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Muehlbacher, Tobias ; Boos, Vinzenz ; Geiger, Leonie-Beatrice ; Rüegger, Christoph M ; Grass, Beate

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Analgosedation for less-invasive surfactant administration: Variations in practice

Tobias Muehlbacher MD | Vinzenz Boos MD | Leonie-Beatrice Geiger MD | Christoph M. Rüegger MD | Beate Grass MD, MSc

Newborn Research, Department of Neonatology, University Hospital and University of Zurich, Zurich, Switzerland

Correspondence
Tobias Muehlbacher, MD, Newborn Research Zurich, Department of Neonatology, University Hospital Zurich, University of Zurich, Frauenklinikstrasse 10, 8091 Zurich, Switzerland.
Email: tobias.muehlbacher@usz.ch

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Abstract

Background: Less-invasive surfactant administration (LISA) is widely used for surfactant delivery to spontaneously breathing preterm infants on nasal CPAP. However, the use of analgesia and/or sedation for the LISA procedure remains controversial.

Methods: We conducted a cross-sectional survey of all tertiary neonatal intensive care units (NICUs) in Austria, Germany, and Switzerland to assess current practices of analgosedation for LISA in preterm infants.

Results: Eighty-eight of 172 (51.2%) NICUs responded to the survey, of which 83 (94.3%) perform LISA. Analgosedation for LISA is used in 60 (72.3%) NICUs. Twenty-eight of those (46.7%) have unit protocols to guide analgosedation while 32 (53.3%) administer medication at the discretion of the attending physician. Ketamine (45.0% of NICUs), propofol (41.7%), fentanyl (21.7%), morphine (20.0%), and midazolam (20.0%) were most frequently used for analgosedation for LISA. Nine (10.7%) NICUs reported the use of pain or distress scores during LISA.

Conclusion: LISA is well established among tertiary NICUs in the German-speaking countries. However, there are considerable variations regarding the use of analgosedation. More evidence is required to guide clinicians seeking to safely and effectively deliver surfactant via a thin catheter to spontaneously breathing preterm infants.

KEYWORDS
analgosedation, LISA, preterm infant, surfactant

1 | INTRODUCTION

Historically, surfactant was given via an endotracheal tube and infants remained intubated and ventilated for some time after the procedure. The increased use of nasal continuous positive airway pressure as primary therapy for preterm infants with respiratory distress syndrome (RDS) led to a search for methods of administering surfactant without the need for ongoing mechanical ventilation.[1] Delivery of surfactant through a thin tube, known as less-invasive surfactant administration (LISA), allowed infants to experience the benefits of surfactant but avoid the risks of intubation and mechanical ventilation.[2–4] During the last decade, LISA has become

increasingly popular.[5] Compared with surfactant administration via an endotracheal tube followed by mechanical ventilation, LISA increases the number of infants who survive without bronchopulmonary dysplasia.[6–8]

However, the LISA procedure involves laryngoscopy, which may be uncomfortable and painful for the infant. The administration of analgesia and/or sedation during the LISA procedure is practiced inconsistently.[9–11] This contrasts with the recommendation to use analgosedation when placing an endotracheal tube.[12,13] The debate surrounding analgosedation for LISA involves the advantages of alleviating pain and stress for the infant and the potential facilitation of the LISA procedure in highly agitated infants. Conversely, concerns have been raised regarding adverse effects on respiratory drive and the unclear long-term consequences associated with the use of potentially neurotoxic drugs.[14–16]

In preterm infants, current evidence on the use of analgosedation for LISA suggests an important reduction of pain-related stress, but also a higher risk of desaturations requiring positive pressure ventilation.[17–20]

We surveyed the current practices among German-speaking countries, the frequency of use, administration of analgosedation and failure rates of the LISA procedure using an online questionnaire.

2 | METHODS

A cross-sectional survey with a maximum of 46 questions (complete survey provided as Supporting Information File) was developed by the authors. The survey had three subcategories: (a) institutional information, (b) information on LISA practices (indication, target population, technique, analgosedation), and (c) information on INSURE practices (indication, target population, analgosedation). This manuscript will report on variations regarding the of LISA procedure, due to very consistent practice and regular use of analgosedation for INSURE.

The survey was sent to the medical directors of all tertiary neonatal intensive care units (NICUs) in Germany ($n = 156$), Austria ($n = 7$), and Switzerland ($n = 9$) in April 2023 using an online survey tool (LimeSurvey, Hamburg, Germany) with one follow-up email 4 weeks later. The medical directors were permitted to share the survey link with another person within their own NICU to complete the questionnaire. Responses were saved anonymously in the database. However, there was an optional comment field where participants could enter the name of their hospital. This served the dual purpose of avoiding reminder emails and allowing for the identification of potential duplicate responses. If multiple responses were received from one hospital, only the first response was considered for analysis.

The focus of the survey was analgosedation; the indication, choice of drug and initial dose. Multiple-choice answers were allowed for the types of drug and the devices that were used for LISA. Finally, estimated LISA failure rates were determined—defined as intubation within 24 h or repeated LISA within 1 h. This definition was used to represent procedural failure, although that most studies report on the need for mechanical ventilation <72 h as the definition for LISA failure.[8]

Descriptive statistics were used for data analysis using SPSS (IBM SPSS Version 29.0). Categorical variables are presented in absolute numbers and percentages. Consent for data collection, evaluation, and publication was waived by the Swiss ethical committee of the Canton of Zurich (KEK-ZH Number 2023-00253). A Consensus-Based Checklist for Reporting of Survey Studies (CROSS) | EQUATOR Network (equator-network.org) CROSS guidelines was followed for reporting this survey.[21]

3 | RESULTS

The survey on LISA was completed by 88 of the 172 (51.2%) tertiary NICUs. A single NICU provided two responses. Consequently, the second response was excluded from the analysis. Characteristics of NICUs performing LISA are presented in Table 1. The vast majority of respondents in Austria and Germany were using LISA regularly and for more than 5 years whereas usage in Switzerland was more recent and less regular. All NICUs in Austria and Switzerland and 64.8% of the responding German NICUs followed a local guideline for LISA. Upper gestational age (GA) thresholds to perform LISA were used in 16.7%, 14.1%, and 16.7% of Austrian, German and Swiss NICUs. Lower GA thresholds were not used in Austria, but in 11.3% and 50% of German and Swiss NICUs, respectively (Table 1). LISA treatment criteria were established in 83.3%, 69.0%, and 83.3% of Austrian, German, and Swiss NICUs, respectively. In all NICUs, FiO_2 levels were employed to determine the initiation of LISA. Additionally, positive end-expiratory pressure (PEEP) levels, with a median PEEP of 6.5 cmH2O, served as the threshold for LISA in 33.3%, 23.9%, and 66.7% of Austrian, German and Swiss NICUs, respectively. Purpose-built LISA catheters (LISAcath®, Neofact®, or Surfcath®) were used in 100.0%, 81.7%, and 100.0% in Austrian, German and Swiss NICUs (Table 1).

Analgosedation was used in 60 of the 83 (72.3%) NICUs performing LISA. In 28 (46.7%) of those, clearly defined indications for analgosedation existed (Table 2a). The remaining 32 (53.3%) units did not have a protocol for the use of analgosedation. The choice of medication and the respective doses varied within and between the countries. Variation also existed within some NICUs. Responses indicated that more than one regime was used in these units; ketamine, opioids or propofol were most frequently administered for the LISA procedure (45.0% vs. 41.7% vs. 41.7%), whereas benzodiazepines were less commonly used (Table 2b). Analgosedation was administered with similar frequency regardless of NICU size, number of infants treated with LISA per year or the use of a Magill forceps to insert the LISA catheter into the trachea. NICUs with longer LISA experience were less likely to use analgosedation than those with shorter LISA experience (Table 3).

Overall, LISA failure rates were estimated to be low among the 80 NICUs who provided an answer: below 10% in 40 (50.0%) NICUs, 10%–25% in 29 (36.3%) NICUs, and above 25% in 11 (13.8%) NICUs.

TABLE 1 Institutional data on NICUs using LISA.

	Austria		Germany		Switzerland	
Total number of tertiary NICUs per country	7		156		9	
Number of responses	6 *(85.7)*		73 *(46.8)*		9 *(100)*	
Number of preterm infants <32 weeks admitted to NICU per year						
Less than 25	0	*(0.0)*	2	*(2.7)*	0	*(0.0)*
25–50	0	*(0.0)*	20	*(27.4)*	1	*(11.1)*
51–75	1	*(16.7)*	29	*(39.7)*	4	*(44.4)*
76–100	4	*(66.7)*	12	*(16.4)*	1	*(11.1)*
More than 100	1	*(16.7)*	10	*(13.7)*	3	*(33.3)*
NICUs using LISA regularly for the treatment of respiratory distress syndrome						
Yes	6	*(100.0)*	71	*(97.3)*	6	*(66.7)*
No	0	*(0.0)*	2	*(2.7)*	3	*(33.3)*
Number of infants treated with LISA per year						
Less than 10	0	*(0.0)*	9	*(12.7)*	1	*(16.7)*
10–30	0	*(0.0)*	28	*(39.4)*	3	*(50.0)*
31–50	2	*(33.3)*	22	*(31.0)*	1	*(16.7)*
51–70	1	*(16.7)*	8	*(11.3)*	0	*(0.0)*
More than 70	3	*(50.0)*	4	*(5.6)*	1	*(16.7)*
Years of experience with LISA						
Less than 2 years	0	*(0.0)*	2	*(2.8)*	4	*(66.7)*
2–4 years	1	*(16.7)*	14	*(19.7)*	2	*(33.3)*
5–7 years	2	*(33.3)*	27	*(38.0)*	0	*(0.0)*
8–10 years	2	*(33.3)*	12	*(16.9)*	0	*(0.0)*
More than 10 years	1	*(16.7)*	16	*(22.5)*	0	*(0.0)*
Standard operating procedure for LISA						
Yes	6	*(100.0)*	46	*(64.8)*	6	*(100.0)*
No	0	*(0.0)*	25	*(35.2)*	0	*(0.0)*
Upper gestational age limit for LISA						
Yes	1[a]	*(16.7)*	10[b]	*(14.1)*	1[c]	*(16.7)*
No	5	*(83.3)*	61	*(85.9)*	5	*(83.3)*
Lower gestational age limit for LISA						
Yes	0	*(0.0)*	8[d]	*(11.3)*	3[e]	*(50.0)*
No	6	*(100.0)*	63	*(88.7)*	3	*(50.0)*
Respiratory thresholds for LISA						
yes	5	*(83.3)*	49	*(69.0)*	5	*(83.3)*
FiO_2[f]	5	*(83.3)*	49	*(69.0)*	5	*(83.3)*
Positive end-expiratory pressure (PEEP) level[g]	2	*(33.3)*	17	*(23.9)*	4	*(66.7)*
no	1	*(16.7)*	22	*(31.0)*	1	*(16.7)*
Use of Magill forceps for LISA						
Yes	0	*(0.0)*	22	*(31.0)*	2	*(33.3)*
No	6	*(100.0)*	46	*(64.8)*	4	*(66.7)*
No answer	0	*(0.0)*	3	*(4.2)*	0	*(0.0)*
Device used for LISA (multiple answers possible)						
Umbilical vein catheter	0	*(0.0)*	13	*(18.3)*	0	*(0.0)*
Angiocath or comparable	1	*(16.7)*	5	*(7.0)*	0	*(0.0)*
Suction tube	0	*(0.0)*	3	*(4.2)*	0	*(0.0)*
Gastric tube	2	*(33.3)*	9	*(12.7)*	1	*(16.7)*
Purpose built catheter (e.g., LISAcath®, Neofact®, Surfcath®)	6	*(100.0)*	58	*(81.7)*	6	*(100.0)*
Others	0	*(0.0)*	2	*(2.8)*	0	*(0.0)*
Nonpharmacologic measures for LISA (e.g., sucrose, facilitated tucking, swaddling)						
Yes	6	*(100.0)*	63	*(88.7)*	6	*(100.0)*
No	0	*(0.0)*	8	*(11.3)*	0	*(0.0)*
Pharmacologic analgosedation for LISA						
Yes	4	*(66.7)*	51	*(71.8)*	5	*(83.3)*
No	2	*(33.3)*	20	*(28.2)*	1	*(16.7)*

Note: Data [n *(%)*] on participating tertiary NICUs. Upper gestational age limits for LISA

Abbreviations: LISA, less-invasive surfactant administration; NICU, neonatal intensive care unit.

[a]28 weeks.

[b]29–35 weeks.

[c]37 weeks; lower gestational age limits for LISA.

[d]25–26 weeks.

[e]23–27 weeks.

[f]Median FiO_2 of 0.30 (range: 0.22–0.50, $n = 49$) or gestational age ($n = 8$).

[g]Median PEEP level 6.5 cmH2O (range: 5–8 cmH2O, $n = 23$).

NICUs not using analgosedation for LISA estimated their failure rates lower compared to NICUs who administer medication for analgosedation (Table 3).

4 | DISCUSSION

The main goal of the survey was to review the current practices regarding LISA with a special focus on analgosedation in the German-speaking countries.

This survey revealed country-specific differences in the timing of implementation of LISA. LISA is routinely used in almost all surveyed

TABLE 2 Analgosedation during LISA.

(a)	Total		Austria		Germany		Switzerland	
	83		6		71		6	
NICUs using LISA	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*
Indication for analgosedation for LISA								
No treatment	23	*(27.7)*	2	*(33.3)*	20	*(28.2)*	1	*(16.7)*
At the discretion of the attending physician	32	*(38.6)*	2	*(33.3)*	29	*(40.8)*	1	*(16.7)*
Routinely for LISA after transfer to NICU	16	*(19.3)*	2	*(33.3)*	13	*(18.3)*	1	*(16.7)*
Routinely above certain gestational age	4	*(4.8)*	0	*(0.0)*	4	*(5.6)*	0	*(0.0)*
Yes for all infants	8	*(9.6)*	0	*(0.0)*	5	*(7.0)*	3	*(50.0)*
(b)								
NICUs using pharmacologic analgosedation for LISA	60	*(72.3)*	4	*(66.7)*	51	*(71.8)*	5	*(83.3)*
Drugs used (multiple answers possible)	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*
Propofol[a]	25	*(41.7)*	3	*(75.0)*	21	*(41.2)*	1	*(20.0)*
Fentanyl[b]	13	*(21.7)*	2	*(50.0)*	8	*(15.7)*	3	*(60.0)*
Remifentanyl	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*
Morphin[c]	12	*(20.0)*	1	*(25.0)*	11	*(21.6)*	0	*(0.0)*
Ketamin and Esketamin[d]	27	*(45.0)*	3	*(75.0)*	22	*(43.1)*	2	*(40.0)*
Midazolam[e]	12	*(20.0)*	1	*(25.0)*	11	*(21.6)*	0	*(0.0)*
Dexmedetomidin	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*
Others[f]	2	*(3.3)*	0	*(0.0)*	2	*(3.9)*	0	*(0.0)*

Note: Analgosedation during LISA, overall and stratified by countries: (a) Comparison of indications for analgosedation and (b) the respective choices of medication with following most common starting doses used (multiple answers were possible).

Abbreviations: LISA, less-invasive surfactant administration; NICU, neonatal intensive care unit.

[a]0.5–1 mg/kg (range: 0.05–2 mg/kg).

[b]1 mcg/kg (range: 0.1–5 mcg/kg).

[c]0.05 mg/kg (range: 0.02–0.1 mcg/kg).

[d]0.5 (−1) mg/kg for ketamine (range: 0.25–1 mg/kg), 0.5 mg/kg for Esketamin (range: 0.25–0.5 mg/kg).

[e]0.05–0.1 mg/kg (range: 0.025–0.1 mg/kg).

[f]Diazepam 0.05–0.25 mg/kg.

tertiary NICUs and can be considered standard of care in Austria and Germany, but not yet in Switzerland. Most NICUs follow a unit-based protocol for the LISA procedure. Only a minority of NICUs apply upper or lower GA thresholds for LISA initiation. Swiss NICUs more frequently use lower GA thresholds, potentially due to the more recent introduction of LISA in Switzerland. While LISA treatment criteria align with current guidelines[14–16] in most Austrian and Swiss NICUs and in about two-thirds of German NICUs, our survey cannot clarify whether the remaining NICUs use LISA prophylactically or with different treatment criteria. However, NICUs adhering to predefined LISA treatment criteria demonstrate median FiO_2 and PEEP levels in accordance with guideline recommendations.[14–16] Various devices for LISA are reported in the literature, but the majority of NICUs across all three countries use purpose-built catheters, with slightly more variability observed in German NICUs.[5,16] Consequently, practical aspects for LISA appear standardized across the three countries, with only minor variations.

In contrast, analgosedation for LISA is less standardized in Austrian and German NICUs, and is more consistent in Swiss NICUs. Fewer than half of the NICUs using analgosedation define specific indications for its administration. The remainder leave it to the discretion of the attending physician. An even higher variation is shown in the choice of the analgosedative drug and its respective initial dose, not only between and within countries, but also within individual NICUs, where the respective respondent provided multiple drugs and dosages administered for analgosedation.

Compared to a survey from 2015/2016, rates of analgosedation for LISA have increased,[9] yet more than half of the NICUs using analgosedation leave it to the discretion of the attending physician without a standardized protocol. Furthermore, our survey suggests that only a minority of NICUs use GA thresholds as indication for analgosedation. This approach contrasts with current recommendations to tailor analgosedation according to GA, as more mature infants (>32 weeks) more often show signs of discomfort.[14,16]

TABLE 3 Subgroup analysis regarding indication for analgosedation for LISA.

Total			Any kind of indication for analgosedation		At the discretion of the attending physician		Routinely for LISA after transfer to NICU		Routinely above certain gestational age		Yes for all infants	
	No treatment											
	23		60		32		16		4		8	
Variable	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*
Number of preterm infants <32 weeks admitted to NICU per year												
Less than 25	1	*(4.3)*	1	*(1.7)*	1	*(3.1)*	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*
25–50	5	*(21.7)*	16	*(26.7)*	7	*(21.9)*	4	*(25.0)*	3	*(75.0)*	2	*(25.0)*
51–75	8	*(34.8)*	24	*(40.0)*	15	*(46.9)*	5	*(31.3*	0	*(0.0)*	4	*(50.0)*
76–100	6	*(26.1)*	10	*(16.7)*	6	*(18.8)*	4	*(25).0)*	0	*(0.0)*	0	*(0.0)*
More than 100	3	*(13.0)*	9	*(15.0)*	3	*(9.4)*	3	*(18.8)*	1	*(25.0)*	2	*(25.0)*
Number of LISA treated infants per year												
Less than 10	3	*(13.0)*	7	*(11.7)*	4	*(12.5)*	1	*(6.3)*	0	*(0.0)*	2	*(25.0)*
10–30	7	*(30.4)*	24	*(40.0)*	13	*(40.6)*	5	*(31.3)*	3	*(75.0)*	3	*(37.5)*
31–50	8	*(34.8)*	17	*(28.3)*	9	*(28.1)*	5	*(31.3)*	1	*(25.0)*	2	*(25.0)*
51–70	3	*(13.0)*	6	*(10.0)*	3	*(9.4)*	3	*(18.8)*	0	*(0.0)*	0	*(0.0)*
More than 70	2	*(8.7)*	6	*(10.0)*	3	*(9.4)*	2	*(12.5)*	0	*(0.0)*	1	*(12.5)*
Use of Magill forceps for LISA												
Yes	6	*(26.1)*	18	*(30.0)*	10	*(31.3)*	3	*(18.8)*	1	*(25.0)*	4	*(50.0)*
No	16	*(69.6)*	40	*(66.7)*	21	*65.6)*	13	*(81.3)*	2	*(50.0)*	4	*(50.0)*
No answer	1	*(4.3)*	2	*(3.3)*	1	*(3.1)*	0	*(0.0)*	1	*(25.0)*	0	*(0.0)*
Years of experience with LISA												
Less than 2 years	2	*(8.7)*	4	*(6.7)*	0	*(0.0)*	1	*(6.3)*	0	*(0.0)*	3	*(37.5)*
2–4 years	1	*(4.3)*	16	*(26.7)*	10	*(31.3)*	4	*(25.0)*	0	*(0.0)*	2	*(25.0)*
5–7 years	9	*(39.1)*	20	*(33.3)*	12	*(37.5)*	3	*(18.8)*	3	*(75.0)*	2	*(25.0)*
8–10 years	5	*(21.7)*	9	*(15.0)*	4	*(12.5)*	5	*(31.3)*	0	*(0.0)*	0	*(0.0)*
More than 10 years	6	*(26.1)*	11	*(18.3)*	6	*(18.8)*	3	*(18.8)*	1	*(25.0)*	1	*(12.5)*
Pain/distress assessment												
General use of pain or distress scores	19	*(82.6)*	49	*(81.7)*	25	*(78.1)*	12	*(75.0)*	4	*(100.-0)*	8	*(100.0)*
Use of pain or distress scores during LISA	2	*(8.7)*	7	*(11.7)*	2	*(6.3)*	3	*(18.8)*	0	*(0.0)*	2	*(25.0)*
Drugs used (multiple answers possible)												
Propofol			25	*(41.7)*	12	*(37.5)*	8	*(50.0)*	1	*(25.0)*	4	*(50.0)*
Fentanyl			14	*(23.3)*	5	*(15.6)*	6	*(37.5)*	0	*(0.0)*	3	*(37.5)*
Morphin			12	*(20.0)*	5	*(15.6)*	5	*(31.3)*	2	*(50.0)*	0	*(0.0)*
Ketamin and Esketamin			25	*(41.7)*	13	*(40.6)*	6	*(37.5)*	3	*(75.0)*	3	*(37.5)*
Midazolam			12	*(20.0)*	8	*(25.0)*	3	*(18.8)*	1	*(25.0)*	0	*(0.0)*
Others			2	*(3.3)*	2	*(6.3)*	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*
Estimated failure rate for LISA												
Less than 10%	13	*(56.5)*	27	*(45.0)*	13	*(40.6)*	10	*(62.5)*	2	*(50.0)*	2	*(25.0)*

(Continues)

TABLE 3 (Continued)

Total	No treatment 23		Any kind of indication for analgosedation 60		At the discretion of the attending physician 32		Routinely for LISA after transfer to NICU 16		Routinely above certain gestational age 4		Yes for all infants 8	
Variable	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*	*n*	*(%)*
10%–25%	6	*(26.1)*	24	*(40.0)*	13	*(40.6)*	6	*(37.5)*	1	*(25.0)*	4	*(50.0)*
26%–33%	2	*(8.7)*	5	*(8.3)*	3	*(9.4)*	0	*(0.0)*	1	*(25.0)*	1	*(12.5)*
34%–50%	1	*(4.3)*	3	*(5.0)*	2	*(6.3)*	0	*(0.0)*	0	*(0.0)*	1	*(12.5)*
More than 50%	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*
No answer	2	*(8.7)*	1	*(1.7)*	1	*(3.1)*	0	*(0.0)*	0	*(0.0)*	0	*(0.0)*

Note: Indication for analgosedation for LISA: Left columns compare analgosedation versus no treatment. On the right the indications for the analgosedation are further differentiated.

Abbreviations: LISA, less-invasive surfactant administration; NICU, neonatal intensive care unit.

Only a minority used a standardized pain or distress assessment to decide whether analgosedation for LISA might be necessary. Unmeasured pain, combined with the concerns of possible respiratory depression as a side effect of analgosedation, and the impossibility of applying a controlled invasive ventilation during LISA, may lead to a restrictive use of analgosedation for LISA.

Existing evidence on analgosedation for LISA is scarce as only two small RCTs ($n = 112$ infants) have been published so far.[17,18] A systematic review and meta-analysis of one RCT and 32 observational studies showed no effect on the duration of the LISA procedure or the need of rescue intubation or mechanical ventilation.[20] Transient effects on respiratory drive occurred more often in infants with analgosedation for LISA compared to no analgosedation resulting in higher rates of apnea, desaturations and need for positive-pressure ventilation. However, quality of evidence for all results was rated very low to low.[20] A further systematic review of one RCT and seven observational studies focusing on safety and the effectiveness of pain reduction and another recent small RCT showed lower pain scores and higher rated comfort for infants treated with analgosedation for LISA.[18,19] As a result, clinicians must carefully consider the trade-off between the potential advantages of improved pain control and the increased risk of apnea, which may necessitate positive pressure ventilation.

As a first step to overcome the current variations, we suggest that infants treated with LISA should receive non-pharmacologic interventions like swaddling and oral sucrose as these effectively reduce procedural pain.[22,23] In a second step, a standardized pain assessment could help identify infants who require additional pharmacologic analgosedation. This approach is feasible because LISA is typically not considered an emergency procedure.[14,24,25]

The question of the "best drug" is still unanswered. Medications with a rapid onset and short duration of analgesic and sedative effects may be preferred since they reduce the duration of depression of respiratory drive. Several RCTs are underway examining analgosedation with ketamine, fentanyl or propofol for LISA. Their results hold the promise of providing essential evidence in this field.[26–29] Finally, national and international guidelines should provide more specific statements on analgosedation for LISA.

Our survey has some limitations: First, the results of this survey represent only the responding NICUs (response rate 51%), leading to a potential selection bias and may not be generalizable to a broader range of settings or practices in other countries. Second, it is important to note that we cannot completely rule out the possibility of multiple responses from the same unit, even with the (optional) comment field for the hospital name. For instance, if the survey link was shared with additional members of the same NICU, this could potentially result in multiple responses from that unit. Third, responses were provided by individuals (with no demographic information on the respondents) and opinions of this restricted group of clinicians may differ from the actual practice in the NICUs.

Future research should focus on the assessment of pain and stress during the LISA procedure to identify infants in need of analgosedation. In addition, adequately powered RCTs in preterm infants comparing different analgosedative strategies during LISA are urgently needed to inform clinical practice guidelines.

5 | CONCLUSION

LISA is well established in the German-speaking countries. Analgosedation for LISA is frequently administered but the considerable variations noted in our survey reflect the lack of evidence on this topic. Nonpharmacologic interventions and standardized pain assessment may be used to improve infant comfort and recognize the need for further pharmacologic treatment until results from ongoing RCTs provide more evidence to inform national and international guidelines.

AUTHOR CONTRIBUTIONS

Tobias Muehlbacher: conceptualization; writing - original draft; writing - review & editing; formal analysis; investigation; methodology; data curation. **Vinzenz Boos**: conceptualization; writing - review

& editing; formal analysis; investigation; methodology; data curation. **Leonie-Beatrice Geiger**: conceptualization; writing - review & editing; investigation; methodology. **Christoph M Rüegger**: conceptualization; writing - review & editing; investigation; methodology. **Beate Grass**: conceptualization; writing - review & editing; investigation; methodology; supervision.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

ETHICS STATEMENT

Consent for data collection, evaluation and publication for this survey was waived by the Swiss ethical committee of the Canton of Zurich (KEK-ZH Number 2023-00253).

ORCID

Tobias Muehlbacher http://orcid.org/0000-0001-8661-9645
Vinzenz Boos http://orcid.org/0000-0001-6895-4861
Christoph M. Rüegger http://orcid.org/0000-0003-1496-2625

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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