

A PROSPECTIVE, MULTICENTER, OBSERVATIONAL STUDY OF PREMEDICATION BEFORE LARYNGOSCOPY IN NEONATES (SUPREMENEO)

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OBJECTIVE

To evaluate the implementation of the 2023 French Society of Neonatology (SFN) guidelines for premedication before laryngoscopy in neonates without life-threatening emergencies.

STUDY DESIGN

A prospective, observational cohort study was conducted across 141 French and Belgian neonatal units. Laryngoscopy data from intubation or less invasive surfactant administration in neonates <45 weeks post-menstrual age were collected. The primary outcome was the proportion of premedication consistent with SFN guidelines. Factors associated with guideline compliance were analyzed using multivariable mixed-effects logistic regression adjusted for neonatal and procedural characteristics.

RESULTS

Six hundred seventy-three laryngoscopies were included. The mean (SD) gestational age was 30.1 (4.8) weeks. Of 506 intubations, 110 (21.7%) were immediate life-threatening emergencies. Among 396 non-life-threatening intubations, 357 (90.1%) were preceded by premedication with 169 (2.7%) consistent with SFN guidelines (propofol alone [$n = 149$, 37.6%]; a fast-acting opioid + muscle blocker [$n = 20$, 5.1%]). Independent factors associated with SFN guidelines compliance were non-emergent intubation (adjusted odds ratio 3.1 [95% CI 1.4–7.0]) and absence of hemodynamic compromise (adjusted odds ratio 31.0 [95% CI 64–150.3]). Propofol and ketamine were the most frequent premedications before intubation, followed by opioids and/or anesthetics. Of the 167 less invasive surfactant administration procedures, 151 (90.4%) were preceded by specific premedication including propofol ($n = 84$, 50.3%), consistent with SFN guidelines.

CONCLUSIONS

Ninety percent of non-life-threatening laryngoscopies were preceded by a premedication but fewer than half complied with SFN guidelines. Further studies on efficacy and tolerance of neonatal anesthetics and drug associations are needed. (*J Pediatr* 2026;290:114967).

ABBREVIATIONS

ELBW	Extremely low birth weight
GA	Gestational age
LISA	Less invasive surfactant administration
NICU	Neonatal intensive care unit
PMA	Postmenstrual age
TRACHEA	Tonus
Reactivity	Awareness, and Conditions of intubation to Help in Endotracheal intubation Assessment
SFN	French Society of Neonatology

Introduction

Laryngoscopy for intubation or less invasive surfactant administration (LISA) in neonates is a stressful and painful procedure that requires premedication, except in the cases of immediate life-threatening emergencies.¹⁻³ However, significant variability exists in premedication practices worldwide, with notable discrepancies between observational and self-reported studies, and awake laryngoscopy remains common prior to these procedures.⁴⁻¹¹ In order to optimize analgesia prior to neonatal laryngoscopy, the French Society of Neonatology (SFN) issued evidence-based practice guidelines in January 2023 for premedication before laryngoscopy in neonates.¹² For intubation, the guidelines recommended either a combination of a fast-acting opioid and a muscle blocker or the use of propofol, provided there was no hemodynamic compromise or hypotension. For LISA, the use of propofol was also recommended under similar hemodynamic conditions.¹²

The implementation of new premedication protocols in neonatal units may be challenging due to entrenched local practices, limited dissemination of the guidelines and insufficient evidence for certain premedication agents. Therefore, we conducted a prospective study following the publication of the SFN best practice guidelines on premedication to assess premedication practice evolution in France, and evaluate the impact and dissemination of the guidelines.

The main objective of this study was to evaluate compliance of premedication administration with the SFN practice guidelines 1 year after their publication. Secondary objectives included description of current premedication practices before laryngoscopy, identification of factors associated with compliance with SFN guidelines and with any premedication use, and evaluation of efficacy and safety of premedications used.

Methods

STUDY DESIGN

We performed an observational, prospective, bi-national cohort study (France and Belgium). Data collection was conducted from March 11 to April 4, 2024 in France and from June 3 to 30, 2024 in Belgium. The study period was chosen to occur approximately 1 year after the publication of the SFN practice guidelines on premedication before laryngoscopy.¹² During the 28 consecutive days of the study in each country, all neonates with a PMA of less than 45 weeks who underwent a laryngoscopy (intubation or LISA) or a laryngeal mask insertion were included regardless of whether they received premedication or not. If a neonate underwent multiple laryngoscopies during the study period, each procedure was included separately. Exclusion criteria were laryngoscopy performed in the operating room, participation in an interventional blinded trial on premedication, or parental refusal to participate. An opt-out parental consent procedure for this study was approved by the ethics committee of the Centre Hospitalier Intercommunal de Créteil on July 7, 2023 for French centers. In the event of either parent declining to participate, data were not collected. Consent from

both parents was obtained in Belgian centers for data collection with approval from the University Hospital Faculty Ethics Committee of Liège ethics committee on May 17, 2024.

DATA COLLECTION AND DEFINITIONS

The following data were collected for each laryngoscopy: neonatal characteristics (sex, GA at birth (weeks), birth weight (g), postnatal age, PMA, and weight at the time of laryngoscopy); circumstances of the procedure (day/night shift (8 AM to 8 PM/8 PM to 8 AM), indication, intubation route, use of videolaryngoscopy, emergency level based on the required delay between decision and intubation (emergent if ≤ 10 minutes; semi-emergent between 10 and 30 minutes, and non-emergent if > 30 minutes), pre-procedural ventilatory support, parental presence, hemodynamic compromise at the time of laryngoscopy (mean arterial blood pressure in mmHg $<$ corrected GA in weeks and/or need for hemodynamic support), location (neonatal intensive care unit (NICU), special care nursery, delivery room or transport unit) and type of facility (level I, II, or III)), and operator's awareness of the SFN guidelines. Data collected for premedication included agents, continuous infusion of sedation or analgesia at the time of the laryngoscopy, reasons for the absence of premedication, atropine use and indication, where applicable, adverse events observed during or within 1 hour following premedication, success at first attempt and TRACHEA score (Tonus, Reactivity, Awareness, and Conditions of intubation to Help in Endotracheal intubation Assessment)⁶ (0 = adequate sedation with excellent conditions of intubation, 10 = inadequate sedation with very poor conditions of intubation), as rated by the operator.

OUTCOMES

The primary outcome was the proportion of laryngoscopies preceded by a first sequence of premedication in compliance with the SFN practice guidelines. When no premedication was administered to the patient, the operator could indicate that the reason was an immediate life-threatening emergency. SFN practice guidelines considered that cardiopulmonary arrest or bradycardia despite efficient ventilation were life-threatening emergencies justifying an immediate intubation without premedication.¹² Thus, life-threatening intubations were excluded from the analysis on premedication. Secondary outcomes included characteristics of premedication used, reasons for absence of premedication, adverse events related to premedication, TRACHEA scores, and success at first attempt.

STATISTICAL ANALYSIS

Quantitative variables were presented as medians (interquartile ranges) or means (standard deviations), and categorical variables as counts and percentages. Group comparisons were conducted using student's t tests for continuous variables and chi-square/Fisher's exact tests for categorical variables. Separate analyses were performed for intubation and LISA procedures.

To identify factors associated with compliance with SFN practice guidelines, we compared the group that received premedication in compliance with SFN guidelines vs the non-compliant group (no

premedication or premedication outside of guidelines). To identify factors associated with the administration of any premedication prior to intubation, we compared the premedication and the no premedication groups. For each analysis, we first performed univariable logistic regression models to identify statistically and clinically relevant variables. Neonatal and procedural characteristics that could influence premedication based on existing literature⁵⁻⁷ or clinical relevance were studied: GA at birth (<28/28-31/32-36/>36 weeks), procedure period (day vs night), type of center (NICU vs level I + II), procedure location (delivery room vs neonatal unit regrouping NICU, special care nurseries or transport unit), degree of emergency (emergent vs non- or semi-emergent), hemodynamic compromise (presence or absence), operator affiliation (transport team or local), awareness of the SFN practice guidelines. GA and variables with *P* values <0.2 in univariable analysis were then included in a multivariable mixed-effects logistic regression model, with center included as a random effect. A sensitivity analysis was conducted for centers that reported at least 5 intubations. To compare efficacy between 3 groups - no premedication, adequate premedication following guidelines, and non-adequate premedication—we compared first attempt's success rates and TRACHEA scores using a threshold ≤ 3 .⁶ We compared the proportion of TRACHEA score >3 in extremely low birth weight (ELBW) (<1000g) vs ≥ 1000 g neonates, and between intubations and LISA procedures.

All analyses were conducted in complete cases (no replacement of missing data) using RStudio-2024.12.1 (Posit PBC). A *P* value less than 0.05 was considered statistically significant.

Results

PATIENT SAMPLE

A total of 190 French neonatal units were contacted, and 122 (64%) agreed to participate in the study: 55 of 70 (78.6%) French level III NICUs, 43 of 86 (50%) French level II special care nurseries and 24 of 34 (70.6%) French pediatric transport teams. All 19 (100%) Belgian level III NICUs participated in the study; level II centers in Belgium do not perform laryngoscopies and transports of newborn are provided by NICU teams. During the study period, 741 laryngoscopies were recorded (581 in France, 160 in Belgium) with 674 laryngoscopies included in the analysis: 506 intubations, 167 LISA procedures, and 1 laryngeal mask insertion (Figure 1). The laryngeal mask insertion was a life-threatening emergency without premedication and was excluded from further analysis.

Patients' characteristics and circumstances of the procedure are presented in Table I. The main indications for intubation were respiratory distress syndrome (31.6%), apnea (15.6%), hypoxic-ischemic encephalopathy (6.9%), and endotracheal tube replacement (6.7%).

Figure 1. Flow chart of the study. Location of the laryngoscopy was missing for 15 intubations and 5 LISA.

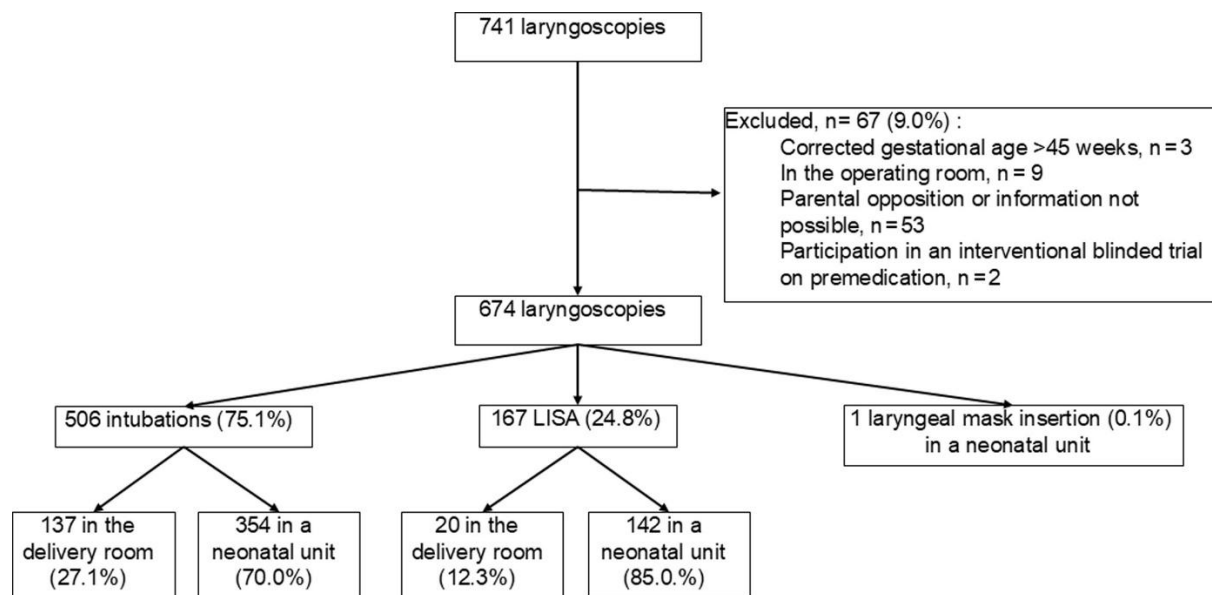


Table I. Patients' characteristics and circumstances of the procedure for all laryngoscopies, LISA, and intubations

Characteristics	Intubation (n = 506)	LISA (n = 167)	All laryngoscopies (n = 673)
Patients' characteristics, n with data (%)			
Sex (M), n = 669 (99.4)	290 (57.4)	88 (53.7)	378 (56.5)
Gestational age at birth (wks), n = 673 (100)	30.4 (5.2)	29.2 (2.9)	30.1 (4.8)
Birth weight (g), n = 671 (99.7)	1602 (1003)	1312 (569)	1530 (923)
Extremely low birth weight, n = 671 (99.7)	203 (40.3)	57 (34.1)	260 (38.7)
Postnatal age at laryngoscopy (d), n = 671 (99.7)	0.4 [0.0-8.1]	0.1 [0.0-0.3]	0.2 [0.0-2.8]
Corrected gestational age (wks), n = 671 (99.7)	31.9 (5.2)	29.6 (2.9)	31.3 (4.8)
Weight at laryngoscopy (g)	1706 (1015)	1306 (569)	1606 (940)
Circumstances of the procedure, n with data (%)			
Type of center, n = 665 (98.8)			
Neonatal intensive care unit (level III)	448 (89.6)	153 (92.7)	601 (90.4)
Special care nursery (level II)	43 (8.6)	11 (6.7)	54 (8.1)
Maternity with no neonatal ward (level I)	9 (1.8)	1 (0.6)	10 (1.5)
Location, n = 653 (97.0)			
Delivery room	137 (27.9)	20 (12.3)	157 (24.0)
NICU	288 (58.7)	110 (67.9)	398 (60.9)
Special nursery care	50 (10.2)	28 (17.3)	78 (11.9)
Transport	16 (3.3)	4 (2.5)	20 (3.1)
Degree of emergency, n = 670 (99.6)			
Emergent	199 (39.6)	2 (1.2)	201 (30.0)
Semi-emergent	208 (41.4)	101 (60.5)	309 (46.1)
Non-emergent	96 (19.1)	64 (38.3)	160 (23.9)
Day shift, n = 668 (99.3)	302 (60.0)	110 (66.7)	412 (61.7)
Type of ventilation before laryngoscopy, n = 670 (99.6)			
NIV/mask ventilation	398 (79.1)	167 (100)	565 (84.3)
Invasive ventilation	62 (12.3)	0 (0.0)	62 (9.3)
Spontaneous ventilation (± 02)	43 (8.6)	0 (0.0)	43 (6.4)
Nasal route (for intubations), n = 663 (98.5)	443 (89.3)	-	-
Videolaryngoscope, n = 628 (93.3)	64 (13.4)	71 (47.7)	135 (21.5)
Hemodynamic compromise, n = 673 (100)	57 (11.3)	15 (9.0)	72 (10.7)
Parental presence, n = 668 (99.3)	51 (10.1)	6 (3.7)	57 (8.5)

Results are expressed as mean (SD), median [IQR], or n (%), as appropriate. For patients' characteristics, even if some patients had multiple intubations, the denominator is the number of laryngoscopies because the number of patients was not available. Extremely low birth weight corresponds to birth weight < 1000g.

NIV, noninvasive ventilation.

PREMEDICATION BEFORE LARYNGOSCOPY AND COMPLIANCE WITH SFN PRACTICE GUIDELINES

Of the 506 intubations, 110 (21.7%) were for a lifethreatening emergency requiring immediate intubation without premedication. Among the 396 intubations for non-life-threatening emergencies, 357 (90.1%) were preceded by specific premedication; the primary reasons for absence of premedication included: lack of venous access (17/39, 43.6%), local habits or protocol (9/39, 23.1%), or ongoing continuous infusion of sedation or analgesia (4/39, 10.3%). Premedication was consistent with SFN practice guidelines in 169 of the 396 (42.7%) non-life-threatening intubations: propofol alone (without hemodynamic compromise) was used in 149 cases (37.6%), and a fast-acting opioid plus muscle blocker in 20 cases (5.1%) (Figure 2). Among the 167 laryngoscopies for LISA procedures, 151 (90.4%) received a specific premedication; reasons for absence of premedication that occurred in 6 of the 141 centers were prescribers' habits or local protocol. Propofol alone was administered in 84 of 167 (50.3%) LISA without hemodynamic compromise or hypotension, consistent with practice guidelines (Figure 2). Operators were aware of the SFN practice guidelines in 286 of 390 (73.3%) non-life-threatening intubations and in 121 of 161 (75.2%) LISA.

Atropine was systematically associated with premedication in 258 of 506 (51.7%) intubations and 111 of 167 (66.9%) LISA procedures. It was used to treat bradycardia in 10 of 506 (2.0%) intubations and 4 of 167 (2.4%) LISA procedures.

Factors associated with compliance with SFN guidelines were nonemergent intubation (adjusted odds ratio [aOR] (95% CI), 3.1 (1.4 – 7.0)) and absence of hemodynamic compromise or hypotension (aOR (95% CI), 31.0 (6.4-150.3)) (Table II). Factors associated with absence of premedication were emergent intubation (aOR (95% CI), 10.4 (2.3 – 46.4)) and procedures performed in the delivery room (aOR (95% CI), 127.8 (12.4 – 1313.3)). Neonates with gestational age (GA) at birth between 32 and 36 weeks were more likely to receive premedication compared with those with GA >36 weeks (aOR (95% CI) 0.08 (0.01 – 0.97)) (Table III). In the delivery room, 24/49 (49%) intubations for non-life-threatening situations did not include premedication, of which 14 of 24 (58%) were for surfactant administration. Reasons for absence of premedication were lack of venous access (n = 14), local practice or protocol in the delivery room (n = 6) or unknown (n = 4). The sensitivity analysis performed in centers with ≥ 5 intubations found similar associations in multivariable analysis except for GA at birth and absence of premedication. Univariable analysis did not identify factors associated with compliance with guidelines for LISA procedures.

Figure 2. Proportion of laryngoscopies according to combinations of agents used for intubations (left) and less invasive surfactant administration (LISA, right). Dark gray squares correspond to propofol used in patients with hemodynamic compromise. Opioids included sufentanil, morphine, fentanyl, and remifentanyl; black squares correspond to non-fast-acting opioids (morphine). Anesthetics used in these combinations included ketamine, propofol, midazolam, etomidate, sevoflurane, diazepam, and gamma-OH. IN, intranasal; MB, muscle blocker.

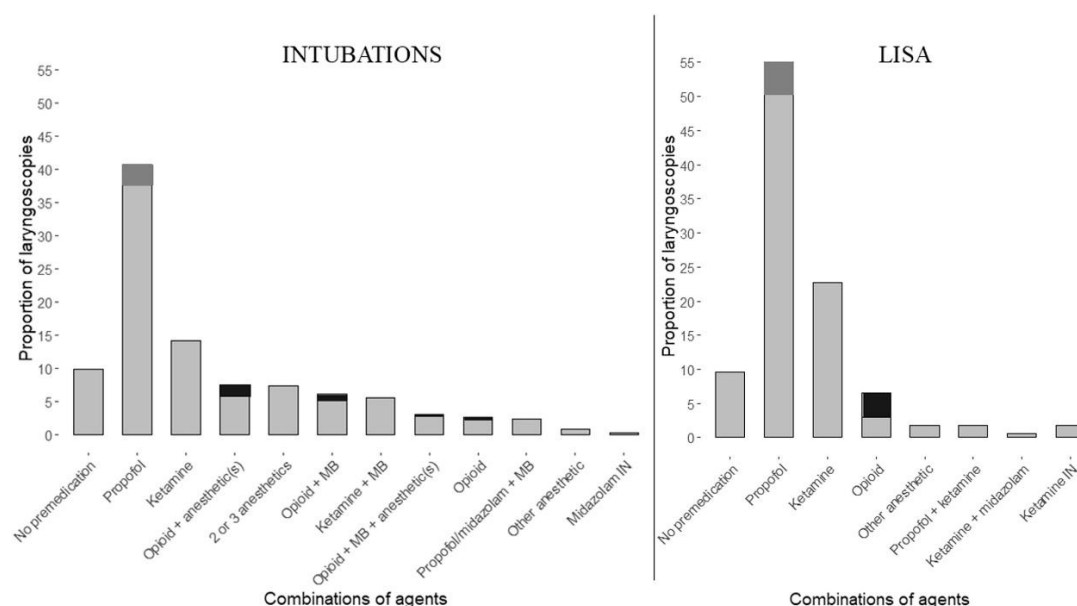


Table II. Univariable and multivariable analysis of factors associated with compliance of premedication to the evidence-based SFN best practice guidelines for non-life-threatening intubations

Factors included in the analysis	n	Compliance n = 169	Non-compliance n = 227	P value*	aOR (95% CI) [†]	P value [†]
Gestational age at birth (wks)	396					
>36		25 (37.3%)	42 (62.7%)		ref	
32-36		30 (36.6%)	52 (63.4%)	.93	0.8 (0.3-2.4)	.72
28-31		28 (39.4%)	43 (60.6%)	.80	1.0 (0.3-3.4)	.93
<28		86 (48.9%)	90 (51.1%)	.11	1.3 (0.5-3.2)	.59
Procedure period	394					
Day shift		101 (41.7%)	141 (58.3%)		-	
Night shift		66 (43.4%)	86 (56.6%)	.74	-	
Type of center	390					
Level III		150 (43.8%)	192 (56.1%)		-	
Level I or II		18 (37.5%)	30 (62.5%)	.41	-	
Degree of emergency	393					
Emergent		30 (30.6%)	68 (69.4%)		ref	
Non-emergent		138 (46.8%)	157 (53.2%)	.006	3.1 (1.4-7.0)	.007
Hemodynamic compromise	396					
Yes		3 (6.0%)	47 (94.0%)		ref	
No		166 (48.0%)	180 (52.0%)	<.001	31.0 (6.4-150.3)	<.001
Operator affiliation	388					
Physician on site		153 (43.6%)	198 (56.4%)		-	
Transport team		14 (37.8%)	23 (62.2%)	.50	-	
Location of the procedure	383					
Neonatal unit		149 (44.6%)	185 (55.4%)		ref	
Delivery room		14 (28.6%)	35 (71.4%)	.04	0.6 (0.2-1.6)	.29
Awareness of the SFN guidelines	390					
Yes		130 (45.5%)	156 (54.5%)		ref	
No		37 (35.6%)	67 (66.4%)	.08	0.5 (0.2-1.2)	.15

Bold characters correspond to significant results.

*P value for univariable analysis, variables were included in multivariable analysis if P value < .2.

[†]Multivariable mixed-effects logistic regression model, with center included as a random effect. Intraclass correlation coefficient: 0.46, 46% of the model variability explained by center effect.

Analysis conducted on complete cases (n = 374).

Table III. Univariable and multivariable analysis of factors associated with the absence of premedication before non-life-threatening intubations

Factors included in the analysis	n	Premedication n = 357	No premedication n = 39	P value*	aOR (95% CI)†	P value†
Gestational age at birth (wks)						
>36	396	58 (86.6%)	9 (13.4%)		ref	
32-36		76 (92.7%)	6 (7.3%)	.22	0.1 (0.01-0.97)	.048
28-31		64 (90.1%)	7 (9.9%)	.51	0.2 (0.01-2.2)	.18
<28		159 (90.3%)	17 (9.7%)	.40	0.8 (0.1-5.5)	.80
Procedure period						
Day shift	394	218 (90.1%)	24 (9.9%)		-	
Night shift		137 (90.1%)	15 (9.9%)	.99	-	
Type of center						
Level III	390	308 (90.1%)	34 (9.9%)		-	
Level I or II		45 (93.7%)	3 (6.3%)	.42	-	
Degree of emergency						
Non-emergent	393	281 (95.3%)	14 (4.7%)		ref	
Emergent		73 (74.5%)	25 (25.5%)	<.001	10.4 (2.3-46.4)	.002
Hemodynamic compromise						
No	396	311 (89.9%)	35 (10.1%)		-	
Yes		46 (92.0%)	4 (8.0%)	.64	-	
Operator						
Physician on site	388	318 (90.6%)	33 (9.4%)		-	
Transport team		33 (89.2%)	4 (10.8%)	.78	-	
Location of the procedure						
Neonatal unit	383	319 (95.5%)	15 (4.5%)		ref	
Delivery room		25 (51.0%)	24 (49.0%)	<.001	127.8 (12.4-1313)	<.001
Awareness of the SFN guidelines						
Yes	390	269 (94.1%)	17 (5.9%)		ref	
No		83 (79.8%)	21 (20.2%)	<.001	1.5 (0.3-8.3)	.66

Bold characters correspond to significant results.

*P value for univariable analysis, variables were included in multivariable analysis if P value < .2.

†Multivariable mixed-effects logistic regression model, with center included as a random effect. Intraclass correlation coefficient: 0.60, 60% of the model variability explained by center effect.

SECONDARY OUTCOMES

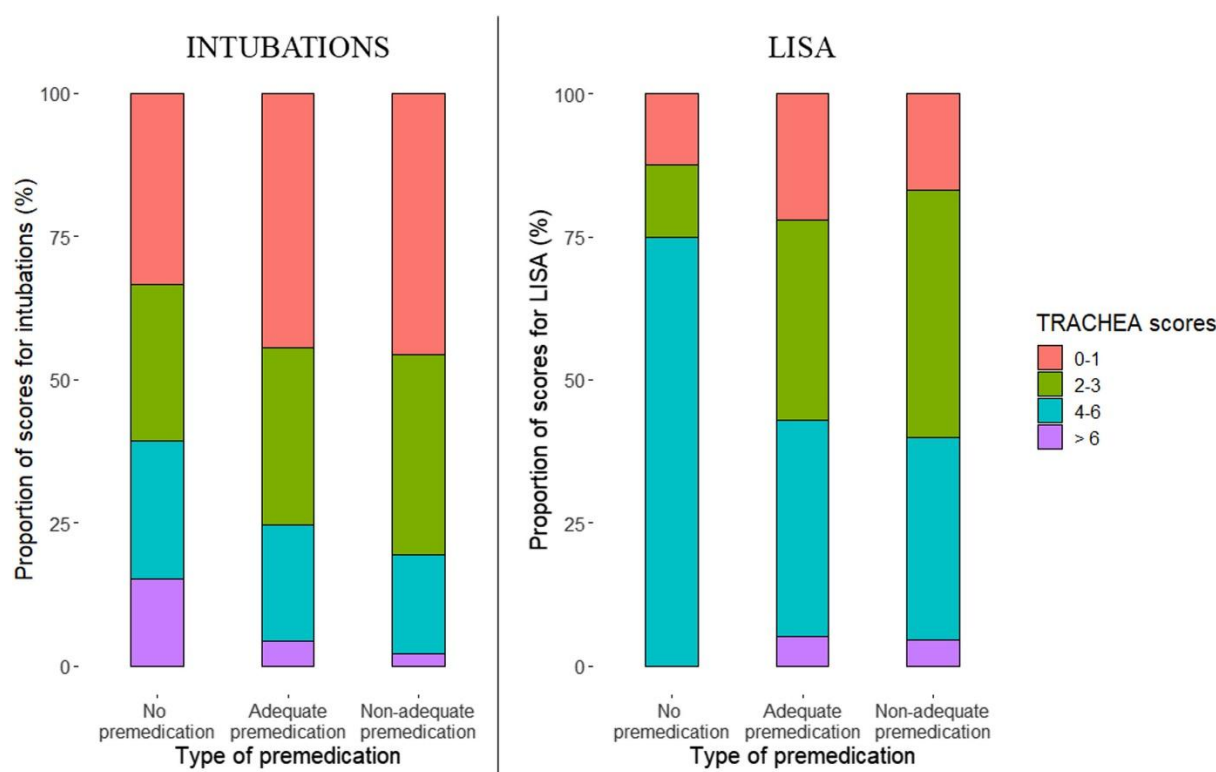
TRACHEA scores were available for 375 of 396 (94.7%) first laryngoscopies for non-life-threatening intubations and for 150 of 167 (89.8%) LISA procedures (8 of 16 of the LISA procedures that were not preceded by a premedication). TRACHEA scores were >3 for 23.7% of non-life-threatening intubations and 43.3% of LISA procedures (Figure 3). When comparing groups with no premedication, adequate premedication according to SFN guidelines, and non-adequate premedication, proportions of TRACHEA scores >3 were significantly different for intubation (41.2% vs 24.7% vs 19.4%, respectively; $P = .02$) but not for LISA (75% vs 42.9% vs 40%, respectively; $P = .19$). Proportions of TRACHEA scores >3 were similar between ELBW and other neonates (21.9% vs 21.9%, $P = .97$).

Overall rates of successful intubation or LISA at first attempt were 56.5% and 54.9%, respectively. When comparing 3 groups: no premedication, adequate premedication, and non-adequate premedication, first attempt success rates were not statistically different for intubation (43.6% vs 59.8% vs 56.2%, respectively; $P = .18$) and for LISA (68.7% vs 50% vs 57.6%, respectively; $P = .33$).

Among the 357 intubations with premedication, adverse events included: desaturation in 159 cases (44.5%), bradycardia < 100/min in 42 cases (11.8%), bradycardia < 60/min in 15 cases (4.2%), chest rigidity in 32 cases (9.0%), hypotension in 32 cases (9.0%) and laryngospasm in 24 cases (6.7%). At least one adverse event was reported in 100/169 (59.2%) and 100/188 (53.2%) of intubations in case of adequate and non-adequate premedication, respectively ($P = .3$). Among the 151 LISA procedures

with premedication, adverse events included: desaturation in 84 cases (55.6%), bradycardia < 100/min in 15 cases (9.9%), bradycardia < 60/min in 2 cases (1.3%), chest rigidity in 13 cases (8.6%), laryngospasm in 8 cases (5.3%) and hypotension in 7 cases (4.6%). At least one adverse event was reported in 49 of 84 (58.3%) and 48 of 67 (71.6%) of LISA procedures in case of adequate and nonadequate premedication, respectively ($P = .13$).

Figure 3. Proportion of TRACHEA scores in the no premedication, adequate premedication and non-adequate premedication groups for non-life-threatening intubations (left) and LISA procedures (right). Conditions of intubation were considered as excellent if the TRACHEA score was 0 or 1, acceptable if it was 2 or 3, poor if it was 4 to 6, and very poor if > 6.⁶ Proportions of TRACHEA scores > 3 differed significantly between intubations and LISA procedures (23.7% vs 43.3%, $P < .001$).



Discussion

In this large prospective observational cohort study, 90.1% of non-life-threatening neonatal intubations and 90.4% of LISA procedures were preceded by a specific premedication, but less than half of these were in line with the 2023 SFN evidence-based guidelines released 1 year earlier.¹² Factors associated with non-compliance with SFN guidelines were emergent intubation and hemodynamic compromise.

This study has several strengths. We objectively assessed the impact of these evidence-based guidelines after their publication. In the United States, a 15-item online questionnaire was sent to

693 neonatologists in 2015,¹³ 5 years after the publication of the American Academy of Pediatrics guidance on premedication for nonurgent tracheal intubation¹: 25% of neonatologists were unaware of these recommendations, and 33% had not changed their practice despite them.¹³ Second, the data collection process was standardized and tested prior to its implementation. It was mandatory for the neonatologist performing the laryngoscopy to submit study data immediately after the procedure to limit any potential memory bias. Finally, the study included many laryngoscopies from 141 French and Belgian centers (83% of all NICUs).

This study also has some limitations. First, this was an observational study that analyzed descriptive data, preventing conclusions on causality. Second, there was large variability in practices between centers, and it is likely that center habits and protocols explain much of the variability in choice of premedication. The precision of the associations is also limited by the low number of laryngoscopies in some centers. Third, the high rate of premedication observed in this study may also be due to selection bias, as 36% of French units did not agree to participate, or did not respond to our invitation to participate in this study. These units may not have had a premedication protocol or may not have been yet aware of the SFN evidence-based practice guidelines and their participation could have reduced the premedication rate. Finally, our cohort had a large proportion of ELBW neonates (38.7%) yet the TRACHEA score was initially developed in a sample of mainly neonates at ≥ 30 weeks GA⁶ In our study, the proportion of TRACHEA scores > 3 did not differ in ELBW neonates. No score currently exists specifically for ELBW neonates and further studies on these patients should be conducted.

Despite these limitations, this study shows the evolution of neonatal premedication practices in France over the last decade. Compared with the French EPIPAIN 2 cohort, premedication before intubation has increased from 47% in 2011 to 71% (and 90% for non-life-threatening intubations) in this 2024 cohort.⁵ Of the 49 non-life-threatening intubations in the delivery room, 25 (51%) received a specific premedication. However, still below the goals of the 2023 SFN guidelines, this rate was also increased compared with the 5% rate of premedication in the delivery room of the 2011 EPIPAGE 2 French cohort.⁷

Even if 75% of operators were aware of the SFN practice guidelines, less than half followed these guidelines. The recommended drugs may partly explain the lack of full compliance. The guidelines recommended the use of propofol in the absence of hemodynamic instability or a fast-acting opioid and a muscle blocker as preferred first-line options.¹² Fear of side effects and lack of experience with their use may explain the reluctance to use muscle blockers, although they are widely studied¹⁴⁻²⁰ and recommended for neonatal, pediatric and adult intubation,²¹⁻²³ in combination with a fast acting opioid.^{1-3,12} In our cohort, the opioid + muscle blocker association was rarely used (6.1%) even if it is the most largely used combination in other countries^{9,11} and preferred option in case of hemodynamic compromise. Muscle blockers have historically been exclusively used in neonates by anesthesiologists in France and neonatologists have not been trained and educated to use them until recently. Propofol has been suggested in other guidelines too, but rather as second line or as conditional recommendation.^{1,2} Very few randomized controlled trials have compared outcomes for specific anesthetic or sedative agents.^{18,24-26} Propofol was the most commonly chosen drug for

laryngoscopy in this study, whether for intubation or LISA, followed by ketamine which is an alternative option in the SFN guidelines,¹² and other opioids and/or anesthetics. Twelve neonates received propofol while hemodynamically compromised, contravening SFN guidelines.¹² Reports of hypotension following premedication by propofol provide justification for careful evaluation of hemodynamic stability before choosing the premedication.²⁷⁻²⁹ The use of morphine or opioids alone is also not recommended, although morphine was used in 10 of 396 intubations and 6 of 167 LISA in our cohort, and was reported in 26% of US NICUs in a recent survey.¹¹ Better dissemination of guidelines could help to optimize the choice of agent and adapt it to the newborn's situation, and the type of procedure (tracheal intubation or LISA). Also, a qualitative survey to better understand reasons for noncompliance with the guidelines could elicit the prescriber perspective on these guidelines.

Despite national and international recommendations,^{1-3,12} the heterogeneity of premedication practices^{4,30} before neonatal laryngoscopy shows that there is still no consensus in neonates and that research needs to continue. The fear of long-term neurodevelopmental effects associated with strong sedatives and analgesics is also likely to be a barrier to their use.³¹⁻³⁵ However, those studies focused on prolonged sedation and analgesia, and very few studies have considered long-term neurodevelopmental outcomes following premedication for laryngoscopy.^{36,37} In adults and children, use of a muscle-blocker is routine and association with anesthetics (usually etomidate or ketamine) and/or opioids are advised.^{21,23} In neonates, data are missing especially on ketamine use and on combinations of opioids, anesthetics and muscle blockers. Further studies would be helpful to broaden possibilities in neonatal premedication.

Dissemination of guidelines and best practices remains a challenge and regular evaluations should be carried out in each country to facilitate their implementation. Simulation sessions including premedication could also prove useful, especially in the delivery room.

Apart from alleviating pain in neonates, premedication was associated with better conditions of intubation for the operator as assessed by the TRACHEA score⁶ in our study. TRACHEA scores were significantly lower for intubations with specific premedication, whether or not SFN practices guidelines were followed. Proportions of TRACHEA scores >3 for LISA procedures were not significantly different between the no premedication and premedication groups, but our sample size may not have been sufficient to provide reliable conclusions. TRACHEA scores above a threshold of 3 were significantly more frequent for LISA procedures compared with intubations. This might be due to the lower level of sedation needed to keep spontaneous breathing in these procedures.

In conclusion, we found that a specific premedication was administered in 90% of non-life-threatening cases in a large contemporary cohort, which is an increase compared with previous French cohorts. Premedication was prescribed in accordance with SFN evidenced-based practice guidelines in less than half of cases. Future randomized controlled trials on premedication with anesthetics alone or in combination with other drugs in neonates to optimize analgesia, sedation, tolerance, conditions of intubation, and long-term safety are needed.

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DECLARATION OF COMPETING INTEREST

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