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Original article

Non-invasive administration of poractant-α in neonatal respiratory distress syndrome via a supraglottic device in the clinical practice in a second level neonatal unit: comparison of LMA® vs iGel® devices

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Abstract. *Introduction:* Non-invasive pulmonary surfactant (SF) administration for neonatal respiratory distress syndrome (NRDS) is a development of administration of SF. Administration of SF via a supraglottic device (SGD) has been shown to be effective. Here the results of administration of SF in NRDS in infants requiring oxygen and nasal-CPAP (n-CPAP) via two types of SGDs, LMA® vs iGel®, in a second level Neonatal Unit are reported in a retrospective study. *Results:* Fourteen infants in the LMA®Group were matched with 21 comparable infants in the iGel® Group (g.a. ≥30 wks and b.w. ≥ 1,500 gr) presenting NRDS with fraction of inspired oxygen (FiO_2) ≥ 0.25 – 0.6, requiring n-CPAP. All infants presented a significant improvement of PaO_2/FiO_2 ratio that was seen earlier in the iGel® Group vs the LMA® Group. There was no severe adverse effect during the maneuver with both SGDs. No baby died, No.2 required endotracheal intubation for a second dose of SF as by protocol, and No. 1 was transferred to a higher level of care. *Conclusion:* Non-invasive SF administration via SGD has been done effectively at a second level Neonatal Unit and very early in the course of the disease therefore limiting transfer of the baby without complications with both SGDs. Improvement in gas exchange was more rapid in the iGel®Group. This result needs confirmation. In our experience iGel® was easier to use than LMA®. (www.actabiomedica.it)

Key words: pulmonary surfactant, poractant-α, neonatal respiratory distress syndrome, supraglottic device

Introduction

Endotracheal pulmonary surfactant (SF) administration via the endotracheal tube has been a milestone in the development of the care of the newborn infant, in particular for premature infants and for those babies presenting with neonatal respiratory distress syndrome (NRDS) and retarded lung maturity as in the infant of diabetic mother and those suffering pneumonia with consequent increased consumption of SF.

After the astonishing effect of SF treatment on survival, with decrease of consequences like air leak syndromes and severe intra-ventricular hemorrhage (1-3) the studies have shifted towards reducing the invasiveness of the method of administration of SF. At present neither artificial or animal derived SFs showed adequate effectiveness when administered via nebulization (4-5), therefore one first successful approach to non-invasiveness was the INSURE method that consists of the rapid sequence **I**ntubation-**SUR**factant administration-**E**xtubation (6) that earned favor of the neonatologists. A second method was an evolution of the INSURE method and consists in the administration of SF through a small catheter that does not occlude the space between the vocal cords, inserted in trachea with the laryngoscope, while maintaining the

baby on nasal-CPAP (n-CPAP) and therefore maintaining the lung recruitment during the maneuver of instillation of SF, then extract the catheter and let the SF distribute with the n-CPAP (7). This second method has been called LISA, an acronym for **L**ess **I**nvasive **S**urfactant **A**dministration. Also this method deserved neonatologists' attention, and it is used in particular for very small babies to avoid intubation with an endotracheal tube that, also positioned for short periods of time, can contribute to the development of chronic lung disease.

Both INSURE and LISA techniques require skilled neonatologists that can intubate in few seconds also the smallest infants. However, such neonatologists are usually found only in the perinatal centers provided with Neonatal Intensive Care Unit (NICU).
Unfortunately:

- not all the very low birth weight infants severely premature babies, whose number is limited to 1-2% of all the newborns, are delivered in perinatal centers with NICU; the few of them delivered in perinatal centers without NICU must be anyway assisted and managed in the best way from the beginning, because it is well known that the first hour of life is critical for outcome;
- in such premature babies the percentage of NRDS is very high, and the lower the gestational age (g.a.) the higher the probability of onset of NRDS;
- the very great majority of babies (98-99%), are delivered in perinatal centers without NICU, and often in centers where the Pediatrician is not a pure Neonatologist, but has to carry out several functions. In these same centers the great majority of the Anesthesiologists have few confidence with the newborn too. Luckily the very great part of the babies delivered in these centers will not develop NRDS. However the estimated percentage of babies between 34-37 wks'gestation developing NRDS is between 5% and 1% (8), and to them fullterm infants of diabetic mothers, those with congenital pneumonia, those with asphyxia at birth and other small categories have to be added. Eventually, the total number of NRDS in these infants is greater than the total number of NRDS in the severe premature infants, but:

a) they are more largely distributed because they can be delivered everywhere, therefore the number for each center can be limited;
b) the very great majority of them cannot be foreseen before birth and therefore transfer to another center will be performed after birth. To transfer an ill baby can worsen his/her outcome while to give SF at the first stages of NRDS and with a non-invasive method might in many cases avoid endotracheal intubation and transfer to another center, while allowing maternal bonding implementation;
c) the dose of SF required by these infants is at least double compared to that of very premature infants, but the increased cost is distributed on many centers and compensated by the reduction of transfers, that have high direct and indirect costs.

One must add to the above observations the facts that SF replacement is not to be anymore considered an experimental treatment of NRDS, that any baby needing it cannot be denied this treatment and that studies (1) have demonstrated that its effectiveness improves when it is administered early in the course of NRDS.

These are the motives that led to the use of a supraglottic device (SGD), a non-invasive device, whose progenitor is the Laryngeal Mask Airway (LMA®), for the airways management in the neonate in a second level Neonatology Unit, and progressively for delivering SF to the lung. LMA® is constituted by an irregular oval mask whose anterior part is more pointed and enters the esophagus sealing it. After inflation of a cuff around the oval mask, this creates a closed chamber over the tongue centered over the larynx. In this point the roof of the mask is opened to a conduit that exits from the mouth and whose distal end can be connected with a self-inflating bag or a flow-inflating bag or a mechanical ventilator. Through the conduit one can inject drugs that go directly in the trachea, and in the present case SF.

The non-invasiveness of this device is due to the followings:

- it can be used when the patient is spontaneously breathing and/or in n-CPAP;
- even if the baby is vigorous it is not necessary to sedate him/her to introduce the mask;
- it is not necessary that the baby is in a particular position to insert the mask: therefore his/her head can stay in a lateral position or in a neutral position during insertion and administration of ventilation or drugs. After the procedure, you can easily take away the mask and let the baby on spontaneous ventilation and/or n-CPAP.

iGel® is a second generation SGD made of soft gel-like material, conceptually equal to LMA®, but the shape, softness and contours accurately mirror the peri-laryngeal anatomy to create the perfect fit. Therefore it does not have any inflatable cuff around the oval mask. This makes iGel® easier to use and eventually more quick to be correctly positioned.

Both SGDs have been used to deliver SF to infants with NRDS with good results (9-13), however no study was done to compare the two devices for administration of SF in NRDS.

In this paper we will report the experience in a second level Neonatology Unit with administration of poractant-α for treatment of NRDS given via LMA® from 2013 to 2015 and via iGel® from 2013 to 2018 to evaluate if any difference was found between the two methods.

Patients and Methods

All babies with birth weight (b.w.) ≥ 1,500 gr consecutively admitted to the second level Neonatal Unit of the Eastern Liguria Hospital of La Spezia, Italy, and presenting clinical or radiological NRDS were eligible for non-invasive administration of SF unless they required endotracheal intubation to sustain ventilation from the onset of NRDS.

Radiological staging of NRDS was defined by plain chest X-ray (14) as:

- Stage 1: fine homogeneous ground glass shadowing
- Stage 2: bilateral widespread air bronchogram
- Stage 3: confluent alveolar shadowing
- Stage 4: alveolar shadowing obscuring cardiac border.

However, because at the analysis of data chest X-ray was not always available before the administration of SF we decided to stage NRDS before SF arbitrarily with a clinical staging: presence of tachypnea + dyspnea + nasal flaring + grunting staged on the basis of oxygen requirement to keep transcutaneous saturation of oxygen ($SatO_{2tc}$) ≥95% and n-CPAP:

- Stage 1: need of fraction of inspired oxygen (FiO_2) <0.25, quite stable on n-CPAP
- Stage 2-3: need of FiO_2 ≥0.25 - ≤ 0.4, with increasing trend of oxygen requirements on n-CPAP
- Stage 3-4: need of FiO_2 > 0.4, with increasing trend of oxygen requirements on n-CPAP.

After having obtained verbal parental consent, a quote of poractant-α of 200 mg/kg was prepared in a syringe. However, some babies were treated in the delivery room and the baby was not weighted: in those cases to define the dose of SF the estimated prenatal weight was used. The infant was fully monitored before and after SF administration. Then a humidified supraglottic device (SGD) was inserted (if LMA® it was also blocked by the inflation of the cuff) without withdrawing any ongoing n-CPAP. When the device was correctly inserted then the chest was rotated on its left (without moving the head) and half dose of SF instilled directly in the conduit. This was done to better distribute SF within the left lung. In fact one can see that SF accumulates a bit in the conduit before the baby inspires and inhales it. From a previous pilot experience (15) it had been seen that without rotating the body of the baby the self- inflation of SF tended to distribute prevalently on the right chest, as usually happens in inhalation. To instill directly in the conduit the SF with a syringe rather than to introduce a thin catheter in the conduit of the SGD [Catheter and Laryngeal Mask Endotracheal Surfactant Therapy (CALMEST) (16)] was preferred. This choice was done to limit manipulation and to reduce time of administration. At this point a self-inflating bag was attached to

the distal part of the conduit and the baby was manually bag ventilated with a pressure of about 20 cmH_2O with the same mixture of O_2 he/she was receiving before the maneuver. After 5-10 inflations with the conduit clean of SF, the baby was rotated on his right, again without rotating the head, and the second half quote of SF was administered with the same method. At the end of the maneuver the SGD was removed (if LMA® after having deflated the cuff) and the baby let in spontaneous breathing on n-CPAP with the same mixture of O_2 than before, checking in continuous $SatO_{2tc}$ to reduce FiO_2 as soon as $SatO_{2tc}$ was above 97-98%, till to when $SatO_{2tc}$ was stable around 95-97%. Immediately after the maneuver, a gastro-esophageal feeding tube was inserted by mouth to evaluate the presence or not of SF in the stomach.

If during the procedure there was a fall of $SatO_{2tc}$ <75% or of heart rate < 100 bpm, then the procedure was paused and manual positive pressure ventilation was guaranteed via SGD until $SatO_{2tc}$ was ≥95% and HR>100 bpm. The protocol established that if stabilization wasn't obtained within 30 sec, then the baby had to be intubated and undergo mechanical ventilation: in the present study 2 cases presented respiratory depression with HR<100 bpm and desaturation but recovery was rapid and no mechanical ventilation was needed.

Arterial blood gases were measured before the administration of SF, within the first 2 hrs after administration, and in the intervals 6-12 hrs and 12-24 hrs after the administration. If more than one sample was taken in each defined time interval the one scoring better was used for data analysis.

Vital parameters as respiratory frequency, heart rate, $SatO_{2tc}$, non-invasive arterial blood pressure as well FiO_2 were monitored in continuous and recorded at the same times as above.

Mean length of hospitalization and complications were recorded at discharge.

Supraglottic devices description

Size 1 autoclavable LMA® model was used (Laryngeal Mask Company Limited, San Diego, California, USA). The brand indicates this mask useful for babies weighing < 5 kg. Before insertion it was humidified with sterile injectable water to facilitate its progression in the mouth. After insertion the cuff

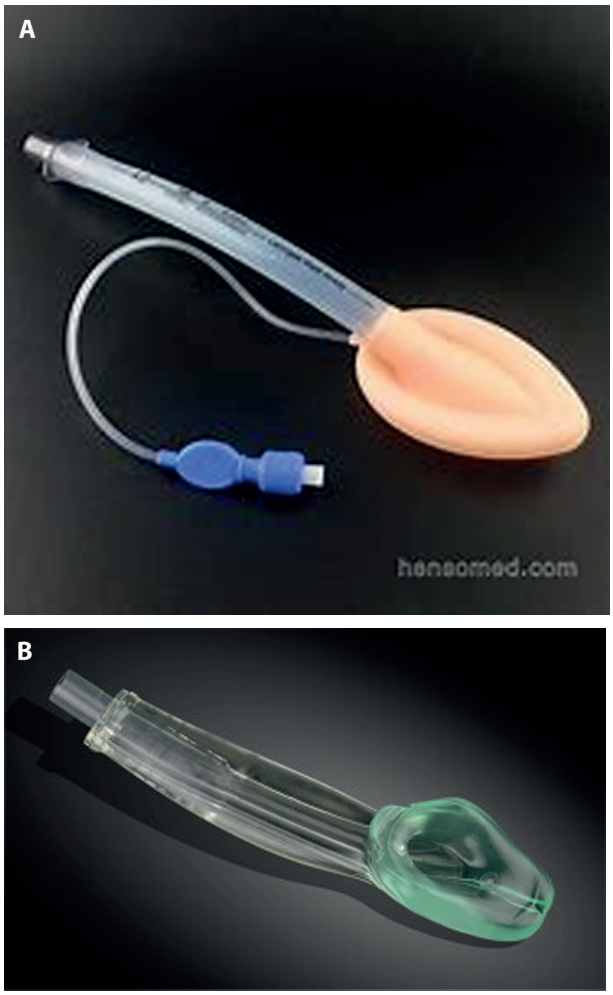

Figure 1. a) LMA ®; b) iGel®

was inflated to stop the mask itself and it was left that the mask had a little bounce-back (17) (Figg. 1, 2). The volume of air inflated was max 4 ml, smaller in the smallest infants. The cuff was deflated before removal of the mask.

Size 1 disposable iGel® mask was used (Intersurgical SpA, Mirandola, Italy), identified also by the pink color of the containing box. The limits of use for mask given by the factory are infants weighing 2-5 kg. However we used it also in infants of 1,500 gr. The mask was humidified before insertion with sterile injectable water or sterile ultrasound gel. Once inserted there was no need to inflate a cuff (that is not present in this device) - and therefore no bounce-back - to fix

it. After administration and distribution of the injected SF the mask was removed.

Statistical analysis

Statistical analysis was done by Student's *t*-test for unpaired data for parametrical data and by exact test of Fisher for non-parametrical data. Chi square was used to evaluate the frequency distribution. Significance was considered for $p < 0.05$.

Results

Thirty-five babies qualified for treatment with SGD: No.14 in the LMA® Group and No.21 in the iGel® Group.

Clinical details of the babies of the two groups are listed in Table 1. No statistically significant difference was found in gender prevalence - with male sex being more frequently represented -, mean g.a. (34.4 wks LMA® Group vs 34.6 wks iGel® Group), mean b.w. (2,371 gr LMA® Group vs 2,355 gr iGel® Group), as well as percentage of antenatal steroid prophylaxis, antepartum hemorrhage, pregnancy induced hypertension, maternal diabetes, chorioamnionitis and other maternal problems.

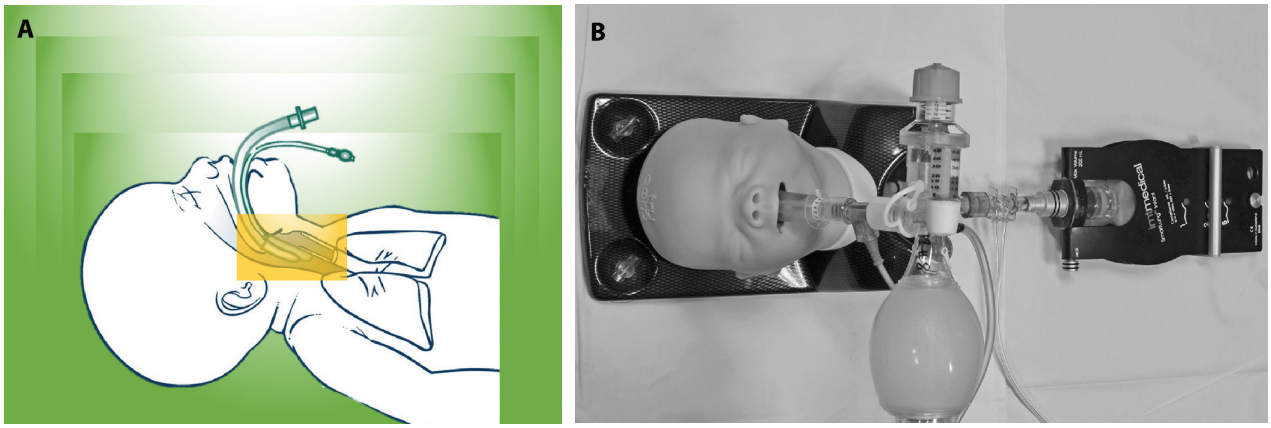

Figure 2. a) positioning of LMA®: note that the opening of the mask is on the larynx ; b) positioning of iGel®: note the widened, flattened stem to reduce axial rotation and mal-positioning.

Table 1. Clinical details of the patients. No statistically significant difference was found.

Parameter	LMA® Group	iGel® Group
No.	14	21
M/F, No.	9/5 = 64.3% M	15/6 = 71.4% M
g.a., wks, mean (range)	34.4 (30 – 40.7)	34.6 (31-41.7)
b.w., gr, mean (range)	2,371 (1,455-3,850)	2,355 (1,500-4,980)
Antenatal steroids, No.	2/12 =16.7%	4/21 = 19.0%
Antepartum hemorrhage, No.	4/14	2/21
Pregnancy induced hypertension, No.	1/14	1/21
Maternal diabetes, No.	1/14	4/21
Chorioamnionitis, No.	0/14	2/21
Other maternal problems No.	2/14	3/21

In Table 2 the main clinical data regarding delivery and conditions at birth are reported. No significant difference was observed in type of delivery, presence of prolonged rupture of membranes (PROM) > 18 hrs, arterial cord pH and base excess, Apgar score at 1st minute after birth. The babies of the iGel®Group had a significantly lower Apgar at 5th minute ($p<0.02$) and presented an increased need of resuscitation maneuvers at birth vs those of the LMA®Group: respectively 90.5% vs 57.1%, $p<0.05$.

Concerning the development of NRDS in both groups (Tab. 2), none presented stage 1 NRDS, and the two groups did not differ for the frequency of stage 2-3 and stage 3-4 NRDS.

As regards the administration of SF (Tab. 3), there was no difference in the mean values of parameters of oxygenation before its instillation, nor in the mean age at administration - even if there was a great SD in the LMA®Group due to one baby treated late, about 52 hrs -, or in the mean quantity of SF/kg body weight administered, whose quantity indeed resulted meanly lower than the foreseen dose in both groups for the real body weight.

One adverse effect at administration, described as bradycardia and desaturation, was recorded in each group, that was treated with manual bag ventilation through the SGD and resolved within 30 seconds.

Table 2. Clinical data of delivery and conditions at birth in the two groups of patients.

Parameter	LMA®Group	iGel® Group	P
Urgent CS, No.	8/14 = 57.1%	11/21 = 50%	NS
CS, No.	3/14 = 21.4%	11/21 = 52.4%	NS
Vaginal, No.	3/14 = 21.4%	10/21 = 47.6%	NS
PROM > 18 hrs, No.	1/14 = 7.14%	2/21 = 9.52%	NS
Cord pH, mean, SD	7.31 (±0.121)*	7.25 (±0.107)	NS
Cord BE, mmol/l, mean, SD	-5.21 (±4.08)*	-6.08 (±4.95)	NS
Apgar score 1', mean	6.57 ± 2.47	5.47 ± 2.42	NS
Apgar score 5', mean	8.64 ± 0.84	7.57 ± 1.50	< 0.02
Resuscitation at birth, No.	8/14 = 57.1%	19/21 = 90.5%	< 0.05
NRDS Max Grade = 2-3, No.	6/14	11/19	NS
NRDS Max Grade = 3-4, No.	8/14	8/19	NS

*9 cases; Legend: CS = cesarean section; PROM = prolonged rupture of membranes; BE = base excess; NRDS = neonatal respiratory distress syndrome

Table 3. Details of administration of surfactant in the two groups of patients. No statistically significant difference was found.

Parameter	LMA® Group	iGel® Group
FiO_2 before SF, mean ± SD, mmHg	0.45 ± 0.12	0.45 ± 0.21
PaO_2 before SF, mean ± SD, mmHg	62.8 ± 17.5	51.0 ± 13.5
$SatO_{2tc}/FiO_2$ ratio before SF ± SD	242 ± 59	235 ± 39
PaO_2/FiO_2 ratio before SF ± SD	155 ± 63	135 ± 79
Mean age at administration of SF ± SD, min	738.1 ± 861.7	331.1 ± 368.5
Mean dose of administered SF ± SD, mg	181 ± 13	189 ± 29
Adverse effects during administration, No.	1 bradycardia + desaturation	1 bradycardia + desaturation
SF in the stomach after administration	None	None

Legend: FiO_2 = fraction of inspired oxygen; PaO_2 = partial pressure of arterial oxygen; $SatO_{2tc}$ = transcutaneous saturation of oxygen; SF = surfactant

In both groups no SF was found in the stomach after the instillation maneuver, an indirect sign of its administration in the lung.

When we evaluated how mean requirement of O_2 changed after SF administration (Tab. 4), no difference in mean FiO_2 given before SF between the groups was observed (see Tab. 3).

In the LMA® Group mean FiO_2 presented a trend towards reduction, without reaching significance even after 12-24 hrs. On the contrary mean FiO_2 was significantly reduced in the iGel® Group already after 60-120 min ($p< 0.005$) remaining statistically significant lower for the whole period of recording (Tab. 4).

As regards PaO_2 changes after SF administration (Tab. 5), no difference in mean PaO_2 before SF between the groups was observed (see Tab. 3).

After administration of SF (Tab. 5), mean PaO_2 in the LMA® Group increased more slowly than the corresponding decrease of FiO_2, presenting a non significant improving trend. Instead mean PaO_2 progressively increased in the iGel® Group, and the

Table 4. Fraction of inspired oxygen (FiO_2, mean value ± SD) in relation to time of administration of surfactant (SF) in the two groups of infants.

TIME	LMA® Group	LMA®: P vs before SF	iGel® Group	iGel®: P vs before SF
Before SF	0.45 ± 0.12		0.45 ± 0.21	
60-120 min after SF	0.36 ± 0.12	NS	0.30 ± 0.10	< 0.005
6-12 hrs after SF	0.34 ± 0.15	NS	0.30 ± 0.11	< 0.005
12-24 hrs after SF	0.35 ± 0.17	NS	0.27 ± 0.06	< 0.001

Table 5. Mean values ± SD of PaO_2 (partial pressure of arterial pressure, mmHg) in relation to administration of surfactant (SF) in the two groups of infants.

TIME	LMA® Group	LMA®: P vs before SF	iGel® Group	iGel®: P vs before SF
Before SF	62.8 ± 17.5		51.0 ± 13.5	
60-120 min after SF	68.4 ± 22.8	NS	61.0 ± 17.1	NS
6-12 hrs after SF	82.3 ± 29.4	NS	65.9 ± 24.7	NS
12-24 hrs after SF	62.3 ± 27.6	NS	70.3 ± 29.6	<0.05

Table 6. Transcutaneous saturation of oxygen/fraction of inspired oxygen ($SatO_{2tc}/FiO_2$) ratio (mean value ± SD) in relation to administration of SF in the two groups of infants.

TIME	LMA® Group	LMA®: P vs before SF	iGel® Group	iGel®: P vs before SF
Before SF	242 ± 59		235 ± 39	
60-120 min after SF	239 ± 62	NS	349 ± 90	<0.001
6-12 hrs after SF	330 ± 105	<0.02	342 ± 104	<0.01
12-24 hrs after SF	322 ± 121	<0.05	387 ± 87	<0.001

Table 7. Partial pressure of arterial oxygen/fraction of inspired oxygen (PaO_2/FiO_2) ratio (mean value ± SD) in relation to administration of SF in the two groups of infants.

TIME	LMA® Group	LMA®: P vs before SF	iGel® Group	iGel®: P vs before SF
Before SF	155 ± 63		135 ± 79	
60-120 min after SF	196 ± 59	NS	205 ± 76	<0.02
6-12 hrs after SF	290 ± 104	<0.02	229 ± 100	<0.01
12-24 hrs after SF	236 ± 172	<0.01	265 ± 87	<0.001

improvement in oxygenation was significant already 12-24 hrs after SF administration. ($p<0.05$)

However, when the changes of $SatO_{2tc}/FiO_2$ ratio (Tab. 6) and PaO_2/FiO_2 ratio (Tab. 7), that represents the alveolar/arterial gas exchange, were analyzed in relation to the time of administration of SF we found that even if there was a more rapid significant improvement of these ratios in the iGel® Group (already after 60-120 min), however the ratios improved significantly also in the LMA® Group already after 6-12 hrs.

In any case no significant difference was found in the parameters FiO_2, PaO_2, $SatO_{2tc}/FiO_2$ ratio, PaO_2/FiO_2 ratio between the two groups of patients at any specific time interval considered.

At discharge no difference was found between the groups, both as duration of hospitalization, transfer to a third level NICU, need of a second dose of SF (given by the INSURE method) and main complications. (Tab. 8). Intubation and mechanical ventilation were needed in one baby in each group only.

Table 8. Outcome at discharge. No statistically significant difference was found.

Parameter	LMA® Group	iGel ® Group
Duration of hospitalization, days, mean±SD (only non transferred infants)	15.7 ± 9.1 (No. 13)	20.9 ± 9.0 (No. 21)
Transfer to NICU, No.	1/14	0/21
Air leak (PTX, PIE), No.	2/14	1/21
Pneumonia, No.	1/14	2/21
Intubation and MV after SF, No.	1/14	1/21
IVH, No.	0/14	1/21 (grade 1)
PDA, No.	6/14 (1* treated with 2 doses of ibuprofen)	4/21
Sepsis, No.	0/14	0/21
NEC, No.	0/14	0/21
ROP, No.	0/14	0/21
PPHN, No.	0/14	0/21
Mortality, No.	0/14	0/21
Need of a 2nd dose of SF, No.	0/14	2/21

Hemodynamically significant

Legend: NICU = neonatal intensive care unit; PTX = pneumothorax; PIE = pulmonary interstitial emphysema; MV = mechanical ventilation; IVH = intra-ventricular hemorrhage; PDA = patent ductus arteriosus; NEC = necrotizing enterocolitis; ROP = retinopathy of prematurity; PPHN = persistent pulmonary hypertension of the neonate.

Discussion

Few studies exist on the use of SGDs for delivering SF in infants for treatment of NRDS. One first proposal of using such a technique came from H. Verder using LMA® (Verder H. Personal communication, 1997, Holbaek) in a time when intubation was the only accepted method to deliver SF, given the relative failure of administering a substitutive surfactant via nebulization (18,19). However he abandoned it for limits due to the measure of the mask that is not affordable in babies <1500 gr and a relative difficulty in its positioning that, in those years, had to be done with a maneuver requiring to insert the mask with the open part looking at the palate, then rotating it in the mouth till to the final positioning, followed by the all around cuff insufflation to avoid leaks around the tongue and the esophagus. Verder et al. then developed the INSURE technique that could be applied in the smallest babies, and published a paper that was a milestone in the history of SF treatment in the neonates with NRDS because demonstrated the possibility of treating NRDS with n-CPAP after INSURE avoiding mechanical ventilation in a significant number of infants (6).

From those years on, the LMA® was used more and more, especially by the Anesthesiologists in the operating theater, and new generations of SGDs were produced. In particular the iGel® was one whose main qualities were the ease of introduction, the pointlessness of an inflated cuff to avoid leaks saving time during the positioning maneuver, and a widened, flattened stem to reduce axial rotation and mal-positioning.

In 2005 Trevisanuto et al. published a paper in which they could observe that poractant-α administered via LMA® was effective in improving oxygenation in 3 cases of NRDS (9).

Parmigiani et al. published 8 cases of infants given poractant-α for NRDS via LMA® showing an increase of oxygenation within 30 minutes after administration and an improvement of PaO_2/FiO_2 ratio >120% (10) whose impressive results were further on improved in

other 5 cases simply introducing the chest rotation at instillation of SF (10).

A randomized controlled study on delivery of SF (calfactant) via LMA® vs INSURE in moderate NRDS in infants 28-36 wks'gestation, b.w. ≥1,250 gr, age ≤36 hrs, requiring FiO_2 0.3-0.4 and n-CPAP showed decrease of FiO_2, significant reduction of endotracheal intubation and mechanical ventilation in the babies given SF via LMA®, without serious adverse effects during the maneuver with SGD (11).

Similar results were obtained in another randomized study of delivery of SF with LMA® vs INSURE in infants with NRDS and FiO_2 0.3-0.6 requiring n-CPAP (12).

Another randomized controlled study evaluated if there was any difference between babies ≥2,000 gr with NRDS on n-CPAP given SF via iGel® or INSURE. The study concluded that the administration of SF (Survanta®) via iGel® was significantly more successful in oxygen improvement than the INSURE method (13).

In the present retrospective study LMA® was used from 2009 to June 2015. The iGel® SGD was preferred from 2013 to 2018 due to its simpler use. Even if in anesthesia and in comparison with a modified LMA® mask (LMA-P®), a systematic review and meta-analysis confirm that iGel® can be correctly inserted in a shorter time and complications during insertion are reduced vs LMA-P® (21). In the present retrospective clinical study we have compared data on oxygenation and outcome at discharge using the above cited SGDs to deliver SF in two groups of babies with NRDS that did not differ in their main clinical characteristics.

What is peculiar is that we report data from the clinical use of two types of SGD used to deliver SF (poractant-α) in No.35 infants with NRDS that are not necessarily premature, whose mean g.a. was 34.4 wks and that were delivered in a second level Neonatology Unit. Only one of them was transferred to NICU while the others thirty-four could be nourished with their mother's milk and could be cared by their parent's hands. In economical terms it was a great sparing of money both for the NHS, that had not to pay for NICU's cares, and the parents that had not to move to another city to take care of their baby nor stopping work.

In particular our study showed that in two groups of patients with NRDS, b.w. ≥ 1,500 gr and g.a. ≥ 30 wks, similar for clinical characteristics (only the iGel®group presented lower 5 min Apgar's score and needed more frequently resuscitation maneuvers at birth) the administration of SF via SGD caused a significant reduction of FiO_2 already at 60-120 after administration and for all the period of observation in the iGel® Group vs the LMA® Group.

PaO_2 was improved too, but given the attention to keep PaO_2 within limit values of safety and efficacy also before SF, it increased slowly in both groups, giving the impression that the improvement of gas exchange was rapid but less traumatic using a SGD to deliver SF, avoiding dangerous peaks of hyperoxygenation that are often seen when SF is given by endotracheal tube.

The PaO_2/FiO_2 ratio improved significantly earlier in the iGel® Group, 60-120 min after SF, vs the LMA® Group, where a significant improvement was recorded 6-12 hrs after SF. A similar trend was shown using the simpler index $SatO_{2tc}/FiO_2$. These results are index of the efficacy of the treatment. The earlier improvement with iGel® needs to be confirmed by a controlled randomized trial.

None of the babies died. No significant difference was found in the incidence of complications nor in the time of hospitalization.

The iGel® was used more frequently than the LMA® for at least two reasons: 1) a curve of learning with LMA® had been done when iGel® was marketed, and the INSURE technique almost abandoned in favor of SGD delivering of SF; 2) the use of iGel® is certainly more intuitive and rapid, and as the present study has shown, without producing negative side effects when compared with LMA®.

Administered SF was given to lung and was not found in the stomach after the procedure in both groups. This indirectly means that positioning of the SGDs was correct. A suggested improvement of the technique is to use a carbon dioxide detector, even a simple colorimetric detector, connected to the stem of the SGD to evaluate the correct positioning of the SGD before instilling SF (21). To avoid insertion of

an oro-gastric feeding tube after the maneuver thanks to the capnometer together with the use of continuous monitoring of $SatO_{2tc}/FiO_2$ ratio instead of invasive and single point in time PaO_2/FiO_2 ratio will further reduce the non-invasiveness of the method.

Apart from the better oxygenation recorded after SF in the iGel®Group data did not show statistically significant differences between the two methods at the specific time intervals taken into account for analysis. Such finding can be due to the sample size and/or to the fact that the use of iGel® followed in time that of LMA®, after a learning curve with the last SGD. Both methods seem therefore effective with few if none difference, even if our experience lead to prefer iGel® in such context because more intuitive and easier to use.

Conclusions

Our retrospective study on two comparable sets of infants with NRDS given SF through a different SGD (LMA® vs iGel®) showed that in a second level Neonatology Unit SF can be administered safely and with very good results in infants ≥ 1,500 gr and ≥ 30 wks' gestation, making it possible to reduce FiO_2, avoiding both mechanical ventilation and transfer of the infant to a higher level of care, allowing him/her to stay with his/her parents, to be breastfed or anyway nourished with his/her mother's raw milk. This kind of administration of SF in a second level Neonatology Unit allows to hasten an effective treatment, to reduce the risks of transport and an useless intubation just for such purpose, to reduce the costs without increasing complications, and eventually also to increase/keep alive the skills of physicians and nurses of the second level Neonatology Unit.

With respect to the SGDs, in the babies treated with iGel® FiO_2 could be reduced significantly earlier than in those treated with LMA®, maintaining PaO_2 within safe limits. Such data needs to be confirmed in a more ample cohort and with a specifically designed study.

A consideration derived from the reported data is that also in well equipped second level Neonatology Units with skilled personnel, SF can be given with a non-invasive easy to learn method, to term or near term babies with NRDS, administering it in the early stages of the disease to avoid worsening of the disease towards more severe respiratory failure that might require a transfer to NICU.

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