RESEARCH ARTICLE

A survey of minimally invasive surfactant therapy in Canada

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Introduction: Minimally invasive surfactant therapy (MIST) can be used to treat neonatal respiratory distress syndrome in neonatal intensive care units (NICUs). Clinical and institutional variances in MIST utilization persist globally with little published research regarding MIST utilization in Canada. Therefore, the objective of this study was to survey MIST utilization in NICUs in Canada.

Methods: An online survey was emailed to the 33 participating centres of Canadian Neonatal Network™ (CNN) Evidence-based Practice for Improving Quality (EPIQ) Lung Health Group (LHG). Site demographics and surfactant therapy procedural details were categorically collected. Free text and multiple-choice questions were utilized to capture perceived barriers and individual preferences for MIST use.

Results: Twenty-eight of 33 participating members of the CNN EPIQ-LHG completed the survey between April 2021 and October 2021 (85%); 17/28 (61%) respondents reported ongoing MIST utilization at their center. Most centers that used MIST techniques administered bovine lipid extract surfactant (68%), commonly using angiocatheters (47%) and purpose-built catheters (41%). MIST was widely used for patients at 26–33 weeks gestational age (88%). Nine centres had never used MIST (32%), and 3 indicated a plan to implement MIST within the next 2 years. Common barriers to MIST use included lack of consensus amongst clinicians (78%), lack of training (56%), and lack of experience with MIST (56%).

Conclusion: While MIST is being increasingly used in Canadian NICUs, universal use is yet to be seen. Clinician inexperience and lack of consensus, formal training, and local guidelines contribute to underutilization of MIST. Training workshops, country-wide data collection, and uniform operating protocols are needed to standardize practice.

Key Words: *neonates; respiratory distress syndrome; surfactant; survey*

INTRODUCTION

The use of surfactant replacement therapy for neonatal respiratory distress syndrome (RDS) has been shown to effectively reduce associated morbidity and mortality in preterm neonates in Canada [1, 2]. Historically, prophylactic intubation and endotracheal surfactant administration were considered routine treatments for many preterm neonates at high risk of RDS. However, studies show that routine stabilization with continuous positive airway pressure (CPAP) therapy with early selective surfactant reduced the risk of bronchopulmonary dysplasia (BPD) and death compared to prophylactic surfactant [3]. Nonetheless, many neonates who require surfactant therapy require additional support beyond CPAP and often undergo intubation. Following its introduction in the 1980s, surfactant was routinely delivered via an endotracheal tube followed by mechanical ventilation. However, due to the associated risks of ongoing mechanical ventilation, the "INSURE" method of intubation followed by surfactant delivery and rapid extubation to CPAP has been used as an alternative to minimize exposure to mechanical ventilation following surfactant administration [4].

More recently, techniques for surfactant administration that eliminate the need for intubation and positive pressure ventilation have been favoured to reduce the risk of BPD and other hypoxia-induced adverse events [5, 6]. Catheter-based techniques, such as the Cologne or Hobart methods, administer surfactant through a gastric tube or vascular catheter in spontaneously breathing neonates who are being supported with nasal CPAP (nCPAP) [7, 8]. The Cologne method delivers surfactant through a gastric feeding tube catheter, with the catheter placement guided by a laryngoscope and secured using Magill forceps [9]. Similarly, the Hobart method also delivers surfactant to neonates supported with nCPAP; however, this method utilizes an angiocatheter and does not require the use of Magill forceps [10]. Both of these techniques allow for the synergistic effect of routine stabilization with CPAP at birth and early selective surfactant for preterm neonates who are at high risk of RDS, CPAP failure, and the development of BPD.

Techniques that deliver surfactant without intubation have various names, including less invasive surfactant administration (LISA), minimally invasive surfactant therapy (MIST) and surfactant without intubation (SWI). These procedures are unique from the INSURE technique because surfactant is administered to a spontaneously breathing neonate through an oral or nasal catheter to the trachea [5, 11]. The feasibility and efficacy of the latter technique, broadly encompassed by the term MIST in this study, has been widely studied in randomized controlled trials and systematic reviews to reduce the incidence of BPD. Nevertheless, institutional variances and low uptake of MIST have persisted despite recommendations for its use for RDS management by the European Consensus Guidelines on the Management of Respiratory Distress Syndrome [12]. A survey of LISA use by neonatologists in the United States of America found wide

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disparities in the use of minimally invasive techniques in clinical care and research [11]. A recent survey by Klotz and colleagues [13] illustrated the widespread use of MIST across European neonatal care centres but with variances in its prevalence in routine clinical practice. However, little is known to date about the prevalence of MIST use in Canadian neonatal units or which methods are used by those who administer MIST. Hence, we designed this study with the objective of collecting information about MIST utilization in Canada.

METHODS

Study design

This study was a national-level, web-based survey conducted between April and September 2021 inquiring about the utilization of MIST, how the procedure is performed, and potential limitations to the use of MIST across Canadian neonatal intensive care units (NICUs).

Survey description

The survey was created and distributed using Qualtrics™. Prior to distribution, the survey was independently reviewed by two neonatologists to assess the validity and representativeness of the listed questions. It consisted of 33 questions, 10 for non-MIST sites (never used/discontinued use), and 22 for MIST sites. Site demographic information such as academic affiliation, level of care, unit admission rate, and type of surfactant routinely used was collected. Representatives were asked to characterize the prevalence of MIST use at their institutions and, if relevant, provide details about the techniques and protocols used. For sites that did not use the MIST procedure, perceived limitations and barriers to MIST utilization, and clinician preference for surfactant delivery were sought. Responses were obtained using multiple choice and free text fields. A copy of the survey used is included as Appendix.[1]

Our survey was sent out to members of the Canadian Neonatal Network's (CNN) Evidence-based Practice for Improving Quality (EPIQ) Lung Health Group (LHG) utilizing the official distribution list of LHG after obtaining appropriate organizational and ethical approval. Participating CNN centres are involved in EPIQ. LHG is a collaborative effort under EPIQ focussing on neonatal respiratory care. The survey was sent to 33 participating centres. There were no specific exclusion criteria. Site representatives were initially approached in April 2021 with an introductory email containing a letter of information and survey link. One set of responses was obtained per site, completed by a physician, Registered Respiratory Therapist, or Registered Nurse member of the LHG. Subsequent reminder emails were sent to sites with incomplete survey responses at 4-week intervals after the initial email. Submitted survey responses were considered to have received implied consent, and incomplete responses were promptly deleted from Qualtrics™. The final reminder email was delivered in September 2021, and the survey was closed in early October 2021.

Data analysis

Results of the survey were uploaded to and collated using Excel v13 (Microsoft, USA). Quantitative data were captured using frequency and proportions. Institutional research ethics board approval was obtained (REB 116750).

RESULTS

This survey was sent out to all 33 participating centres of the CNN between May 2021 and October 2021. Out of the 33 centers, we obtained a response from designated representatives of 28 centers (85%). Table 1 summarizes the details of the participating centers. The vast majority of the centers were academic (82%) and represented Level 3/3+ NICUs (96%), with 39% of the centers reporting average annual admission for neonates less than 29 weeks gestation to be 50 or above. The survey was primarily completed by physicians (64%) and respiratory therapists (29%).

[1]Supplementary materials are available at https://www.cjrt.ca/wp-content/uploads/Supplement-cjrt-2022-011.docx.

TABLE 1
Description of participating centers and respondents

Description of survey responders (*N* = 28)	*N* (%)
Type of setting	
Academic	23 (82)
Non-academic	5 (18)
Highest level of NICU care provided	
Level 2	1 (3.6)
Level 3	18 (64.3)
Level 3+	9 (32.1)
Respondentr	
Physician	18 (64.3)
Respiratory therapist	8 (28.6)
Nurse Practitioner	2 (7.1)
Registered Nurse	0
Average annual number of neonatal admissions below 29 weeks gestation per year at each site	
Less than 50	16 (57.1)
50 to 100	5 (17.9)
Greater than 100	6 (21.4)
No response	1 (3.6)

Note: NICU = neonatal intensive care units.

MIST utilization and procedural details

Seventeen out of 28 responding centers (61%) reported MIST utilization, whereas nine (32%) centers reported never using MIST. MIST utilization became more widespread in 2018 and onwards at centers that reported successful implementation and use (Figure 1). Procedural details are summarized in Table 2. Bovine lipid extract surfactant (BLES; 68%) was the predominant type of surfactant used among centers that used the MIST technique, whereas angiocath (47%) and purpose-built catheters (41%) were the most common catheters for delivery of surfactant. Four centers (24%) reported previous use of feeding tubes for surfactant delivery, which was later switched to either angiocath or purpose-built catheters. Most respondents (71%) did not report using Magill forceps to aid intratracheal catheter placement. The use of video-laryngoscopy was reported by eight (47%) MIST users. Most centers reported using nasal continuous positive airway pressure (NCPAP) or nasal intermittent positive pressure ventilation (NIPPV) before and in conjunction with the procedure. Only one center reported not using any premedication. However, there was considerable variation in the use of premedication between sites. Overall, atropine (59%), fentanyl (47%), and ketamine (35%) were the most reported drugs used as premedication during surfactant delivery.

To assess the procedural success or successful intratracheal instillation, most centers (53%) used an approach of clinical response and aspiration of gastric contents. Some centers only assessed clinical response (29%), while one center also used pre- and post-procedure lung ultrasonography. Amongst the centers that use MIST, the perceived efficacy was high or very high among 82% of respondents. The most common gestational age group where MIST is consistently used across the centers appears to be 26–33 weeks. Only nine centers among 17 reported use at 24–25 weeks gestation, and only two reported use at less than 24 weeks (Figure 2).

Procedural adverse effects and barriers to implementation

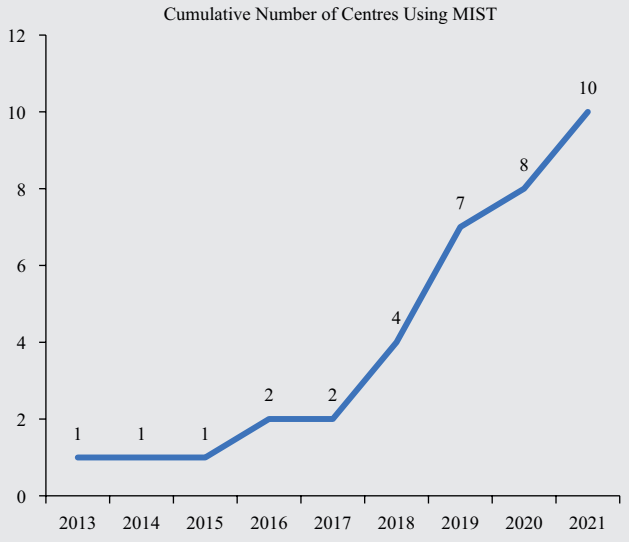
Centers reported surfactant reflux and hypoxia as the most encountered procedural adverse effects (Table 3). Only one center reported discontinuation of MIST due to a lack of training/experience and guidelines. Of the nine centers that did not utilize MIST, common reasons for non-utilization included lack of consensus (78%), lack of training (56%), and lack of experience (56%) with the technique. Three out of the nine centers that currently do not use MIST indicated they plan to implement the method within the next 2 years.

DISCUSSION

The present study represents the first national, site-specific survey of MIST techniques within tertiary-level NICUs in Canada. The survey response rate was relatively high at 85%, generating a reasonably accurate representation of national-level practices and providing crucial data

FIGURE 1

The number of Canadian Level 3/3+ NICUs using MIST over time. Numbers represent the centers (*N* = 10) that provided response regarding year of MIST implementation.



to identify current strengths, gaps, and future directions on using MIST for RDS management.

Our study shows that the utilization rate of MIST techniques amongst Canadian NICUs has rapidly increased in the last 3 years. Seventeen out of twenty-eight (61%) responding sites in Canada reported the use of MIST. Overall utilization in Canada found in our study appears to be considerably higher than in the United States, where only 15% of 2550 practicing neonatologists reported using the technique in 2019 [11]. Although the survey had a considerably larger sample size compared to our study, the low response rate (472/2250 respondents, 18%) may not have fully captured MIST utilization across the United States [11]. As our study was conducted after 2019, a more current survey in the United States may show increased uptake. In the meantime, a survey of 37 European countries reported that 52% of centers utilized the MIST technique as early as 2016 (165/324 respondents, 51%) [13]. A similar distribution of MIST use in the United Kingdom was found in 2019, where 11% of surveyed NICUs (144/150 respondents, 96%) reported MIST utilization, and an additional 78% were planning future implementation [14]. In addition, a recent survey of NICUs in Spain reported MIST utilization in 89% of the 44 responding centres (66% response rate) in 2020 [15]. Overall, the literature suggests an increasing uptake of these techniques worldwide.

In 2021, the Canadian Pediatric Society published a position statement outlining "Guidelines for Surfactant replacement in neonates" where MIST methods were recommended as the preferred method of surfactant delivery in spontaneously breathing neonates [16]. Despite these recommendations and an increasing rate of MIST utilization reported in this study, universal use across all Canadian NICUs is yet to be achieved. Only 14 out of 28 centers (50%) report a consistent use supported by formal institutional guidelines. The greatest barriers in this regard appear to be a lack of consensus, training, and experience in the technique. In addition, utilization rates were notably lower in neonates less than 26 weeks gestation, despite the highest risk of respiratory complications such as BPD and higher potential benefit from the procedure compared to later preterm neonates. More research is needed on the use of MIST on outcomes in the extremely preterm infant less than 26 weeks before use can become more widespread in this population. Results from the OPTIMIST trial suggest that intratracheal surfactant administration via a thin catheter did not result in a statistically significant reduction in the likelihood of the composite outcome of death or BPD compared to continued support with CPAP [7, 17]. However, the results demonstrated a reduction in the incidence of BPD alone among survivors at 36 weeks. Additionally, amongst secondary outcomes analysed in this study, there was reduced need of intubation, reduction in pneumothorax needing drainage with reduced need for oxygen at discharge in the MIST group. These findings continue to support judicious use of noninvasive/minimally invasive approach to surfactant instillation.

In terms of the procedural details collected in this survey, our results showed that a vast majority of Canadian centers use the higher volume BLES compared to other surfactants of higher concentration. While our group had published the local use of higher volume surfactant [1], this national data support that the MIST procedure may be successfully used regardless of the surfactant volume. Similar to previous survey-based studies, premedication prescription in MIST use remains a highly variable practice and future research exploring ideal agents is needed [18].

TABLE 2
MIST uptake and procedural details

Centers that responded to survey (*N* = 28)	***N* (%)**
MIST/LISA utilization	
Yes – Consistently used based on local guidelines	14 (50.0)
Yes – Occasionally used but in the absence of local guidelines	3 (10.7)
Never	9 (32.1)
Previously used, now discontinued or suspended	1 (3.6)
No response	1 (3.6)
Type of surfactant	
Cursurf (poractant alpha) only	3 (10.7)
Bovine lipid extract surfactant (BLES) only	19 (67.9)
Survanta (Beractant) only	1 (3.6)
Bles and Curosurf	3 (10.7)
Bles and Survanta	1 (3.6)
No response	1 (3.6)
Centers using MIST (*N* = 17)	
Type of catheter	
Purpose built catheter for MIST delivery (e.g. SurfCath, BLES Catheter)	7 (41.2)
Angio catheter	8 (47.1)
Multi-access catheter	1 (5.9)
Feeding tube	1 (5.9)
Umbilical catheter	0
Others	0
Premedication	
No premedication	1 (5.9)
Atropine	10 (58.8)
Propofol	0
Fentanyl	8 (47)
Ketamine	6 (35.3)
Remifentamil	0
Caffeine	0
Sucrose	1 (5.9)
Other	3 (17.6)
Operators	
Respiratory therapists	9 (53%)
Trainee physicians/fellows	7 (41.2)
Consultants/neonatologists	13 (76.5)
Time for surfactant delivery via MIST	
Less than 1 minute	5 (29.4)
1–2 minutes	4 (23.5)
2–3 minutes	3 (17.7)
≥3 minutes	3(17.7)
No response	2(11.8)
Perceived success	
Very high	5 (29.4)
High	9 (53)
Medium	1 (5.9)
Low/very low	0
No response	2 (11.8)

Note: MIST = Minimally Invasive Surfactant Therapy; LISA = Less Invasive Surfactant Administration.

FIGURE 2

Bar chart showing gestational age break down for MIST use.

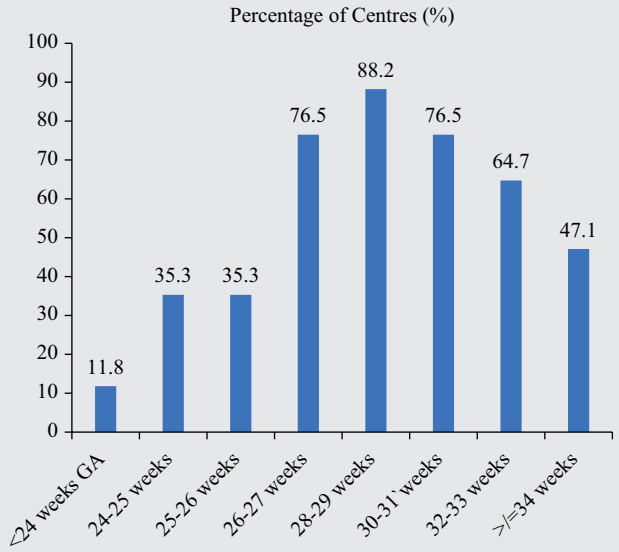


TABLE 3

Reports of procedural adverse effects and perceived efficacy barriers to implementation

	Proportion (%)
Adverse effects frequently/Very frequently seen (Centers using MIST, *N* = 17)	
Surfactant reflux	8/17 (47%)
Hypoxia	5/17 (29.4)
Bradycardia	6/17 (35.3)
Apnea	2/17 (11.8)
Need to intubate during procedure	0
Missing response = 2 centers	
Reasons for non-utilization (centers not using MIST, *N* = 9)	
Lack of consensus among neonatologist to use technique	7/9 (77.8)
Lack of experience in technique	5/9 (55.5)
Lack of evidence to support MIST	3/9 (33.3)
Lack of purpose-built catheter for MIST/Off label use of catheter not permitted	2/9 (22.2)
Lack of training	5/9 (55.5)
Low perceived efficacy of MIST	0
Other (please specify)	Fear about minimal sedation/ analgesia
Discontinuation rate of MIST	1/28 (3.6)

Note: MIST = Minimally Invasive Surfactant Therapy.

Furthermore, the relative popularity of video laryngoscope use was a notable finding. The ability to confirm the proper placement of the MIST catheter in real-time using a video laryngoscope may be particularly beneficial during training and implementation, as it may increase user confidence and procedural success. However, few studies have explored the utility of a video laryngoscope as an educational and procedural tool for MIST, and further research is required before universal recommendations can be concluded.

Many centers reported using purpose-built catheters that were only recently approved for use in Canada in early 2019. The lack of commercially available surfactant delivery products in the Canadian market prior to 2019 may have been a barrier to implementation in Canadian NICUs. Lack of availability may lead to the use of off-label products to complete the MIST procedure, which carries additional risk. While our group has previously reported that the procedural success remains similar with either the rigid vascular catheter or more flexible catheters such as multi-access catheters [19], specific procedural data pertaining to the use of various purpose-built catheters is yet to be published.

It is important to note the potential limitations of using a survey design for this study. As site surveys were based on input from one or two representative individuals, responses may be subject to bias and inaccuracies. However, the respondents were representatives of the CNN EPIQ-LHG and thus, hold leadership positions that would require familiarity with their site's procedures. Moreover, the moderately high response rate to the survey provided an excellent representative overview of tertiary level NICUs across Canada. Although the sample size of our survey was smaller than previously published surveys of MIST use in North America and Europe, the findings of this study provide a detailed snapshot of institutional practices and policies within the Canadian context.

Overall, the findings of this survey identified a need for national initiatives and data collection to support uniform MIST utilization across Canadian NICUs. While the recently published national position statement will go a long way to generate and support consensus, other potential interventions that may improve uptake nationally could be workshops and national in-person and virtual training sessions. Fostering cooperation and educational sessions between more experienced centers and centers with limited experience by national focus groups and national quality improvement initiatives could also be effective. Additionally, as more Canadian centers adopt this technique, short- and long-term data trends and impact on critical patient-related outcomes such as BPD should be monitored in national surveillance through initiatives such as the CNN.

CONCLUSION

This survey exploring surfactant delivery methods in Canada found rising rates of MIST utilization among the NICUs that are part of the CNN. However, a considerable variation is reported on catheter choice, premedication use, and the gestational age of neonates where MIST is consistently used; 32% of NICUs that completed the survey reported no use of MIST, citing a lack of consensus, training, and experience. National endeavours focusing on data collection, training workshops, and development of standard operating protocols would go a long way to increase uptake of this method and standardize practice. Future studies are needed to explore MIST utilization in preterm neonates less than 26 weeks gestation, optimal premedication and ideal catheter choice.

DISCLOSURES

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Contributors

All authors contributed to the conception or design of the work, the acquisition, analysis, or interpretation of the data. All authors were involved in drafting and commenting on the paper and have approved the final version.

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Competing interests

All authors declare no conflict of interest.

Ethical approval

Institutional research ethics board approval was obtained (REB 116750).

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