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ORIGINAL ARTICLE

Awareness in children: a secondary analysis of five cohort studies

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Summary

Five recent cohort studies have shown a frequency of awareness in paediatric anaesthesia of between 0.2% and 1.2%, but they were not individually large enough to identify risk factors. This study pooled raw data from these five studies to identify factors associated with awareness in children. The outcome of awareness was taken as the cases judged to be most likely awareness cases in each study. Logistic regression was used to identify awareness-associated factors. A combined sample of 4486 anaesthetics revealed 33 cases of awareness. Unadjusted analysis demonstrated weak evidence that nitrous oxide used as an anaesthetic maintenance adjunct was associated with awareness (OR 2.04 (95% CI 0.97–4.33), p = 0.06), and some evidence that use of a tracheal tube was associated with awareness (OR 2.78 (95% CI 1.11–6.94), p = 0.03). Multivariable regression analysis revealed that nitrous oxide maintenance and use of a tracheal tube were independently associated with awareness (nitrous oxide, OR 2.4 (95% CI 1.08–5.32), p = 0.03; tracheal tube, OR 3.0 (95% CI 1.20–7.56), p = 0.02).

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Awareness under general anaesthesia is a rare complication but has the potential to cause adverse psychological consequences. Several studies have evaluated the incidence and risk factors for awareness in adults, the incidence being roughly 0.1–0.2% [1–12]. Paediatric data are less complete. Five recent cohort studies have reported the incidence of awareness in children to be between 0.2% and 1.2% [13–17], considerably higher than the reported incidence in adults. It is unknown why the incidence is higher in children. In each of the paediatric studies the number of children with awareness is too small to allow meaningful analysis

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of risk factors for awareness. Identification of factors that place children at risk for awareness is important because it may enhance understanding of the causative mechanisms that may in turn guide practice aimed at preventing this adverse outcome. Such information may also inform which population to use in future intervention studies aimed at reducing awareness in children. The aim of this study was to pool the data from these five cohort studies to identify factors associated with awareness in children.

Method

Raw unidentifiable data from five independently conducted cohort studies were combined [13–17]. The original studies were conducted with the approval of local institutional review boards or ethics committees and children were enrolled after informed consent from their parents. Where needed, there was exemption or approval (and waiver of consent) from the relevant institutional review boards or ethics committees for the transfer of data for this analysis. Two of the studies were conducted at Royal Children's Hospital, Melbourne, Australia [13, 15]; one was at University Hospitals, Geneva, Switzerland [14]; another was at Sophia Children's Hospital, Rotterdam, The Netherlands [16]; and another was a multicentre study in the USA (conducted at Emory University, Atlanta, University of Colorado, Denver, and University of Michigan Health Systems, Ann Arbor, Michigan) [17]. All the original cohort studies were designed to determine the incidence of awareness in children, where awareness was defined as the free recall of events that occurred during general anaesthesia. They all used one or more semi-structured interviews at varying time points following anaesthesia. The format of the interviews was different at each site but all included questions designed specifically to elicit information related to recall of intra-operative events.

Standardised risk factor variables were derived from the five study datasets following discussion and consensus among study investigators. The definition of awareness and how awareness was judged varied between cohorts. For analysis we took the outcome 'adjudicated awareness' to be the cases in each study that were considered to have the greatest likelihood in each study of representing awareness i.e. recall of intra-operative events. In the respective papers these groups were called 'true awareness' [13], 'confirmed awareness' [14], 'awareness' [15], 'true awareness' [16] and 'possible/probable awareness' [17]. De-identified datasets of standardised variables from all five studies were then combined into a single large dataset. Only children who had at least one assessment for awareness were included.

The following variables were available in all datasets: record identifier; age of child at time of anaesthesia; sex; emergency or non-emergency surgery; use of sedative premedication; use of inhalational induction as opposed to intravenous induction; use of neuromuscular blocking agents; use of total intravenous anaesthesia; and use of nitrous oxide (N_2O). Age was recalculated from dates of birth and procedure dates where these variables were available. All studies recorded whether or not there were critical events, complications, or intra-operative interventions, though these were rarely defined explicitly.

The ASA classification was recorded for all studies except the second Australian study [15], whereas use of a tracheal tube was recorded for all studies except the first Australian study [13]. Use of regional nerve blockade was only available for the Swiss, Dutch and second Australian studies [14–16]. In the other studies, this was either not recorded, or it was impossible to determine if local anaesthesia was used for regional blockade or local infiltration. The US, Dutch and first Australian studies [13, 16, 17] reported whether or not ketamine was used; this was not reported in the Swiss and second Australian study [14, 15]. Duration of anaesthesia was recorded for all studies except the first Australian study [13], where duration of procedure was available and used as a proxy. Durations were recalculated from start and finish times where available.

The classification of procedure type differed substantially between studies. Only a few procedure groups were clearly and uniformly defined. These were: cardiac surgery; gastrointestinal endoscopy; ear, nose and throat surgery; radiological procedure (CT or MRI); neurosurgery; ophthalmology; and orthopaedics. All other procedures were classified as 'other'. Procedure type for the Swiss study was recorded in French; this variable was translated to English and categorised by bilingual clinicians.

A hospital identifier for each patient was available for all except the Swiss and second Australian studies [14, 15]. Where available, hospital and study identifiers were cross-checked. Hospital identifiers were unique within the US [17] and first Australian [13] studies.

The Dutch study [16] comprised 889 children, of whom 29 contributed two records and five contributed three. The time between successive operations for children contributing multiple records ranged from 14 to 350 days (median 147 days). The 73 records from

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children who contributed multiple records comprised 1.6% of records in the combined dataset; as this is a small percentage, it was deemed unnecessary to model within-patient correlation.

Associations between each risk factor and awareness were initially investigated in a logistic regression model with no other covariates. Covariates achieving the value of $p < 0.10$ in these analyses were then included in a multivariable model.

Logistic regression models included a random intercept for each study to account for potential within-study correlation (logistic mixed effects regression). The US study [17] was conducted at three different sites, each of which was treated as a separate study, as were the two Australian studies [13, 15]. If the random effect did not improve model fit ($p < 0.10$ for a likelihood ratio test vs logistic regression), then the results of the logistic regression are reported. Two sets of sensitivity analyses were also performed; these were (i) adjusted for study and (ii) stratified by study, with the combined odds ratio (OR) calculated using Mantel-Haenszel weights. The latter approach is equivalent to a fixed effects meta-analysis.

As awareness is rare, sometimes no individuals in a particular category experienced awareness. In this case, the OR is zero; the p value was obtained from the chi-squared test and the upper confidence limit using the Cornfield approximation. Analyses were performed using STATA version 11.1 (StataCorp. 2009, Stata Statistical Software: Release 11, College Station, TX, USA: StataCorp LP).

Results

The combined sample included 4486 children with a total of 33 cases of adjudicated awareness (0.74% with exact 95% binomial CI 0.49–1.00%) (Table 1). Descriptive statistics for the factors possibly associated with adjudicated awareness are provided in Tables 2 and 3.

Models with a random intercept (to allow for within-study correlation) did not fit better than logistic regression models for any of the risk factors examined. Hence, the OR and 95% CI from the latter analyses are reported. There was no evidence that the incidence of awareness differed between sites, with a Wald test yielding little evidence against the null hypothesis that all sites have the same odds of awareness ($p = 0.62$).

Table 4 shows the results of unadjusted analyses of the outcome of adjudicated awareness for the factors that might be associated with awareness. Each covariate is entered into a separate regression model as the only predictor. Two factors showed some evidence ($p < 0.10$) of association with adjudicated awareness. There was some evidence for an association with use of a tracheal tube ($p = 0.03$), and weaker evidence than for use of N_2O for maintenance ($p = 0.06$). Both were estimated to increase the odds of awareness, and both remained associated with awareness when sensitivity analyses were performed ($p \leq 0.06$). Most results changed little when sensitivity analyses were performed, with two exceptions: the evidence for sedative premedication increasing the odds of awareness attenuated to $p = 0.44$, while the evidence for complications increasing the odds of awareness strengthened to $p \leq 0.10$.

Table 1 Number of children recruited at each site and rates of adjudicated awareness for each site. Values are number or number (proportion).

Site	Children interviewed	Number of adjudicated aware cases
Melbourne 1 [13]	864	7 (0.81%)
Geneva [14]	410	5 (1.22%)
Melbourne 2 [15]	500	1 (0.20%)
Rotterdam [16]	928	6 (0.65%)
Michigan [17]	944	8 (0.85%)
Denver [17]	706	4 (0.57%)
Emory [17]	134	2 (1.49%)
Total	4486	33 (0.74%)

Nitrous oxide maintenance and use of a tracheal tube were entered into a multivariable model as covariates. Whereas N_2O maintenance was recorded by all studies, use of a tracheal tube was not recorded in the first Australian study [13]. As the multivariable analysis could only consider patients who had non-missing values for the outcome and all covariates, patients from the first Australian study [13] were not included in this model. In the multivariable analysis ($n = 3497$) both N_2O maintenance and use of a tracheal tube were independently associated with adjudicated awareness after adjusting for the other covariate. The adjusted OR for use of N_2O was 2.40 (95% CI 1.08–5.32, $p = 0.03$), while the adjusted OR for use of tracheal tube was 3.02 (95% CI 1.20–7.56, $p = 0.02$). Under the sensitivity analyses, the evidence remains similar for N_2O ($p \leq 0.03$), but becomes weaker for use of a tracheal tube ($p \leq 0.06$). There was only a weak correlation between these two covariates (Pearson correlation coefficient −0.113).

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Table 2 Descriptive statistics for factors possibly associated with adjudicated awareness; continuous variables. Values are median (IQR [range]).

	Melbourne 1 [13]	Geneva [14]	Melbourne 2 [15]	Rotterdam [16]	Michigan [17]	Denver [17]	Emory [17]	Total
Age; years	8 (7–11 [5–13])	11 (9–13 [5–17])	9 (7–11 [5–13])	10 (7–13 [5–22])	10 (7–13 [5–15])	10 (7–13 [5–15])	10 (8–13 [5–15])	10 [5–22]
Duration of anaesthesia; min	N/R*	80 (60–130 [10–475])	30 (18–48 [4–209])	60 (30–80 [7–540])	66 (43–106 [10–602])	65 (48–105 [19–370])	57 (37–68 [16–153])	53 [4–602]
Duration of procedure; min	30 (20–45 [5–360])	40 (25–85 [5–400])	N/R	N/R	42 (24–73 [0–525])	34 (20–62 [1–320])	26.5 (15–45 [4–100])	35 [0–525]
Weight; kg	N/R	36 (28–49 [17–110])	31 (23–38 [13–98])	34 (25–50 [14–106])	37 (26–53 [13–131])	37 (25–53 [14–130])	40 (29–53 [11–232])	35 [11–232]
Height; cm	N/R	143 (131–159 [19–195])	N/R	N/R	142 (125–157 [56–193])	144 (126–160 [53–188])	145 (130–157 [41–193])	143 [19–195]

N/R, not recorded.
*Duration of procedure used as duration of anaesthesia for analysis purposes.

While both factors associated with awareness have a large OR, it should be kept in mind that as adjudicated awareness has a low prevalence, the probability of awareness remains low even if the odds of the outcome are multiplied by a large factor. Table 5 shows the absolute risk, or probability, of adjudicated awareness predicted by this multivariable model under each combination of risk factors. Even for the highest risk combination of patients with both N_2O maintenance and a tracheal tube, the probability is 0.0162, so fewer than 1 in 62 children in this category would be expected to experience adjudicated awareness.

Discussion

In this pooled analysis we found the overall rate of awareness in children to be 0.74%. Two independent factors were found to be associated with awareness; use of a tracheal tube for the airway and use of N_2O as part of maintenance of anaesthesia.

The incidence of awareness in this pooled study is higher than that observed in most studies in the adult population [3, 4, 8, 11, 12]; in the adult population the incidence of awareness is roughly 1:1000, although in some studies it has been reported as much lower. Why is the incidence in children higher? Firstly, are at-risk groups identified in the adult population represented more frequently in children? In the adult population the incidence of awareness is higher during anaesthesia for trauma, bronchoscopy, caesarean section and cardiac surgery [1, 2, 5, 6, 18]. In this pooled analysis there were no cases of awareness in these groups, so the higher overall incidence in children is not due to an increased relative frequency of these types of procedure in children. Similarly, while in adults the use of neuromuscular blocking agents is a recognised risk factor for awareness, this was not found to be a risk factor in our pooled analysis, so even if there were an increased use of these in children this cannot explain the higher incidence of awareness in children. In summary, the risk factors identified in adults do not explain the higher incidence in children [1–3, 5–7, 10, 11, 18, 19]. In our sample, the incidence of awareness seems to be related to factors that are different from those seen in adults.

Identifying factors associated with awareness helps identify causative mechanisms for awareness. In the adult population, these factors are indeed consistent with plausible mechanism of awareness. For example, in adults it is plausible that awareness may be a result of inability to deliver adequate anaesthesia due to

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Table 3 Descriptive statistics for factors possibly associated with adjudicated awareness; categorical variables. Values are number (proportion).

	Melbourne 1 [13]	Geneva [14]	Melbourne 2 [15]	Rotterdam [16]	Michigan [17]	Denver [17]	Emory [17]	Total
Sex (male)	493 (57.1%)	247 (60.2%)	311 (62.2%)	507 (54.6%)	513 (54.3%)	375 (53.1%)	82 (61.2%)	2528 (56.4%)
ASA classification								
1	636 (73.6%)	255 (62.5%)	N/R	838 (90.3%)	486 (51.5%)	337 (47.7%)	62 (46.3%)	2614 (65.6%)
2	175 (20.3%)	152 (37.3%)	N/R	83 (8.9%)	423 (44.8%)	286 (40.5%)	67 (50%)	1186 (29.8%)
3	52 (6.0%)	1 (0.2%)	N/R	7 (0.8%)	33 (3.5%)	81 (11.5%)	4 (3.0%)	178 (4.5%)
4	1 (0.1%)	0	N/R	0	2 (0.2%)	2 (0.3%)	1 (0.7%)	6 (0.1%)
Emergency surgery	7 (0.8%)	17 (4.2%)	15 (3.0%)	3 (0.3%)	0	0	0	42 (0.9%)
Procedure type								
Cardiac	0	0	0	0	6 (0.6%)	1 (0.1%)	0	7 (0.2%)
Gastro-intestinal endoscopy	105 (12.2%)	23 (6.7%)	107 (21.4%)	59 (6.4%)	105 (11.1%)	46 (6.5%)	48 (35.8%)	493 (11.2%)
Gynaecology	1 (0.1%)	4 (1.2%)	0	0	6 (0.6%)	1 (0.1%)	0	12 (0.3%)
Ear, nose and throat	184 (21.3%)	12 (3.5%)	1 (0.2%)	172 (18.5%)	209 (22.1%)	203 (28.8%)	4 (3.0%)	785 (17.8%)
MRI/CT	13 (1.5%)	0	0	24 (2.6%)	41 (4.3%)	1 (0.1%)	0	79 (1.8%)
Neurosurgery	4 (0.5%)	0	0	10 (1.1%)	3 (0.3%)	0	0	17 (0.4%)
Ophthalmology	53 (6.1%)	1 (0.3%)	0	29 (3.1%)	107 (11.3%)	33 (4.7%)	6 (4.5%)	229 (5.2%)
Orthopaedics	108 (12.5%)	162 (47.5%)	149 (29.8%)	142 (15.3%)	174 (18.4%)	202 (28.6%)	8 (6.0%)	945 (21.4%)
Other	396 (45.8%)	139 (40.8%)	243 (48.6%)	492 (53.0%)	293 (31.0%)	219 (31%)	68 (50.7%)	1850 (41.9%)
Sedative premedication	136 (15.7%)	328 (80.0%)	51 (10.7%)	0	374 (39.6%)	82 (11.6%)	103 (76.9%)	1074 (24.1%)
Tracheal tube airway	N/R	211 (51.5%)	77 (15.4%)	455 (50%)	675 (71.7%)	462 (66%)	85 (63.9%)	1965 (54.7%)
Inhalational induction	396 (45.8%)	180 (43.9%)	281 (56.3%)	69 (7.5%)	429 (45.4%)	367 (52.0%)	91 (67.9%)	1813 (40.5%)
Neuromuscular blocking agents used	100 (11.6%)	176 (45.2%)	40 (8.0%)	404 (43.5%)	272 (28.8%)	77 (10.9%)	24 (17.9%)	1062 (23.9%)
Total intravenous anaesthesia	24 (2.8%)	25 (6.1%)	1 (0.2%)	97 (10.9%)	197 (20.9%)	348 (49.3)	80 (59.7%)	772 (17.4%)
Nitrous oxide induction	N/R	N/R	456 (91.6%)	0	734 (77.8%)	655 (92.8%)	130 (97.0%)	1975 (86.6%)
Nitrous oxide maintenance	724 (94.5%)	234 (68.2%)	443 (88.6%)	0	544 (57.6%)	161 (22.8%)	120 (89.6%)	2226 (52.0%)
Nitrous oxide use recorded at any time	724 (94.5)	234 (68.2%)	484 (96.8)	0	832 (88.1%)	664 (94.1%)	134 (100%)	3072 (71.7%)
Ketamine used	14 (3.7%)	19 (4.7%)	7 (1.4%)	37 (4.0%)	N/R	N/R	N/R	77 (3.5%)
Regional nerve blockade	N/R	80 (19.6%)	70 (14.0%)	109 (11.9%)	N/R	N/R	N/R	259 (14.2%)
Any complications or critical events	72 (16.8%)	274 (7.9%)	39 (10.0%)	25 (2.9%)	101 (10.7%)	33 (4.7%)	4 (3.0%)	274 (7.9%)

N/R, not recorded.

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Table 4 Results of the unadjusted analysis examining factors possibly associated with adjudicated awareness. Values are frequencies for categorical variables or median lower quartile, upper quartile for continuous variables.

	Not aware	Aware	Odds ratio (95% CI)	p value
Study/site				
Melbourne 1 [13]	864	7	1 (ref)	0.62*
Geneva [14]	410	5	1.51 (0.48–4.79)	
Melbourne 2 [15]	500	1	0.25 (0.03–2.00)	
Rotterdam [16]	928	6	0.80 (0.27–2.38)	
Michigan [17]	944	8	1.05 (0.38–2.90)	
Denver [17]	706	4	0.70 (0.20–2.39)	
Emory [17]	134	2	1.85 (0.38–9.02)	
Sex				
Male	2509	19	0.95 (0.48–1.90)	0.89
Female		14		
ASA				
1	2597	17	1 (ref)	0.23*
2	1172	14	1.82 (0.90–3.71)	
3 or 4	183	1	0.83 (0.1–6.31)	
Age; years	9.7 [7.0, 12.1]	9.5 [7.1, 11.0]	0.95 (0.85–1.07)	0.42
Emergency surgery				
No	4410	33	0 (0–12.31)	0.57†
Yes	42	0		
Procedure type‡				
Cardiac	7	0	0 (0–75.84)	0.82†
Gastro-intestinal endoscopy	489	6	1.80 (0.74–4.38)	0.20
Gynaecology	12	0	0 (0–43.93)	0.77†
Ear, nose and throat	782	5	0.84 (0.32–2.18)	0.72
MRI/CT	78	1	1.75 (0.24–12.99)	0.58
Neurosurgery	17	0	0 (0–30.84)	0.72†
Ophthalmology	229	0	0 (0–2.15)	0.18†
Orthopaedics	950	8	1.18 (0.53–2.62)	0.69
Other	1883	13	0.89 (0.44–1.79)	0.74
Sedative premedication				
No	3369	21	1.81 (0.89–3.70)	0.10
Yes	1062	12		
Duration of anaesthesia; min§	53 [30, 86]	60 [35, 105]	1.14 (0.83–1.56)	0.43
Tracheal tube				
No	1622	6	2.78 (1.11–6.94)	0.03
Yes	1945	20		
Inhalational induction				
No	2644	20	0.95 (0.47–1.92)	0.897
Yes	1800	13		
Neuromuscular blocking agents used				
No	3350	22	1.55 (0.75–3.20)	0.24
Yes	1082	11		
Total intravenous anaesthesia				
No	3647	27	1.06 (0.44–2.57)	0.901
Yes	766	6		
Nitrous oxide induction				
No	303	4	0.42 (0.13–1.34)	0.14
Yes	1964	11		
Nitrous oxide maintenance				
No	2048	10	2.04 (0.97–4.33)	0.06
Yes	2204	22		
Nitrous oxide use recorded at any time				
No	1206	6	1.72 (0.70–4.18)	0.24
Yes	3046	26		
Ketamine used				
No	2115	14	1.99 (0.26–15.31)	0.51
Yes	76	1		

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Table 4 (*Continued*).

	Not aware	Aware	Odds ratio (95% CI)	p value
Regional nerve blockade				
No	1557	11	0.55 (0.07–4.27)	0.57
Yes	258	1		
Any complications or critical events				
No	3169	22	2.13 (0.73–6.24)	0.17
Yes	270	4		

*p value from Wald test of the joint null hypothesis (all odds ratios are one).
†p value from chi-squared test, OR 95% CI calculated using Cornfield's formula.
‡OR for each category calculated vs all other categories combined.
§Analysed following logarithmic (base 2) transformation.

Table 5 Probability of awareness with each combination of factor.

Tracheal tube	Nitrous oxide maintenance	Probability of adjudicated awareness
No	No	0.0023
Yes	No	0.0068
No	Yes	0.0054
Yes	Yes	0.0162

restrictions imposed by the patient's condition (as seen in trauma or obstetrics), or inability to monitor delivery (as seen with bronchoscopy) or to monitor surrogate measures of anaesthesia depth (as seen when a patient is on cardiopulmonary bypass in cardiac surgery and with paralysis). In this paediatric study, factors associated with awareness were use of nitrous oxide and use of a tracheal tube. It is difficult to explain with certainty the mechanism why these factors might be associated with awareness. It is possible that intubation of the patient's trachea causes intense stimulation that increases the risk of awareness if anaesthesia is light. Furthermore, it is well described that children require a higher dose of anaesthetic. It may be that they are more prone to awareness during induction if anaesthetists do not allow sufficient time for adequate effect site concentrations to be achieved before intubation. The mechanism for explaining why use of nitrous oxide is associated with awareness is also unclear. A possible explanation is that compared to a volatile agent, nitrous oxide has greater anti-nociceptive action relative to hypnotic action. Relatively high doses of volatile agents are required to prevent movement to stimulus or cardiovascular response to stimulus. If nitrous oxide is used, a lower dose of volatile agent may be required to prevent response to stimuli which may result in the child receiving less total hypnotic than they would be given if nitrous oxide had not been used. This could possibly increase risk of awareness. As the actual doses given in these studies were not recorded, this remains a speculative assertion.

There are substantial limitations to this study. First, there were different assessments for awareness across the contributing studies. Awareness is a subjective phenomenon and various methods of detecting awareness have been described. It is unclear if any particular method is superior [20]. It was not possible to have a single novel assessment system that could be identically applied across the studies, as the studies used different interviews and different numbers of adjudicators, and asked adjudicators to rank likelihood of awareness with different possible descriptors. We contemplated giving all raw accounts of the awareness experience to a new batch of adjudicators, but the nature of the original reports differed substantially in format and language, making any uniform delivery of the raw experience impossible.

Another limitation was the difficulty encountered in standardising variables between studies. In particular, it was necessary to classify 41.9% of procedures as 'others' due to difficulties in reconciling procedure classifications between studies. There was also possibly some difference across studies in what was classified as a complication, adverse event or need for an intervention. On the other hand, many covariates were unambiguous and could be combined in a straightforward manner, including demographic variables and peri-operative variables such as ASA classification, emergency surgery, induction method and use of a tracheal tube. Finally, some possible risk factors of interest could not be investigated because definitions varied to the extent that the derivation of a standardised variable was not deemed possible.

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In spite of the large number of children examined in this study, awareness remains a relatively unusual event. The low incidence of the outcome event inevitably reduces the power of the study to detect factors associated with awareness. The study would have had 90% power to detect a hypothetical factor present in 50% of children and increasing the risk of awareness from 0.5% to 1.5%. There would be less power to detect a smaller difference, a less frequent risk factor or a risk factor not recorded for all children studied. The implication is that covariates cannot be excluded as potential risk factors, particularly those with moderately low p values and high odds ratios such as endoscopy, use of neuromuscular blocking agents and complications/critical events.

Lastly, in all such cohort studies, there is always the possibility that confounding factors exist that are unknown. Therefore, it cannot be conclusively stated that use of nitrous oxide or a tracheal tube increases the risk of awareness in children. There could be other unknown factors associated with both awareness and the risk factors identified. Only a prospective trial could definitively determine if these are indeed causative factors or just associated factors.

One rationale for the study was to identify at risk groups to aid prevention. While use of nitrous oxide and tracheal intubation may be associated with awareness, the possibility of confounding factors means it is not proven that avoiding these would decrease the risk. At most, all that can be recommended is that extra care should be taken to ensure adequate anaesthesia in these children. Another rationale for the study was to recognise a higher risk group where further intervention studies using processed EEG devices may be warranted. Therefore, from this study it could be argued that future intervention studies should focus on children undergoing tracheal intubation. Such a future study would also have to take care to use a single standardised method of awareness assessment.

In conclusion the pooled analysis of five recent cohort studies suggests the incidence of awareness in children is approximately 0.7%. Although causation cannot be assumed, use of nitrous oxide and tracheal intubation were both independently associated with increased risk of awareness.

Competing interests

No external funding and no competing interests declared.

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