al. Cornell assessment of pediatric delirium: A valid, rapid, observational tool for screening delirium in the PICU. *Critical Care Medicine* 2014; **42**: 656–663
14. Plambech MZ, Afshari A. Dexmedetomidine in the pediatric population: a review. *Minerva Anesthesiologica* 2015; **81**: 320-32.

Table 1. Baseline characteristics and intra-operative details of patients included in the study. Values are median (IQR [range]), number (proportion) or mean (SD).

		Dexmedetomidine premedication group n=82	**Dexmedetomidine intra-operative group n=81**	**Control group n=84**
Age; y		4 (3-6 [2-7])	4 (3-6 [2-7])	4 (3-5 [2-7])
Weight; kg		18 (15-22 [10-34])	18 (15-21 [10-37])	19 (15-21 [12-36])
Sex; male		51 (62%)	46 (57%)	55 (66%)
Previous operations	*0*	54 (66%)	44 (54%)	52 (62%)
	1	16 (19%)	23 (29%)	15 (18%)
	2 or more	12 (15%)	14 (17%)	17 (20%)
Indigenous	*Yes*	6 (7%)	8 (10%)	8 (10%)
	No	76 (93%)	73 (90%)	76 (90%)
Highest level of parent education*:*				
Primary school		0 (0%)	1 (1%)	0 (0%)
High School		21 (27%)	21 (27%)	18 (23%)
TAFE/diploma		29 (37%)	27 (34%)	29 (37%)
Bachelor		19 (24%)	24 (30%)	20 (26%)

Postgraduate		6 (8%)	6 (8%)	9 (11%)
Rather not say		3 (4%)	0 (0%)	2 (3%)
Type of surgery	*General*	40 (49%)	35 (44%)	40 (48%)
Orthopaedics		7 (9%)	5 (6%)	7 (8%)
ENT		12 (15%)	11 (13%)	6 (7%)
Eyes		10 (12%)	12 (15%)	9 (11%)
Plastics		3 (4%)	6 (7%)	11 (13%)
Gastro		4 (5%)	3 (4%)	3 (4%)
Respiratory		1 (1%)	1 (1%)	2 (2%)
Radiology		3 (4%)	4 (5%)	4 (5%)
Other		1 (1%)	4 (5%)	2 (2%)
Child anxiety				
Baseline SDQ		9.5 (5-14 [0-22])	7 (4-10 [0-28])	7 (4-12 [0-30])
Child temperament				
EAS score		63.5 (5.3)	63.6 (5.8)	63.6 (5.8)
Parental anxiety				
STAI score		16.5 (12-18 [10-28])	15 (12-20 [10-30])	15 (13-21 [10-29])
Type of induction	*Inhalational*	79 (99%)	79 (99%)	83 (100%)
Intravenous		1 (1%)	1 (1%)	0 (0%)
Intra-*op analgesia*	*Paracetamol*	53 (65%)	41 (51%)	47 (56%)
NSAID		14 (17%)	9 (11%)	8 (10%)
Fentanyl		68 (83%)	65 (80%)	68 (81%)
Morphine		7 (9%)	6 (7%)	9 (11%)

Tramadol	1 (1%)	0 (0%)	1 (1%)
Surgery time; min	37 (31-53 [14-153])	36 (27-57 [22-173])	39 (33-52 [16-113])

EAS, Emotionality Activity Sociability Temperament Survey; STAI, State-Trait Anxiety Inventory; NSAID, non-steroidal anti-inflammatory drug; TAFE, technical and further educationTable 2. Behavioural change as measured by the PHBQ-AS and SDQ on postoperative day 3. Values are number (proportion) or median (IQR [range]).

Behaviour change	**Dexmedetomidine premedication group n=78**	**Dexmedetomidine intra-operative group n=78**	**Control group n=78**	**Adjusted p value**
PHBQ-AS score day 3				
Improved	6 (8%)	13 (17%)	8 (10%)	
No change	35 (45%)	31 (40%)	30 (39%)	
Worse	37 (47%)	34 (44%)	40 (51%)	0.99
SDQ score day 3	7.5 (3-12 [0-26])	6 (3-11 [0-23])	8 (4-12 [0-26])	0.99
Increased risk of problem behaviour (score >13)	16 (21%)	11 (14%)	13 (17%)	

PHBQ-AS, Post-Hospitalisation Behaviour Questionnaire for Ambulatory Surgery; SDQ, Strength and Difficulties Questionnaire

Table 3. Behavioural changes as measured by the PHBQ-AS and SDQ on postoperative days 14 and 28 and anxiety at induction. Values are number (proportion) or median (IQR [range]).

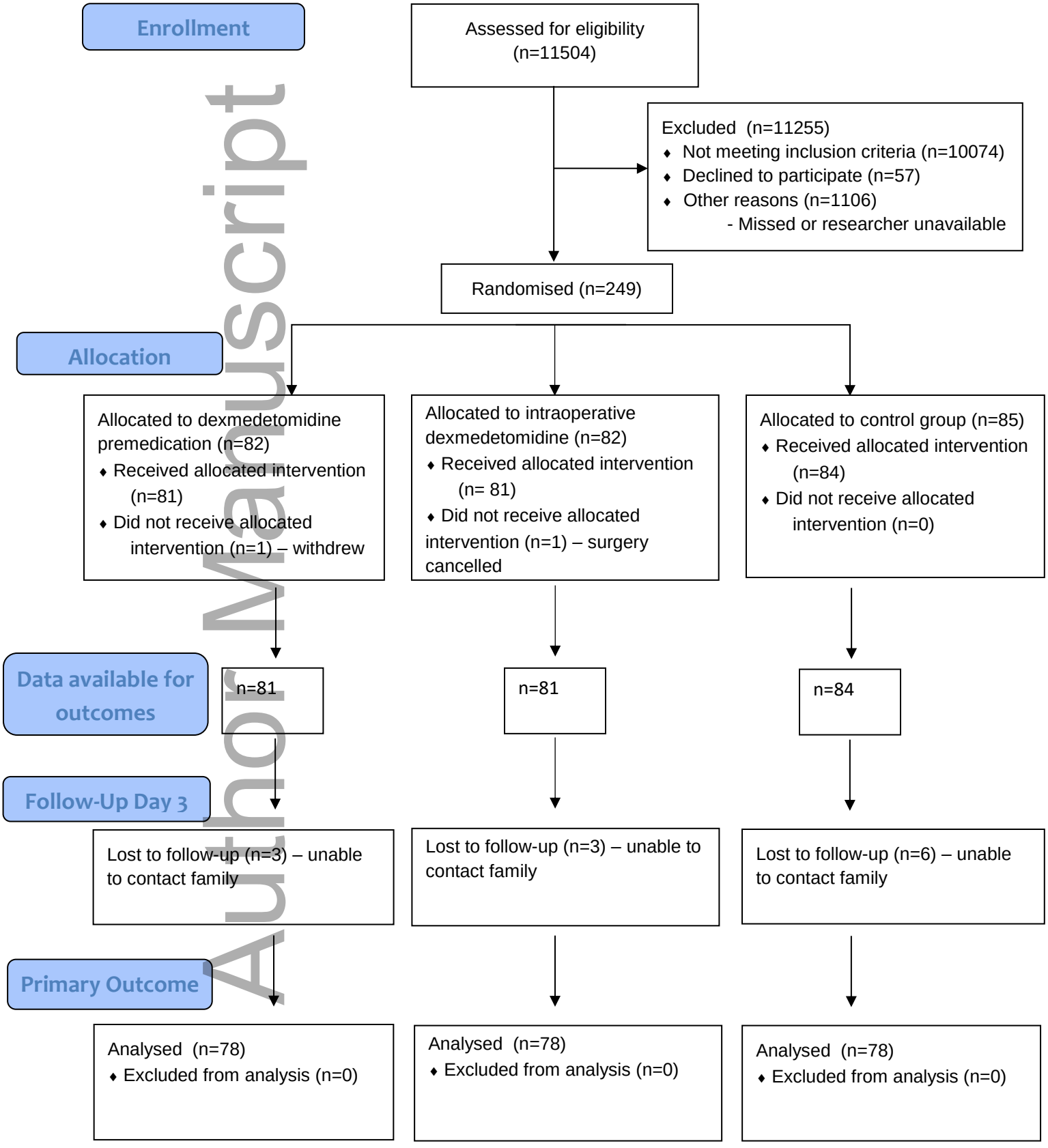
	Dexmedetomidine premedication group	**Dexmedetomidine intra-operative**	**Control group**	**p value**

		group		
Behaviour change day 14	Total = 68	Total = 71	Total = 69	
(PHBQ-AS):				
Improved	5 (7%)	6 (8%)	8 (12%)	
No change	35 (52%)	41 (58%)	32 (46%)	
Worse	28 (41%)	24 (34%)	29 (42%)	0.68
Behaviour change day 28	Total = 62	Total = 62	Total = 65	
(PHBQ-AS):				
Improved	7 (11%)	4 (6%)	9 (14%)	
No change	32 (52%)	49 (79%)	29 (45%)	
Worse	23 (37%)	9 (15%)	27 (41%)	<0.001
Baseline SDQ score	Total = 82	Total = 81	Total = 84	
	9.5 (5-14 [0-22])	7 (4-10 [0-28])	7 (4-12 [0-30])	
Increased risk of problem behaviour (score >13)	25 (31%)	16 (20%)	18 (21%)	
SDQ score day 14	Total = 68	Total = 71	Total = 69	
	7 (3-13 [0-27])	6 (2-10 [0-25])	5 (3-14 [0-30])	0.85
Increased risk of problem behaviour (score>13)	15 (22%)	9 (13%)	19 (28%)	
SDQ score day 28	Total = 62	Total = 62	Total = 65	
	6 (2-10 [0-22])	6 (2-9 [0-25])	7 (3-11 [0-34])	0.29
Increased risk of problem behaviour (score>13)	8 (13%)	8 (13%)	13 (20%)	

Baseline anxiety *(mYPAS score)*	23 (23-23 [23-100])	23 (23-23 [23-97])	23 (23-23 [23-83])	
Anxiety at induction *(mYPAS score)*	23 (23-40 [23-100])	23 (23-49 [23-100])	23 (23-52 [23-100])	0.96
High anxiety at induction *(mYPAS > 30*)	27 (33%)	26 (32%)	29 (34%)	0.99

PHBQ-AS, Post-Hospitalisation Behaviour Questionnaire for Ambulatory Surgery; SDQ, Strength and Difficulties Questionnaire; mYPAS, Modified Yale Preoperative Anxiety Scale

Figure 1: Study flow diagram.



Author/s:
Lee-Archer, PF; von Ungern-Sternberg, BS; Reade, M; Betts, M; Haenke, D; Keys, A; Rance, T; Gibbons, K; Long, D

Title:
The effect of dexmedetomidine on postoperative behaviour change in children: a randomised controlled trial.

Date:
2020-11

Citation:
Lee-Archer, P. F., von Ungern-Sternberg, B. S., Reade, M., Betts, M., Haenke, D., Keys, A., Rance, T., Gibbons, K. & Long, D. (2020). The effect of dexmedetomidine on postoperative behaviour change in children: a randomised controlled trial.. Anaesthesia, 75 (11), pp.1461-1468. https://doi.org/10.1111/anae.15117.