ACTA PÆDIATRICA
NURTURING THE CHILD

Acta Pædiatrica ISSN 0803-5253

REGULAR ARTICLE

Five-country manikin study found that neonatologists preferred using the LISAcath rather than the Angiocath for less invasive surfactant administration

Laura Fabbri (l.fabbri@chiesi.com)[1], Katrin Klebermass-Schrehof[2], Marta Aguar[3], Catherine Harrison[4], Ewa Gulczyńska[5], Debora Santoro[1], Marco Di Castri[1], Vincent Rigo[6]

1.Research & Development – Neonatology, Chiesi Farmaceutici SpA, Parma, Italy
2.Division of Neonatology, Pediatric Intensive Care and Neuropediatrics, Department of Pediatrics and Adolescent Medicine, Medical University Vienna, Vienna, Austria
3.Division of Neonatology, Hospital Universitari i Politècnic la Fe, Valencia, Spain
4.Neonatology Division, Leeds Teaching Hospitals NHS Trust, Leeds, UK
5.Department of Neonatology, Polish Mother's Memorial Hospital – Research Institute, Łódź, Poland
6.Neonatology Division, CHU de Liège - CHR de la Citadelle, University of Liège, Liège, Belgium

Keywords
Catheter, Continuous positive airway pressure, Less invasive surfactant administration, Neonatology, Respiratory distress syndrome

Correspondence
Laura Fabbri, Global Clinical Development, Research & Development – Neonatology, Chiesi Farmaceutici SpA, Largo Belloli 11/A, 43122 Parma, Italy.
Tel: +390521 279722 |
Fax: +39 0521 279333 |
Email: l.fabbri@chiesi.com

Received
4 September 2017; revised 20 November 2017; accepted 3 January 2018.

DOI:10.1111/apa.14214

ABSTRACT

Aim: Less invasive surfactant administration (LISA) has been shown to decrease the risk of death and bronchopulmonary dysplasia in preterm neonates. The LISAcath is the first catheter to be specifically developed for LISA, and we compared the clinical impressions of neonatologists using the LISAcath and the commonly used Angiocath in a simulated setting.

Methods: This was a multinational, multicentre study, conducted in October 2016, which involved 39 neonatologists who were recruited by employees of the sponsor from large, well-recognised neonatal intensive care units across Europe. LISA was not the standard of care in these units in Austria, Belgium, Poland, Spain and the United Kingdom at the time of the study. After training, participants simulated LISA on a neonatal manikin, once with the LISAcath and once with Angiocath, then answered a 10-item questionnaire.

Results: The responses to nine of 10 questions showed that 67-95% of the respondents preferred the LISAcath to the Angiocath, with most of the remainder indicating no preference. The only exception was the luer connection question, with two-thirds expressing no preference. The LISAcath was considered potentially safer by 33 of 39 participants, with no votes for the Angiocath.

Conclusion: Overall, neonatologists preferred using the LISAcath rather than the Angiocath on a neonatal manikin.

INTRODUCTION

Respiratory distress syndrome is a life-threatening condition, which occurs almost exclusively in preterm neonates with a deficiency, dysfunction or inactivation of pulmonary surfactant (1). Surfactant replacement therapy has become the standard care for the prevention and treatment of respiratory distress syndrome in preterm neonates (1), as its use has been shown to decrease the risk of mortality, bronchopulmonary dysplasia and air leaks (2).

Methods of surfactant administration have been developed to avoid prolonged intubation as a result of the increased focus on avoiding mechanical ventilation. The intubation–surfactant–extubation method consists of brief intubation to administer surfactant, rapidly followed by extubation to nasal continuous positive airway pressure. The less invasive surfactant administration (LISA) method permits maintenance of continuous positive airway pressure support and spontaneous breathing during tracheal catheterisation and drug application. LISA has been

Abbreviation
LISA, Less invasive surfactant administration.

Key notes

- Less invasive surfactant administration (LISA) has been shown to decrease the risk of death and bronchopulmonary dysplasia in preterm neonates.
- This multinational, multicentre study involved 39 European neonatologists who compared the LISAcath, the first catheter customised for LISA, with the Angiocath.
- Overall, neonatologists preferred using the LISAcath rather than the Angiocath on a neonatal manikin and 33 of 39 felt the LISAcath was safer, with none voting for the Angiocath.

developed to avoid positive pressure ventilation and to facilitate more gentle intubation.

Meta-analyses of studies comparing the intubation–surfactant–extubation method and LISA have found a decreased risk of early mechanical ventilation requirements and, more importantly, a decreased risk of the composite outcome of death and bronchopulmonary dysplasia with LISA (3,4). Many devices are currently used to perform LISA. These include gastric tubes, angiography catheters and vascular catheters, such as the Angiocath (Becton, Dickinson and Company, New Jersey, USA), which was the vascular catheter used by Dargaville et al. in their Hobart method for LISA (5,6). However, at the time that method was developed, there was no tool available that had been specifically designed for LISA.

LISAcath (Chiesi Farmaceutici SpA, Parma, Italy) is an optimised version of the Angiocath (Fig. 1) (7,8). It was designed to provide LISA for preterm neonates with respiratory distress syndrome, in combination with poractant alfa, and one of its aims was to improve handling characteristics for healthcare operators. Both of the catheters are straight, although they can be shaped into curves, have identical 5 French shaft diameters and both have a similar working length of 130 mm for the LISAcath versus 133 mm for the Angiocath. In an unpublished *in vitro* study, carried out during the development process, the LISAcath demonstrated better mechanical properties than the Angiocath. Importantly, the blue shaft colour of the LISAcath and the addition of depth markers may facilitate better visualisation and insertion. Moreover, in an unpublished physical–chemical compatibility study, conducted to comply with regulatory requirements, the quality and efficacy of poractant alfa were not affected by contact with either the LISAcath or the Angiocath, thus supporting administration using the LISA technique.

The aim of this study was to compare the clinical impressions of neonatologists using the LISAcath and Angiocath in a standardised and representative simulated setting.

METHODS

This was a multinational, multicentre study conducted in countries where LISA was not the standard of care when the study took place in October 2016. Employees of the sponsor recruited a broad, representative group of neonatologists with a range of experience from 10 years to more than 30 years, working in large, well-recognised neonatal intensive care units. A total of 39 neonatologists completed the study: five in Austria, five in Poland, six in Spain, 11 in Belgium and 12 in the United Kingdom.

At each study site, training was carried out using a training video and reading the LISAcath instructions for use. The participant was asked to simulate LISA with a supplied LISAcath, following the instructions for use and the steps in the training video. The procedure was then repeated with an Angiocath. The procedures were performed on a Premature Anne Task Trainer manikin (Laerdal Medical AS, Stavanger, Norway) in a dedicated neonatal incubator.

Participants then completed a questionnaire (Appendix S1) that was designed by the study sponsor, and included 10 questions related to the main characteristics of the catheters: colour, insertion depth markers and distance markings, tip softness and rounding, stiffness, kinkability, luer attachment, potential safety and overall design. Nine of the questions offered three possible responses: the LISAcath was better or preferred, the Angiocath was better or preferred or there was no difference. The 10th question, which was on overall design, had two responses: the overall design of the two catheters was comparable or that there were significant differences. Respondents who said there were significant differences were then asked which catheter they preferred.

The results of the questionnaire were analysed descriptively, and the number and percentage of participants selecting each response were reported. There was no formal sample size calculation.

RESULTS

All 39 participants completed all 10 questionnaire items. The majority of participants (67-95%) preferred the LISAcath to the Angiocath when responding to nine of the 10 questions (Fig. 2), with most of the remaining participants indicating no preference. Only five responses to three questions indicated a preference for the Angiocath: one participant preferred the white colour of the Angiocath over the blue of the LISAcath, two participants felt that the distal markings of the LISAcath complicated the procedure in

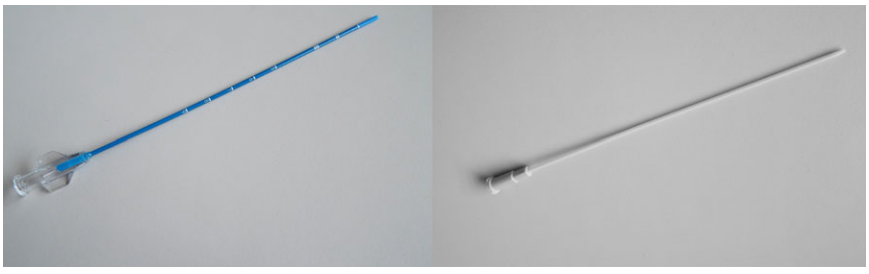

Figure 1 The LISAcath catheter (left) and Angiocath catheter (right).

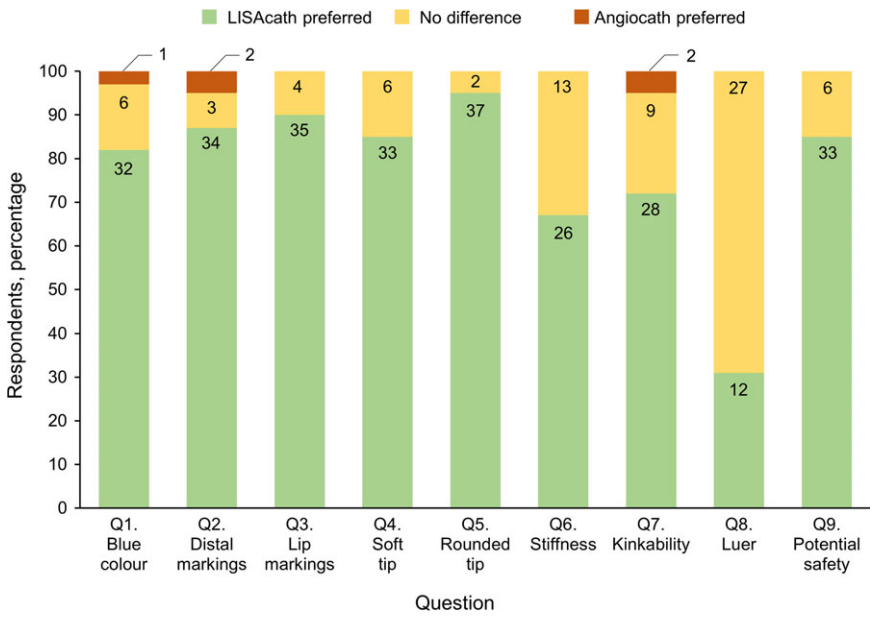

Figure 2 Answers to questions 1 to 9 of the questionnaire (n = 39). Data plotted are percentages and the values in the columns are the numbers of participants with the indicated response.

comparison with the Angiocath and two participants indicated a preference for the kinkability of the Angiocath.

The only question for which there was no clear preference for the LISAcath was when the participants were asked for their opinion on the luer connection. The LISAcath has a standard luer connection, which may explain why approximately two-thirds of the participants indicated no preference. When it came to the important question of potential safety, 33 (85%) of the participants considered the LISAcath to be potentially safer than the Angiocath, with the remainder having no preference. None of the respondents considered the Angiocath to be potentially safer.

Finally, participants were asked whether the overall design of the LISAcath was comparable to the Angiocath. Of the 39 participants, 26 (67%) had an overall preference for the LISAcath and the remainder had a neutral opinion. None of them preferred the Angiocath.

DISCUSSION

This study describes the clinical impressions of neonatologists who simulated LISA on an extremely premature manikin to compare the new purpose-built LISAcath, and the commonly used Angiocath. The characteristics of the LISAcath were preferred by most participants in the study, and its overall design was rated more highly by two-thirds of the participants. Importantly, the participants also felt that its features made it a potentially safer device.

Although the Angiocath and the LISAcath have a number of similarities, many of the LISAcath features were specifically designed to facilitate and secure tracheal intubation. Another study investigated different devices used for LISA and found that more rigid catheters, such as the Angiocath, permitted faster laryngeal catheterisation than gastric tubes (5). In the same study, the subjective ease of use of rigid catheters was also reported to be better. Using the Angiocath as a control was important as it allowed us to compare the LISAcath with the current best available device and focus on specific improvements in design. Feeding tubes for LISA are mostly handled with Magill forceps (9), but if we had used them as controls, the answers to the questionnaire would probably have focused on differences in handling techniques.

The subjective nature of this study was a limitation. However, the inclusion of 39 neonatologists from five different European countries who had different backgrounds is likely to have improved the generalisability of their observations. Secondly, the study involved *in vitro* testing, with no live infants being treated. This had the advantage of standardising the methodology used and meant that the participants could use two catheters in quick succession. However, although the manikin used has been rated as having a high functional fidelity for intubation training, clinical impressions of the relative merits of the two devices during real-life intubation could be different (10). Finally, it was not possible to blind participants to the fact that a new device was being investigated.

CONCLUSION

The future availability of the LISAcath, which has been specifically developed for LISA, will be an important tool in the care of neonates with, or at risk of, respiratory distress syndrome. Its development could potentially help to standardise providing surfactant replacement therapy by LISA.

ACKNOWLEDGEMENTS

The authors would like to thank the investigators at the investigative sites and other colleagues from Chiesi Farmaceutici SpA for their collaboration in this study, together with David Young for writing support.

FUNDING

This study was funded by Chiesi Farmaceutici SpA, the manufacturer of LISAcath, including the writing support.

CONFLICTS OF INTERESTS

LF, DS and MDC are employees of Chiesi Farmaceutici SpA, the sponsor of the study. KKS received speaker honoraria for lectures and workshops and travel grants to attend scientific meetings from Chiesi, not related to this study. No honorarium was received for this study. CH has received speaker honoraria and travel costs to attend meetings about LISA from Chiesi. VR received speaker honoraria and travel grants to attend scientific meetings from Chiesi Belgium, which were not related to this study. The other authors have no conflicts of interest to declare.

References

1. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Plavka R, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2016 Update. *Neonatology* 2017; 111: 107–25.
2. Seger N, Soll R. Animal derived surfactant extract for treatment of respiratory distress syndrome, Seger N, editor. *Cochrane Database Syst Rev* 2009; (2): CD007836.
3. Aldana-Aguirre JC, Pinto M, Featherstone RM, Kumar M. Less invasive surfactant administration versus intubation for surfactant delivery in preterm infants with respiratory distress syndrome: a systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed* 2017; 102: F17–23.
4. Rigo V, Lefebvre C, Broux I. Surfactant instillation in spontaneously breathing preterm infants: a systematic review and meta-analysis. *Eur J Pediatr* 2016; 175: 1933–42.
5. Rigo V, Debauche C, Maton P, Broux I, Van Laere D. Rigid catheters reduced duration of less invasive surfactant therapy procedures in manikins. *Acta Paediatr* 2017; 106: 1091–6.
6. Aguar M, Nuñez A, Cubells E, Cernada M, Dargaville PA, Vento M. Administration of surfactant using less invasive techniques as a part of a non-aggressive paradigm towards preterm infants. *Early Hum Dev* 2014; 90: S57–9.
7. Dargaville PA, Aiyappan A, De Paoli AG, Kuschel CA, Kamlin COF, Carlin JB, et al. Minimally-invasive surfactant therapy in preterm infants on continuous positive airway pressure. *Arch Dis Child Fetal Neonatal Ed* 2013; 98: F122–6.
8. Dargaville PA, Aiyappan A, Cornelius A, Williams C, De Paoli AG. Preliminary evaluation of a new technique of minimally invasive surfactant therapy. *Arch Dis Child Fetal Neonatal Ed* 2011; 96: F243–8.
9. Klotz D, Porcaro U, Fleck T, Fuchs H. European perspective on less invasive surfactant administration-a survey. *Eur J Pediatr* 2017; 176: 147–54.
10. Sawyer T, Strandjord TP, Johnson K, Low D. Neonatal airway simulators, how good are they? A comparative study of physical and functional fidelity. *J Perinatol* 2016; 36: 151–6.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Questionnaire used in the study.