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ORIGINAL ARTICLE

Peri-operative respiratory adverse events in children with upper respiratory tract infections allowed to proceed with anaesthesia

The French national study

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BACKGROUND Peri-operative respiratory adverse events (PRAEs) in paediatric patients with upper respiratory tract infections (URTIs) remain inadequately explored in patients allowed to proceed to anaesthesia and surgery.

OBJECTIVE To determine the incidence and risk factors of PRAE in children with URTI allowed to proceed to anaesthesia.

DESIGN Multicentre cohort study performed over 6 months in France.

SETTING Sixteen centres with dedicated paediatric anaesthetists.

PATIENTS Eligible patients were aged from to years with URTI symptoms on admission or history of such over the preceding 4 weeks.

MAIN OUTCOMES The primary outcome of the study was to determine predictors of PRAE. Secondary outcomes were: predictors of peri-operative arterial desaturation and of the decision to proceed with anaesthesia and surgery in children with URTI.

RESULTS Overall, 621 children were included and 489 (78.7%) anaesthetised. Of those anaesthetised, 165 (33.5%) and 97 (19.8%) experienced PRAE and arterial desaturation, respectively. Factors predictive of PRAE included patient age, tracheal intubation and the absence of midazolam premedication. Factors predictive of peri-operative arterial desaturation included patient age, anaesthetist experience, endoscopic procedures and the presence of other PRAE. Factors predicting proceeding to anaesthesia in the context of URTI included anaesthetist experience, emergency procedures and the absence of severe URTI symptoms.

CONCLUSION The risk of PRAE in patients anaesthetised in the presence of URTI was similar to previous publications – close to 30%. In the light of our findings, first, current rescheduling indications should be questioned, and second, further medical and organisational strategies should be investigated to reduce PRAE in children with URTI.

TRIAL REGISTRATION The study was registered in the European Networks of Centers for Pharmacoepidemiology and Pharmacovigilance (EUPAS16436).

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Introduction

Deciding whether to proceed with anaesthesia in children and infants with upper respiratory tract infections (URTIs) is a significant aspect of daily paediatric anaesthesia practice.[1,2] Given the frequency of URTIs in children, this can result in major organisational issues associated with rescheduling the procedures. Although many studies have found URTIs to be associated with an increased incidence of peri-operative respiratory adverse events (PRAEs),[2–5] no clear consensus or formal recommendations exist to assist physicians in deciding whether to proceed with or to reschedule anaesthesia.[1,2]

The decision whether or not to proceed with anaesthesia and surgery is often the result of a multidisciplinary discussion between the anaesthetist, surgeon and family, and many factors are taken into account. These include the specific URTI symptoms at time of admission or over the preceding weeks, associated comorbidities, the anaesthetist's knowledge regarding the respiratory consequences of each URTI symptom, anaesthetist experience, institutional protocols, the degree of procedural urgency and family constraints.[2] With different anaesthetists and different institutions, such numerous parameters lead to a wide variability in the decision whether or not to proceed with anaesthesia. As an illustration, a recent survey in our institution found the rate of rescheduling for URTI represented 19% of all rescheduling events, although this rate appears to be lower elsewhere.[1]

Rescheduling surgery in patients with URTI is implemented in the expectation that PRAE will be reduced.[3] However, the literature is lacking in robust data exploring such a result, especially when high rescheduling strategies, as applies generally in France,[6] are used. The main outcome of this national cohort study was to determine factors predictive of PRAE in patients with URTI who proceeded to anaesthesia. Secondary outcomes included the factors predictive of proceeding with anaesthesia and surgery in paediatric patients with URTIs, and risk factors for peri-operative arterial desaturation in such patients undergoing anaesthesia.

Material and methods

Ethics

The current study was approved nationally by our IRB (Comité d'Evaluation de l'Ethique des projets de Recherche Biomédicale Hôpital Robert Debré; # 2015/315, chairperson: Professor Yannick Aujard, on the 5 December 2016) and declared to the national data management authority (Commission nationale de l'informatique et des libertés # SMQ1971457B). It was registered in the European Networks of Centers for Pharmacoepidemiology and Pharmacovigilance (EUPAS16436, http://www.encepp.eu/encepp/studySearch.htm). Parents were informed about known risks of peri-operative complications, their management and major issues such as the possibility of admission to a high-dependency unit (HDU) or intensive care unit (ICU). Informed written consent was obtained from all patients or their parents.

Methods

This was a multicentre prospective observational cohort study of paediatric patients admitted to French paediatric tertiary care centres from January 2017 to June 2017 for a procedure requiring general anaesthesia and who presented with URTI or a history of URTI within the preceding 4 weeks. The recruiting centres were either specialist paediatric or mixed adult/paediatric hospitals with dedicated paediatric anaesthetists. Anaesthetists agreeing to take part in the study were recruited by the head of the department in paediatric hospitals or by the paediatric anaesthesia team leader in mixed adult/paediatric hospitals. Those anaesthetists who agreed to participate in the study within each centre were asked to recruit patients in a consecutive manner. Patient inclusion criteria were: children aged less than 18 years at the time of surgery with the concurrent presence of URTI or URTI in the past 4 weeks (these were verified on the day of surgery for ambulatory procedures, and on the day before surgery for inpatients). Symptoms of current or previous URTI included: fever (>38.5%), cough (moist or clear), runny nose (clear or green), wheezing and abnormal auscultation. Lethargy was only enquired about in the context of other symptoms and may be underreported as a result. The definition of URTI in the current study was the presence of any one of these symptoms and signs upon presentation or the description of any of them by parents. There was no standardisation of the decision process to proceed with anaesthesia nor of anaesthetic protocols. However, the decision to reschedule patients was the result of discussion between the anaesthetist, the operator and family. When patients were rescheduled for a reason other than URTI, they were excluded from the analyses. Finally, there was no standardisation of the pre-operative care of patients with URTI or wheezing. Standard practice in France involves referring rescheduled patients to a paediatrician for assessment and treatment. For patients proceeding with anaesthesia, pre-operative nebulised salbutamol, nebulised corticosteroids and chest physiotherapy are commonly prescribed. Given the frequent prescription of chest physiotherapy, most French paediatric services have dedicated physiotherapy teams available in the peri-operative area at least during autumn and winter.

Data collected

The following data were collected and analysed: age, former prematurity (defined as a gestational age <37 weeks), weight, type of surgery/procedure, comorbidities (cardiac or respiratory disease, identified by the presence of a specific medical follow-up for the specific illness), ASA physical status, anaesthetist experience (resident or fellow

versus senior anaesthetist, and years of practice as a paediatric anaesthetist), rescheduled surgery in the preceding 4 weeks and the reason (URTI versus other), the decision to proceed with anaesthesia or to reschedule and the reason for rescheduling (URTI versus other), sedative premedication, pre-operative nebulised bronchodilators or corticosteroids, pre-operative chest physiotherapy, anaesthetist workload at the time of the procedure (i.e. was the anaesthetist responsible for one or two operating theatres: the latter is common in France, with a nurse anaesthetic practitioner present in each operating room), method of anaesthetic induction (intravenous, inhalational or combined), intra-operative analgesia (opioid agents and/or regional analgesia), airway device used (endotracheal tube, laryngeal mask or face mask), type of ventilation (controlled ventilation, assisted ventilation or spontaneous ventilation), use of muscle relaxants for intubation and/or surgical relaxation, depth of anaesthesia during airway device removal (awake or anaesthetised) and adverse peri-operative events (at induction, intra-operatively or in the postanaesthetic care unit, PACU). PRAEs were laryngospasm (defined as a partial or complete airway occlusion whether or not requiring medical intervention), bronchospasm (defined as an increased respiratory effort or airways pressures whether or not requiring medical intervention), severe cough (defined as three consecutive coughs and/or lasting more than 10 s), stridor (defined as a noisy inspiratory sound during spontaneous ventilation) and arterial desaturation defined as [SpO_2] less than 90% for more than 15 s. Bradycardia was defined as a decreased heart rate for more than 30 s: less than 90 bpm from 0 to 1 months of age, less than 80 bpm from 2 months to 2 years, less than 70 bpm from 2 to 4 years, less than 60 bpm from 4 to 9 years and less than 50 bpm from 9 to 18 years. Given the potential for interanaesthetist variability in definitions, we decided to define severe PRAE as the presence of arterial desaturation, as this outcome was considered to carry a major risk of neurological complications and long-lasting postoperative disability. A specific analysis for arterial desaturation was performed (see below).

Postoperative medical management for the consequences of URTI was also recorded. This included the administration of drugs [inhaled corticosteroids, bronchodilators (inhaled or systemic) and epinephrine (inhaled or systemic)], delayed PACU discharge, ICU or HDU admission, invasive or noninvasive postoperative ventilation. The presence of any long-term neurological sequelae or disability related to deep and prolonged arterial desaturation and/or haemodynamic complications or ICU/HDU stay in relation to URTI was reported at discharge from hospital.

Statistical analysis

The primary outcome of this study of children with a current or recent URTI was the incidence of PRAE and its predictive factors in patients proceeding to anaesthesia. Secondary outcomes included the incidence of arterial desaturation and its predictive factors in patients who proceeded to anaesthesia and the proportion of children proceeding to anaesthesia and the factors predictive of this.

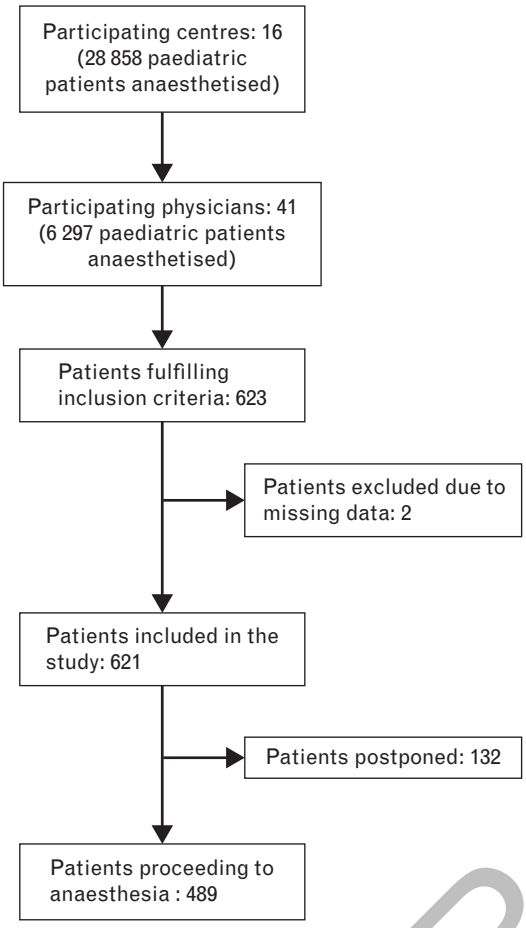
Univariate analyses were performed using analysis of variance (ANOVA) and the chi-squared or Fisher's exact test for categorical variables. If a statistical association was found between a continuous variable and a study outcome, the continuous variable was converted to a discrete variable by categorising it according to its J-point (the maximal value of the Youden index = sensitivity + specificity) following receiving operator characteristics (ROC) analysis. Although multivariate analysis can be performed using continuous variables, transforming continuous variables to discrete values allows the determination of a cut-off value and results that are easier to interpret.[7]

Given that statistical analyses were repeated on the same cohort of anesthetised patients for both peri-operative respiratory complications and arterial desaturation outcomes, a Bonferroni correction was applied to univariate analyses concerning the outcomes of respiratory adverse events and arterial desaturation before multivariate analyses. Accordingly, variables with a P value of 0.2 or less were analysed using stepwise multivariate logistic regression for the outcome of proceeding with anaesthesia, whereas variables with a P value of 0.1 or less post-Bonferroni correction were analysed using stepwise multivariate logistic regression for the outcomes of PRAEs and peri-operative arterial desaturation. Odds ratios were determined for each significant factor, as were goodness of fit (Hosmer–Lemeshow test with a $P > 0.2$), C-statistics (ROC analysis of the model)[8] and sensitivity, specificity, positive predictive value, negative predictive value [and their 95% confidence intervals (CI)] of the logistic regression model.[9] Finally, to avoid collinearity, correlations between predictive factors were analysed and one of the two correlated factors were removed if the correlation was at least 0.7. Statistical analysis was performed using SPSS 22.0 software (IBM Company, Chicago, Illinois, USA).

Number of patients to be included

The sample size of this study was calculated so that the primary outcome of this study (PRAE) could be analysed and data overfeeding avoided. According to a recently published survey on patient rescheduling in one of our centres,[6] 220 patients presented to the ambulatory surgical unit with current or recent URTI symptoms from January to June 2014, and of these, 65 (29.5%) were rescheduled. Given that 30% of anesthetised patients with URTI were estimated to experience a respiratory adverse event[5,10] and that statistical analyses on those respiratory adverse events were expected to include at least 10 cofactors,[11] 100 patients with adverse events (10 patients per variable) were required for logistic regression analysis – a total of 330 anesthetised patients with current or recent URTI. Allowing for 30% rescheduling, a total

Fig. 1



Flow-chart of the study.

number of 470 patients with current or recent URTI was targeted for analyses.

All 16 participating centres were presumed to have the same caseload and URTI rate as in the previously surveyed ambulatory unit (220 patients with URTI per 6 months).[6] Based on the number of anaesthetists expected to participate in the study (25 to 50% in each centre), we predicted a study inclusion rate of 82 to 164 patients per month. Accordingly, a 6-month period was required to enrol the desired number of patients.

Results

Sixteen centres participated in the current study. Overall, 28 858 procedures in patients less than 18 years of age were performed in these centres under general anaesthesia. The proportion of participating anaesthetists was 21.4% (41 of 184 paediatric anaesthetists across the 16 centres) which enabled data for 6297 procedures to be analysed. Overall, 623 patients fulfilled the inclusion criteria: only two patients were excluded during statistical analyses, both because of missing data (Fig. 1).

Table 1 Descriptive statistics of included patients (n=621)

Factor	
Age (months)	43 ± 40
Weight (kg)	16 ± 10.5
Senior anaesthesiologist	521 (83.9)
Experience in paediatric anaesthesiology (years)	10 ± 11
Surgery or procedure	
Imaging	33 (5.3)
Central venous catheter insertion	11 (1.8)
Endoscopy (digestive/respiratory)	19 (3.1)
General surgery	77 (12.4)
Neurosurgery	5 (0.8)
Ophthalmological surgery	13 (2.1)
Ear–nose–throat surgery	87 (14)
Orthopaedic surgery	122 (19.6)
Plastic surgery	49 (7.9)
Dental surgery	28 (4.5)
Urological surgery	173 (27.9)
Thoracic surgery	4 (0.6)
Emergency surgery	100 (16.1)
Ambulatory surgery	377 (60.5)
ASA status	
ASA I	44 (7.1)
ASA II	552 (88.9)
ASA III	25 (4)
Medical condition	
Former prematurity	34 (5.5)
Pulmonary hypertension	3 (0.5)
Cyanotic cardiopathy	6 (1)
Noncyanotic cardiopathy	11 (1.8)
Asthma	80 (12.9)
Other pulmonary conditions	40 (6.4)
Atopy	22 (3.5)
Parental smoking	60 (9.7)
Previous rescheduling of same surgery	
Previous URTI	66 (10.6)
All causes	73 (11.8)
Signs of URTI at admission	563 (90.7)
Fever	67 (10.8)
Wheezing	11 (1.8)
Dry cough	129 (20.8)
Moist cough	234 (37.7)
Auscultation abnormalities	47 (7.6)
Clear runny nose	177 (28.5)
Green runny nose	52 (8.4)
Lethargy	17 (2.7)
Signs of URTI in the preceding 4 weeks	58 (9.3)
Fever	9 (1.4)
Wheezing	20 (3.2)
Dry cough	3 (0.5)
Moist cough	17 (2.7)
Auscultation abnormalities	2 (0.3)
Clear runny nose	20 (3.2)
Green runny nose	1 (0)

Data are mean ± SD or number (%). URTI, upper respiratory tract infection.

The percentages of patients recruited per centre are shown in Supplementary file 1, http://links.lww.com/EJA/A170. As expected, the number of patients recruited decreased progressively from January through June (Supplementary file 2, http://links.lww.com/EJA/A170) as the beginning of the inclusion period coincided with the peak of winter respiratory tract infections in France. Included patients characteristics are displayed in Table 1.

Among anaesthetised patients (n=489, Fig. 1), PRAE occurred in 165 patients (33.5%) and peri-operative

Table 2 Peri-operative adverse events occurring during induction, maintenance, recovery and the postoperative acute care unit

	Induction, *n* (%)	Maintenance, *n* (%)	Recovery, *n* (%)	PACU, *n* (%)
Bronchospasm	18 (3.7)	17 (3.5)	26 (5.3)	4 (0.8)
Laryngospasm	18 (3.7)	2 (0.4)	13 (2.6)	0 (0)
Cough	27 (5.5)	15 (3.1)	0 (0)	37 (7.6)
Stridor	0 (0)		8 (1.6)	6 (1.2)
Desaturation	35 (7.2)	21 (4.3)	55 (11.2)	13 (2.7)
Bradycardia	0 (0)	0 (0)	5 (1)	0 (0)
Any complication	68 (13.1)	38 (7.8)	71 (14.5)	49 (10)

PACU, postoperative acute care unit.

arterial desaturation in 97 patients (19.8%). The details of adverse events and their timing are displayed in Table 2. Bradycardia occurred in five patients (1%) and was always associated with arterial desaturation (Table 2). Postoperatively, in PACU 74% of patients with PRAE were managed with nebulised beta-2 agonists and/or corticosteroids. Nine patients received noninvasive ventilation postoperatively. Finally, 20 patients (4.1%) required a prolonged PACU stay (6 h maximum), one patient (0.2%) required overnight monitoring in HDU and two (0.4%) patients required reintubation with 24 h postoperative ventilation in ICU. On postoperative day 2 all patients were discharged, and no patient had any postoperative disability. All complications, prolonged PACU stay, HDU or ICU admission were attributable to URTI. Univariate and multivariate analyses of factors associated with PRAE are displayed in Table 3. Multivariate analyses identified the following factors as associated with the occurrence of PRAE: age of 58 or less months and tracheal intubation (Table 3). Premedication with midazolam was protective against respiratory adverse events. No correlation was found between predictive factors. *C*-statistic was 0.7 (95% CI: 0.65 to 0.75). The *P* value for the Hosmer–Lemeshow test was 0.6.

Arterial desaturation was the most frequent event (Table 2), and 67 of 97 patients with arterial desaturation also experienced another adverse event: laryngospasm, bronchospasm, severe cough or stridor. Consequently, the presence of one of these events was analysed as a potential predictor of the occurrence of peri-operative arterial desaturation. Assuming that the presence of laryngospasm, bronchospasm, cough or stridor was statistically associated with factors identified by multivariate analysis for respiratory complications, all predictive factors of respiratory complications were not entered in the multivariate analysis for peri-operative arterial desaturation. Table 4 displays univariate and multivariate analyses of factors associated with arterial desaturation. Identified factors included age of 21 or less months, experience of the anaesthetist of 15 years or less, endoscopic procedures and the presence of one of the following: laryngospasm, bronchospasm, severe cough or stridor. No correlation was found between predictive factors. *C*-statistic was 0.83 (95% CI: 0.78 to 0.87). The *P* value for the Hosmer–Lemeshow test was 0.89.

Anaesthesia proceeded in 489 patients presenting with current or recent URTI symptoms (78.7%, Fig. 1). The percentage of patients proceeding to anaesthesia did not differ significantly among centres (data not shown). Table 5 displays univariate and multivariate analyses of factors associated with proceeding with anaesthesia despite URTI symptoms. The following factors were predictive of proceeding with anaesthesia in this cohort of children with URTI: experience of anaesthetist at least 8 years, emergency surgery or procedure, the presence of a clear runny nose and the absence of fever, moist cough, abnormal auscultation or lethargy. No correlation was found between predictive factors. The *C*-statistic was 0.88 (95% CI: 0.85 to 0.9). The *P* value for the Hosmer-Lemeshow test was 0.24.

Discussion

The main finding of this study was that in patients with URTI allowed to proceed to anaesthesia and surgery, adverse events and arterial desaturation occurred in 33.5 and 20%, respectively. Predictors of PRAE included younger patient age, anaesthetist experience, premedication and tracheal intubation. About 80% of paediatric patients with current or recent URTI symptoms proceeded with anaesthesia. Factors associated with the decision to proceed with anaesthesia included anaesthetist experience, emergency procedures and type of URTI symptoms at presentation.

About 30% of patients with URTI who proceeded to anaesthesia had respiratory adverse events, a result similar to published data in comparable cohorts when more patients were rescheduled (three and four). This indicates that despite rescheduling for specific risk factors, the residual risk of respiratory adverse events still remains high when compared with cohorts with lower rescheduling rates (five). Such a result questions the protective effect of high rescheduling rates for patients with URTI, as commonly performed in France. This point of view is supported by the rarity of serious peri-operative consequences (0.6% when considering HDU or ICU admission) and the high number of URTI episodes experienced in children (two). One important point to make is the necessity for parental involvement in the decision to proceed with surgery in the context of URTI

Table 3 Univariate and multivariate logistic regression analyses of factors associated with peri-operative respiratory adverse events in anaesthetised children with upper respiratory tract infection

Factor	Univariate analysis			Multivariate analysis
	PRAE, *n*=164	No PRAE, *n*=325	*P*	OR (95% CI)
Age (months)	33 ± 29	48 ± 43	<0.001	
Age ≤ 58 months	**147 (89.6)**	**228 (70.2)**	**<0.001**	4 (2 to 8)
Weight (kg)	13 ± 8	17 ± 11	<0.001	
Senior anaesthetist	137 (83.5)	281 (86.5)	0.231	
Experience in paediatric anaesthesia (years)	11 ± 11	12 ± 11	0.6	
Surgery or procedure				
Imaging	6 (3.7)	17 (5.2)	0.5	
Central venous catheter insertion	2 (1.2)	7 (2.2)	0.7	
Endoscopy (digestive/respiratory)	9 (5.5)	8 (2.5)	0.115	
General surgery				
Neurosurgery	18 (11)	43 (13.2)	0.56	
Ophthalmological surgery	3 (1.8)	1 (0.3)	0.112	
ENT	4 (2.4)	6 (1.8)	0.74	
Orthopaedic surgery	27 (16.5)	44 (13.5)	0.4	
Plastic surgery	32 (19.5)	60 (18.5)	0.8	
Dental surgery	15 (9.1)	29 (8.9)	1	
Urological surgery	9 (5.5)	13 (4.0)	0.5	
Thoracic surgery	38 (23.2)	96 (29.5)	0.163	
	1 (0.6)	1 (0.3)	1	
Emergency surgery	**45 (27)**	**54 (16.6)**	**0.006**	
Ambulatory surgery	**87 (53)**	**204 (62.8)**	**0.04**	
ASA status				
ASA I	13 (7.9)	29 (8.9)		
ASA II	148 (90.2)	281 (86.5)	0.27	
ASA III	3 (1.8)	15 (4.6)		
Medical condition				
Former prematurity	10 (6.1)	17 (5.2)	**0.7**	
Pulmonary hypertension	0 (0)	1 (0.3)	1	
Cyanotic cardiopathy	1 (0.6)	1 (0.3)	1	
Noncyanotic cardiopathy	3 (1.8)	[illegible]	0.4	
Asthma	22 (13.4)	40 (12.3)	0.8	
Other pulmonary conditions	**15 (9.1)**	**14 (4.3)**	**0.04**	
Atopy	6 (3.7)	13 (4.0)	1	
Parental smoking	**10 (6.1)**	**36 (11.1)**	**0.1**	
Previous rescheduling of same surgery				
Previous URTI	20 (12.2)	[illegible]	0.135	
All causes	**23 (14)**	**28 (8.6)**	**0.08**	
Current signs of URTI	148 (90.2)	285 (87.7)	0.45	
Fever	14 (8.5)	15 (4.6)	0.1	
Wheezing	3 (1.8)	2 (0.6)	0.34	
Dry cough	39 (23.[illegible])	74 (22.8)	0.8	
Moist cough	**63 (38.4)**	**98 (30.2)**	**0.08**	
Auscultation abnormalities	[illegible] (7.4)	13 (4)	0.130	
Clear runny nose	[illegible] (32.9)	111 (34.2)	0.8	
Green runny nose	10 [illegible]	25 (7.5)	0.6	
Lethargy	[illegible] (1.2)	6 (1.8)	0.7	
Signs of URTI in the past 4 weeks	[illegible] (9.8)	40 (12.3)	0.45	
Fever	[illegible] (1.2)	7 (2.2)	0.7	
Wheezing	6 (3.7)	12 (3.7)	1	
Dry cough	0 (0)	3 (0.9)	0.5	
Moist cough	5 (3)	12 (3.7)	0.8	
Auscultation abnormalities	0 (0)	1 (0.3)	1	
Clear runny nose	5 (3)	14 (4.3)	0.6	
Green runny nose	1 (0.6)	0 (0)	1	
Premedication				
Midazolam	**49 (29.9)**	**144 (44.3)**	**0.002**	0.6 (0.4 to 0.9)
Hydroxyzine	4 (2.4)	9 (2.8)	1	
Clonidine	10 (6.1)	60 (6.1)	1	
Pre-operative nebulised salbutamol	48 (29.3)	78 (24)	0.23	
Pre-operative nebulised corticosteroids	6 (3.7)	24 (7.4)	0.1	
Pre-operative physiotherapy	4 (2.4)	12 (3.7)	0.33	
Anaesthetist covering 2 rooms	69 (42.1)	150 (46.2)	0.224	
Induction				
Inhalational	132 (85.5)	258 (79.4)		
Intravenous	15 (9.1)	38 (11.7)	0.4	
Inhalational and intravenous	17 (10.4)	28 (8.6)		
Airways				
Intubation	**100 (61)**	**127 (39.1)**		2.5 (1.7 to 3.8)
Laryngeal mask	**47 (28.7)**	**134 (41.2)**	**<0.001**	
Face mask	**17 (10.4)**	**64 (19.7)**		
Ventilation				
Controlled	**112 (68.3)**	**185 (56.9)**		
Pressure support	**25 (15.2)**	**66 (20.3)**	**0.04**	
Spontaneous ventilation	**26 (15.9)**	**74 (22.8)**		
Muscle relaxation at induction	**17 (10.4)**	**12 (3.7)**	**0.004**	
Intra-operative opioids	69 (42.1)	113 (34.8)	0.137	
Intra-operative regional anaesthesia	59 (36)	138 (42.5)	0.173	
Intra-operative muscle relaxant	14 (8.5)	17 (5.2)	0.2	
Awake removal of ventilation device	**89 (54.3)**	**139 (42.8)**	**0.017**	

Bold script indicates factors included in the multivariate model. Data are mean ± SD, OR (95% CI), or *n* (%). PRAE, peri-operative respiratory adverse event; URTI, upper respiratory tract infection.

Table 4 Univariate and multivariate logistic regression analyses of factors associated with arterial desaturation in anaesthetised children with upper respiratory tract

Factor	Univariate analysis Yes, *n*=97	No, *n*=392	*P*	Multivariate analysis OR (95% CI)
Age (months)	29 ± 31	46 ± 41	<0.001	
Age ≤ 21 months	**58 (59.8)**	**124 (31.6)**	**<0.001**	3 (1.7 to 4.9)
Weight (kg)	13 ± 8	17 ± 11	<0.001	
Senior anaesthesiologist	80 (82.5)	338 (86.2)	0.34	
Experience in paediatric anaesthesiology (years)	9 ± 10	12 ± 11	0.05	
Experience in paediatric anaesthesia ≤ 15 years	**72 (74.2)**	**240 (61.2)**	**0.02**	2 (1.1 to 3.6)
Surgery or procedure				
Imaging	2 (2.1)	21 (5.4)	0.3	
Central venous catheter insertion	2 (2.1)	7 (1.8)	0.7	5.4 (1.6 to 18.2)
Endoscopy (digestive/respiratory)	**8 (8.2)**	**9 (2.3)**	**0.009**	
General surgery	9 (9.3)	52 (13.3)	0.4	
Neurosurgery	1 (1)	3 (0.8)	0.6	
Ophthalmological surgery	3 (3.1)	7 (1.8)	0.4	
ENT	15 (15.5)	56 (14.3)	0.7	
Orthopaedic surgery	16 (16.5)	76 (19.4)	0.56	
Plastic surgery	9 (9.3)	35 (8.9)	0.8	
Dental surgery	4 (4.1)	18 (4.6)	1	
Urological surgery	27 (27.8)	107 (17.3)	0.9	
Thoracic surgery	1 (1)	1 (0.3)	0.36	
Emergency surgery	**27 (27.8)**	**72 (18.4)**	**0.05**	
Ambulatory surgery	**50 (51.5)**	**241 (61.5)**	**0.08**	
ASA status				
ASA I	6 (6.2)	36 (9.2)		
ASA II	89 (91.8)	340 (86.7)	0.4	
ASA III	2 (2.1)	16 (		
Medical condition				
Former prematurity	8 (8.2)	(4.8)	0.2	
Pulmonary hypertension	0 (0)	(0.3)	1	
Cyanotic cardiopathy	0 (0)	2	1	
Noncyanotic cardiopathy	2 (2.1)	4 (1	0.3	
Asthma	12 (12.4)	(12.8)	1	
Other pulmonary conditions	10 (10.3)	19 (4.8)	0.53	
Atopy	5 (5.2)	14 (3.6)	0.5	
Parental smoking	6 (6.2)	40 (10.2)	0.33	
Previous rescheduling of same surgery				
Previous URTI	1 (14.4)	(7.9)	0.52	
All causes	**(15.5)**	**36 (9.2)**	**0.09**	
Current signs of URTI	9 (91.8)	344 (87.7)	0.4	
Fever	(5.2)	24 (6.1)	1	
Wheezing	(2.1)	3 (0.8)	0.26	
Dry cough	26	87 (22.2)	0.34	
Moist cough	36 (37.1)	125 (31.9)	0.34	
Auscultation abnormalities	**9 (9.1)**	**16 (4.1)**	**0.07**	
Clear runny nose	(1)	129 (32.9)	0.5	
Green runny nose	7 (7.2)	28 (7.1)	1	
Lethargy	1 (1)	7 (1.8)	1	
Signs of URTI in the past 4 weeks	8 (8.2)	48 (12.3)	0.4	
Fever	0 (0)	9 (2.3)	0.2	
Wheezing	4 (4.1)	14 (3.6)	0.8	
Dry cough	0 (0)	3 (0.8)	1	
Moist cough	3 (3.1)	14 (3.6)	1	
Auscultation abnormalities	0 (0)	1 (0.3)	1	
Clear runny nose	2 (2.1)	17 (4.3)	0.4	
Green runny nose	1 (1)	0 (0)	0.2	
Premedication				
Midazolam	26 (26.8)	167 (42.6)	0.00	
Hydroxyzine	1 (1)	12 (3.1)	0.5	
Clonidine	5 (5.2)	25 (6.4)	0.8	
Pre-operative nebulised salbutamol	27 (27.8)	99 (25.3)	0.6	
Pre-operative nebulised corticosteroids	3 (3.1)	27 (6.9)	0.23	
Pre-operative physiotherapy	2 (2.1)	14 (3.6)	0.7	
Anaesthetist covering 2 rooms	**37 (38.1)**	**180 (46.4)**	**0.087**	
Induction				
Inhalational	77 (79.4)	313 (79.8)		
Intravenous	9 (9.3)	44 (11.2)	0.3	
Inhalational and intravenous	11 (11.3)	34 (8.7)		
Airway				
Intubation	61 (62.9)	166 (42.3)		
Laryngeal mask	27 (27.8)	154 (39.3)	0.001	
Face mask	9 (9.3)	72 (18.4)		
Ventilation				
Controlled	**67 (69.1)**	**230 (58.7)**		
Pressure support	**11 (11.3)**	**80 (20.4)**	**0.03**	
Spontaneous ventilation	**18 (18.6)**	**82 (20.9)**		
Muscle relaxation at induction	**10 (10.3)**	**19 (4.8)**	**0.05**	
Intra-operative opioids	36 (37.1)	146 (37.2)	1	
Intra-operative regional anaesthesia	32 (33)	165 (42.1)	0.11	
Intra-operative muscle relaxant	**10 (10.3)**	**21 (5.4)**	**0.1**	
Awake removal of ventilation device	**55 (56.7)**	**173 (44.1)**	**0.03**	
Peri-operative laryngospasm, bronchospasm, cough or stridor	**67 (69.1)**	**30 (30.9)**	**<0.001**	10.7 (6.2 to 18.2)

Bold script indicates factors included in the multivariate model. Data are mean ± SD, OR (95% CI), or *n* (%). PRAE, peri-operative adverse event; URTI, upper respiratory tract infection

Table 5 Univariate and multivariate logistic regression analyses of factors associated with the decision to proceed with anaesthesia in patients with upper respiratory tract infection

Factor	Univariate analysis			Multivariate analysis
	Rescheduled, *n*=132	Proceeded, *n*=489	*P*	OR (95% CI)
Age (months)	40 ± 43	43 ± 39	0.48	
Age <1 year	27 (20.5)	88 (18)	0.55	
Weight (kg)	15 ± 10	16 ± 11	0.38	
Senior anaesthetist	103 (78)	418 (85.5)	0.045	
Experience in paediatric anaesthesia (years)	8 ± 10	11 ± 11	0.013	
Experience in paediatric anaesthesia ≥8 years	**47 (35.6)**	**249 (50.9)**	**0.002**	2 (1.2 to 3.2)
Surgery or procedure				
Imaging	10 (7.6)	23 (4.7)	0.193	
Central venous catheter insertion	2 (1.5)	9 (1.8)	0.575	
Endoscopy (digestive/respiratory)	2 (1.5)	17 (3.5)	0.392	
General surgery	16 (12.1)	61 (12.5)	1	
Neurosurgery	1 (0.8)	4 (0.8)	1	
Ophthalmological surgery	3 (2.3)	10 (2)	0.7	
Ear–nose–throat surgery	16 (12.1)	71 (14.5)	0.57	
Orthopaedic surgery	30 (22.7)	92 (18.2)	0.32	
Plastic surgery	5 (3.8)	44 (9)	0.067	
Dental surgery	6 (4.5)	22 (4.5)	1	
Urological surgery	39 (29.5)	134 (27.4)	0.66	
Thoracic surgery	**2 (1.5)**	**2 (0.4)**	**0.2**	
Emergency surgery	**1 (0.8)**	**99 (20.2)**	**<0.001**	279 (28 to 2700)
Ambulatory surgery	86 (65 0.2)	[illegible] (59.5)	0.27	
ASA status				
ASA I	**2 (1.5)**	**[illegible]**		
ASA II	**123 (93.2)**	**[illegible] (87.7)**	0.15	
ASA III	**7 (5.3)**	**18 [illegible]**		
Medical condition				
Former prematurity	7 (5.3)	[illegible] (5.5)	0.5	
Pulmonary hypertension	2 (1.5)	[illegible] (0.2)	0.11	
Cyanotic cardiopathy	4 [illegible]	2 (0.4)	0.21	
Noncyanotic cardiopathy	**5 [illegible]**	**6 (1.2)**	**0.06**	
Asthma	18 [illegible].6)	62 (12.7)	0.8	
Other pulmonary conditions	11 [illegible]	29 (5.9)	0.32	
Atopy	[illegible] (2.3)	19 (3.9)	0.6	
Parental smoking	[illegible] (10.6)	46 (9.4)	0.7	
Previous rescheduling of same surgery				
Previous URTI	**21 (15.9)**	**45 (9.2)**	**0.04**	
All causes	22 (16.7)	51 (10.4)	0.07	
Signs of URTI at admission	[illegible] (98.5)	433 (88.5)		
Fever	**38 (28.8)**	**29 (5.9)**	**<0.001**	0.02 (0.008 to 0.06)
Wheezing	**6 (4.5)**	**5 (1)**	**0.015**	
Dry cough	**16 (12.1)**	**113 (23.1)**	**0.005**	0.2 (0.1 to 0.4)
Moist cough	**73 (55.3)**	**161 (32.9)**	**<0.001**	0.2 (0.1 to 0.5)
Auscultation abnormalities	**22 (16.7)**	**25 (5.1)**	**<0.001**	
Clear runny nose	**12 (9.1)**	**165 (33.7)**	**<0.001**	4 (2 to 9)
Green runny nose	**17 (12.9)**	**35 (7.2)**	**0.05**	0.07 (0.02 to 0.3)
Lethargy	**9 (6.8)**	**8 (6.1)**	**0.004**	
Signs of URTI in the preceding 4 weeks	2 (1.5)	56 (11.5)		
Fever	0 (0)	9 (1.8)	0.115	
Wheezing	2 (1.5)	18 (3.7)	0.17	
Dry cough	0 (0)	3 (0.6)	0.48	
Moist cough	0 (0)	17 (3.5)	0.016	
Auscultation abnormalities	1 (0.8)	1 (0.2)	0.38	
Clear runny nose	1 (0.8)	19 (3.9)	0.4	
Green runny nose	0 (0)	1 (0)	0.8	

Bold script indicates factors included in the multivariate model. Data are expressed as mean ± SD; odds ratio with 95% confidence intervals, and *n* (%). URTI, upper respiratory tract infection.

in the understanding of the increased but nonetheless small risk of serious peri-operative events.

Factors associated with PRAEs and arterial desaturation were mostly unsurprising and previously published, that is younger age, tracheal intubation and experience of the anaesthetist.[3,5,10,12–14] However, the current study identified midazolam premedication as protective against PRAE in children with URTI. Although, this result is in contrast with recent studies in which the drug was associated with higher PRAE rates irrespective of the presence of URTI,[5,15] no trial has specifically investigated midazolam premedication in children with URTIs. One can hypothesise that the depth of anaesthesia induced by

the addition of midazolam might prevent the occurrence of PRAE. Alternatively, midazolam has been experimentally found to produce a spasmolytic effect on constricted airways[16] and clinically to induce pharyngeal relaxation.[17] Such effects could contribute to the protective effect of this agent observed in our study.

Most arterial desaturation events were associated with reported respiratory complications (laryngospasm, bronchospasm, cough and stridor). The number of arterial desaturation episodes was lower than the total of all PRAE because of the concomitant occurrence of multiple complications in one patient, and of course, not all complications led to arterial desaturation. Anaesthetist experience has been previously identified as a preventive factor against peri-operative adverse events during paediatric anaesthesia, albeit with a very small risk-reduction benefit.[3,5] Significantly, anaesthetist experience was associated with a reduced incidence of arterial desaturation in our study but not of PRAE overall. This may mean that the anaesthetist's experience is useful when managing adverse events[3,18] after they occur. This result supports training efforts, such as simulation, that standardise the management of respiratory adverse events with the aim of preventing arterial desaturation during paediatric anaesthesia.[18,19] It also suggests the availability of an experienced anaesthetist is beneficial when patients with URTI are anesthetised.[5,14] This is of particular importance given the near-future shortage of anaesthetists in Europe. Both complicated and uncomplicated patients were anaesthetised by an anaesthetist working between two operating rooms in almost 45% of patients. The most probable explanation for the lack of association between anaesthetist experience and the occurrence of a peri-operative complication was that during anaesthesia of patients with URTI, anaesthetists were focusing on the room containing the patient with URTI. In fact, given that working across two operating rooms occurs commonly in France, anaesthetists are advised to carefully assess safety conditions and the ability to summon help when deciding to proceed with anaesthesia in two operating rooms when one patient requires special attention. A solution widely employed in France is the presence of a 'floating anaesthetist' who is not rostered to any one operating room and is therefore available to help in such circumstances.

Finally, endoscopic procedures were associated with increased arterial desaturation rates. Hypotheses to explain this result include a potentially remote anaesthetic environment away from central operating theatres and involving limited or unfamiliar equipment, and direct stimulation to the pharynx or bronchi during the procedure. Lastly, one can imagine that patients scheduled for endoscopic procedures might be less well prepared due to the supposedly less invasive nature of the procedure – with resulting less rigorous management both pre and intra-operatively.

Although it may seem surprising that 20% of patients presenting with current or recent URTI symptoms were rescheduled, this result is not dissimilar to a previously published survey in France that found 30% of patients rescheduled when presenting with URTI.[6] Such proportions are high in comparison with other countries[2] but reflect current management of patients with URTI in France. This observation is supported by the relative lack of variability of rescheduling rates across participating centres and the high accuracy of the logistic regression model for predicting factors associated with the decision to proceed with anaesthesia. The latter indicates shared reasoning processes employed by physicians when presented with children suffering from URTIs. Otherwise, the high proportion of rescheduled patients might reflect the lack of screening of patients with previous URTIs resulting in the selection of the most severe patients. Given the high proportion of rescheduling observed in our study, some solutions might be undertaken to reduce this rate or at least to anticipate rescheduling and avoid parents and patients presenting on the day of the surgery. These solutions might consist of giving parents clear information about the necessity of calling the surgical centre in case of URTI, providing the paediatrician or the family physician simple guidelines allowing them to judge the signs that mandate surgical rescheduling and specific follow-up of patients before a new surgery appointment is provided.

Among predictive factors for proceeding with anaesthesia, emergency surgery and triaging by specific symptoms of URTI are unsurprising. Both have been proposed in recent decisional algorithms for managing children with URTI.[2] The level of experience of the treating anaesthetist was associated with an increased rate of proceeding to anaesthesia in patients with URTIs was at odds with a previous survey on this topic performed in the USA in 1995[20] which demonstrated that anaesthetists with more than 10 years of experience were more likely to reschedule than those who had been in practice for less than 10 years. Such results may indicate a divergence between North American and French practice or changes in knowledge and practice in patients with URTI over time.

The current study suffers from some limitations. First, the number of patients included in this study varied widely between centres (range: 4 to 109 patients). Although there was no difference in rescheduling rates or respiratory adverse events across centres, one cannot exclude a centre-effect. In fact, even though statistical analyses indicate stability in factors leading to the postponement of anaesthesia and surgery, heterogeneity in individual practice might be present among participating anaesthetists. Moreover, results of the current study concerning rescheduling can probably not be applied easily to other countries given the heterogeneity of management of patients with URTI worldwide. Participating physicians anaesthetised 6297 patients during the study period with some 10% of the children presenting with URTI. Our local data indicates that this proportion is normally around 4.7%.[6] There could

be regional or temporal URTI prevalence differences leading to this higher figure. Also, as the proportion of participating physicians was only 21.4%, one cannot exclude the risk of selection bias, given that inclusion of patients was physician-dependant. Most patients included in the study presented with current signs of URTI (91%) rather than a history of URTI in the preceding 4 weeks. This strongly suggests that patients with recent URTI symptoms were inadequately screened. Moreover, this might have resulted in an overestimate of the incidence of PRAE and rescheduling. Finally, the ratio of one analysed factor per 10 events was not respected for the multivariate analysis regarding peri-operative arterial desaturation. However, this is unlikely to have caused collinearity given the number of predictors identified and the lack of significant correlation between them.

In conclusion, the current study indicates that despite rescheduling those patients with URTI thought to be at the highest risk of respiratory adverse events, a high rate of peri-operative adverse events continued to occur in those that proceed to anaesthesia. This result questions the efficacy of postponing anaesthesia in the context of URTI, especially when symptoms are present. The presence of an experienced paediatric anaesthesiologist significantly reduces the incidence of peri-operative arterial desaturation. Specific pre-operative therapies such as premedication with midazolam appear protective and should be further investigated in the aim of reducing PRAE during anaesthesia in patients with URTI.

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