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TITLE PAGE

French Neonatal Society issues recommendations on preventing nasal injuries in preterm newborn infants during non-invasive respiratory support.

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Abstract

Aim: To issue practical recommendation regarding the optimal care of nasal skin when non-invasive ventilation support is used.

Methods: We performed a systematic search of PubMed to identify relevant papers published in English or French through December 2019. Different grades of evidence were evaluated.

Results: Forty-eight eligible studies. The incidence in preterm infants was high. The lesions were more frequent for preterm infants born under 30 weeks of gestational age and/or below 1500 grams. The lesion was most often located on the skin of the nose but could also be found on the intranasal mucous membranes or elsewhere on the face. Nasal injuries appear early after the beginning of non-invasive ventilation at a mean of two to three days for cutaneous lesions and eight or nine for intranasal lesions. The most effective strategies to prevent trauma are the use of a hydrocolloid at the beginning of the support ventilation, the preferential use of a mask and the rotation of ventilation interfaces.

Conclusion: Nasal injuries with continuous positive airway pressure treatment in preterm newborns infants were frequent and can induce pain, discomfort and sequelae. Immature skin of the preterm newborn infants needs specific attention from trained caregivers and awareness by parents.

Keywords

Continuous Positive Airway Pressure; Guidelines; nasal trauma; Preterm infant; Prevention

Key notes

- The use of non-invasive respiratory support in preterm newborns infants imposes constant pressure on immature skin leading to early and frequent nasal lesions.
- The most effective nasal lesions prevention strategies are the use of a hydrocolloid at the beginning of the support ventilation, the preferential use of a mask and the rotation of ventilation interfaces.
- Guidelines for good practice are proposed and strategies to implement these guidelines.

Abbreviation

GREEN: Group of Reflection and Evaluation of the Environment of Newborns

BACKGROUND

Severe bronchopulmonary dysplasia is diagnosed in 26% of children born at less than 26 weeks of gestational age and 5% of those born between 27 and 31 weeks of gestational age.[1–3] Mechanical ventilation can lead to chronic inflammation. Therefore, the use of less aggressive ventilation to preserve the immature lungs of premature newborns infants is a daily challenge for neonatologists.[4] For several decades, the use of non-invasive ventilator support increased, particularly nasal continuous positive airway pressure. Non-invasive ventilator support has become the gold standard for respiratory support therapy in premature newborns infants.[5,6] In 2016, the European guidelines recommended reducing the duration of invasive ventilation in preterm infants, which corresponds to the current trend in neonatology units. [6] Therefore, in this very vulnerable population, the duration of non-invasive ventilation has increased and is very long.

This ventilation mode, although very protective for lung parenchyma has been associated with cutaneous lesions related to the use of an interface consistently applied on a still immature skin.[7,8] Ensuring optimal ventilation requires maintaining constant and prolonged contact on the patient's nose. However, the pressure exerted on the delicate tissues of the nostrils and nasal septum can cause internal and external nasal complications.[7,8] Nasal lesions can cause pain, discomfort, may require a change in ventilation mode, and sometimes require surgery.[9]. The main sequelae reported in the literature were hyperaemia, pressure sores, necrosis and changes in the structure of the nose like enlarged nostril, upturned nose, involvement of the tip of the nose causing asymmetry and nasal obstruction.[7–10]

The aim of this review was to evaluate skin injuries associated with the non-invasive ventilation interfaces and strategies to limit it. Our goal was also to issue practical guidelines that can optimise the care and monitoring to limit skin lesions and to propose strategies to implement these guidelines.

METHODS

The methods used were previously described by the Group of Reflection and Evaluation of the Environment of Newborns, GREEN, of the French Neonatology Society [11]. The published literature was searched using PubMed to identify papers published in English or French through December 2019. The selection of papers is presented in the flow chart (see Figure 1). We found a Review with meta-analysis on the subject [12]. After guidelines were made available on the French Neonatal Society web site in 2020, we performed an additional systematic review between December 2019 to October 2022. No additional paper compromised our guidelines. To be as exhaustive as possible on the type of lesions encountered, certain studies presenting clinical cases were retained for this question specifically.

We only briefly discuss the comparison of the different ventilation supports in terms of effectiveness and do not address the impact of the use of adhesives, which is the subject of another GREEN paper. This work focused on the use of continuous positive airway pressure which is an occlusive system distinguishing itself from high flow canulae systems. In fact, high flow canulae have smaller cannula and are not totally occlusive.[13]

We asked several specific questions. How can we characterize nasal lesions related to a ventilation interface? What are the incidence and the risk factors of these skin lesions? When does the lesion appear? What are the strategies to prevent and treat these injuries? And finally, what are the best monitoring and care procedures to prevent them?

Three successive versions of the text were written after discussion within the working group. The last version was reviewed by 13 external reviewers. External reviewers scored all sections of the text and each recommendation between zero and nine. Any score below three required a major modification of the written text and re-discussion within the group. A second review was then sent to the reviewers for validation of the changes. Each comment requesting a modification of the text should be scientifically argued and the modifications were then validated by the group. The scores of the evaluation of the external review were between four and nine on a scale from zero to nine. There were no major changes in the guidelines performed after this review.

The guidelines resulting from the analysis of the literature were classified according to the grades retained by the High Authority of Health in France (as shown in Table 1 and already described in the general methodology of the GREEN study group. [11] Grade A corresponded to establish scientific evidence. Grade B and C corresponded respectively to a scientific presumption and to low scientific evidence.

RESULTS

Characterization of nasal injury related to a ventilation interface

Three stages of severity of skin lesions were described [14]. Stage one corresponds to erythema not blanching; Stage two when the lesion is bleeding, a superficial ulcer or erosion with partial thickness skin loss; Stage three to deep lesions such as skin detachment, loss of skin substance or necrosis.

Figure 2 defines the different parts of the nose that can be damaged. Endonasal mucosal lesions have been described in the anterior nasal vestibule: ulcerations, granulations or vestibular stenoses.[15] The first sign of mucosal damage is erythema, then oedema, which can progress to thickening of the mucosa. In the more severe stage, stenosis or bleeding can be observed.

Incidence of lesions, risk factors and timing of onset of skin lesions

Eleven studies answered this question. They are summarised in Table 2. They include four observational studies focusing on premature newborns infants, including one multicentric study.[14,16–18] Three randomized controlled trials looked at a preventive method or different type of interface to compare the incidence of skin lesions.[15,19,20] Four case studies included one to seven newborns infants. [10,21–23] Isolated cases of non-nasal skin lesions were also described. A clinical case showed lesions of the cartilage of the ear secondary to an inadequate cap fixation. [24] Frontal lesions on the pressure point of cap bindings were also described. [25] Exceptional ophthalmic lesions could be linked to the use of ventilation interfaces. [26] Peribuccal lesions or eye flows could be observed in clinical practice, but no publication has recorded their incidence or determined their risk factors. Concerning cutaneous lesions after the

use of a bi-narinal cannula, only one case was reported. This lesion was not directly related to the use of this interface, but disinfection with 2.5% glutaraldehyde of a lesion on the entire cheek was incriminated after two days of treatment. [27]

In total, these studies highlighted four interesting elements.

First, these lesions have high and variable incidence, with a predominance of lesions grade one: from 20% to 100%, depending on the study with variable population, equipment, and care strategy. Among the four larger-scale studies looking at both the overall incidence and the incidence of lesions according to their severity, three were specifically interested in skin lesions related to a ventilation interface. As compared with the Swiss study [14], the two Brazilian studies [16,18] concluded a higher overall incidence, 42% versus 56% to 100%. However, the distribution according to the severity of the lesions seemed almost similar. Most lesions were Grade one, 80% in three of the four studies. Lesions of Grade three were found in less than 1% of cases in two studies and in 9% and 11% in the other two.

Second, different risk factors were identified. In fact, risk factors for lesions of Grades one and two were being born before 30 weeks of gestational age or having a birth weight below 1500 grams. [15,19,28] Moreover, the opacity of the device [19], immaturity of the skin, humidity and temperature of the incubator and the number of changes in position of the child [17] were highlighted and incriminated.

Third, we identified a delay in the appearance of nasal lesions early after the beginning of non-invasive ventilation. For superficial cutaneous lesions, the

trauma appeared at a mean of two to three days after the onset of continuous positive airway pressure treatment and even as early as 18 hours in one publication.[18] The intranasal lesions, like ulcerations, granulomas and stenoses appeared later, from eight to nine days after the onset of the treatment. [15]

Finally, the location of the lesion was described. For the nostrils, the lesion was most often on the skin, on the outside, clearly visible, but also in the interior part at the level of the nasal vestibule corresponding to the anterior part of the nasal fossae. [15] Ear lesions were also described.

Two papers were found on the evolution of these lesions. [9,10] The authors revealed three problems that are aesthetic and functional: snubbed nose, an enlargement of the nostrils and columellar necrosis/septal necrosis. [10] Nostril asymmetry, columellar asymmetry, nasal tip deviation, nasal tip projection defect, and nasal obstruction were described. [9].

Strategies to prevent and treat injuries.

Skin protection has been the main strategy described. A total of five studies evaluating the usefulness of setting up a barrier were identified. Different strategies and materials used were silicone gel, polyvinyl chloride foam, and hydrocolloids pre-cut or cut by caregivers.

In two randomized controlled studies with a total of 244 newborns infants included in the meta-analysis, [12] A hydrocolloid barrier was applied for premature newborns infants (n=65, born between 28 and 37 weeks of gestational age [29] and silicone gel for small-for-gestational-age newborns infants (n=179, birth weight < 1,500 g [30]). The result was a risk difference of -0.12 (95% CI -

0.20; -0.04) in favour of application of a skin barrier (n=6/125) as compared with the absence of protection (n=20/119).

A third clinical trial confirmed this result. Indeed, 56% of premature newborns infants (n=31/55) presented a skin lesion without protection as compared with 34% (n=18/53) when benefitting from hydrocolloid protection, $p = 0.02$. [31] Thus, the three randomized controlled studies showed a benefit in favour of application of a skin protection when using a continuous positive airway pressure on the incidence of lesions and their severity. This was not found for the use of hydrocolloids in infants less than 1,500 grams during the use of high-flow canulae, perhaps due to the low incidence of skin lesions in the study population (n = 26 in the control group; n = 27 in the protection group). [32]

In addition, two other studies concern this subject with a lower level of evidence because of a non-randomized for the first and including continuous positive airway pressure and high flow canulae for the second. The first was a retrospective study focusing on polyvinyl chloride patch use in 101 preterm newborns infants. The reduction in nasal trauma was 24% to 6%, $p = 0.01$. [33] In 132 very preterm neonates infants with non-invasive respiratory high-flow canulae or continuous positive airway pressure, no difference were seen between hydrocolloids on the nose and up to the upper lip and “Velcro-coated”, hydrocolloid covering the upper lip. [13]

The benefit of hydrocolloids is also supported by a randomized trial including 33 newborns infants with a mean of 32 weeks of gestational age. The effectiveness of hydrocolloids was compared and found superior to that of a silicone gel screen applied in a thick or thin layer. [34]

The use of high flow canulae has been also promoted to prevent nasal lesion. In certain conditions, high flow canulae can be used as an alternative to continuous positive airway pressure. Indeed, a Cochrane review from 2016 including 15 randomized studies compared high-flow canulae to continuous positive airway pressure devices. [35] It found that high flow canulae are similarly effective to other forms of non-invasive ventilation in preterm infants in preventing treatment failure and death and preventing bronchopulmonary dysplasia. Most studies focused on the evaluation of high flow canulae as post-extubation ventilatory support. Further adequately powered randomized controlled trials should be undertaken in preterm infants to compare high flow canulae with other forms of non-invasive ventilatory support after birth and for weaning infants from non-invasive support. Further evidence is also needed to assess the safety and effectiveness of high-flow canulae in extremely preterm and mildly preterm subgroups and to compare different high-flow canulae devices. Two studies have since been published. The first in 2017 did not show any difference on the main endpoint, which was reintubation in a group of 49 children born less than 32 weeks of gestational age. [36] A second showed the inferiority of high flow canulae in a larger cohort of 272 children over 28 weeks of gestational age and over 1,000 grams. In this study, this ventilation mode was applied at birth and the judgment criterion was the need for more aggressive ventilation in the first 72 hours. [37] Seven randomised controlled studies [38–44] comparing continuous positive airway pressure and high-flow canulae reported nasal lesions as secondary outcomes during the use of these two types of respiratory support. The authors found a significant reduction in nasal lesions during the use of high-flow

canulae (n=768) -0.14 (95% CI -0.17 to -0.1) as compared with continuous positive airway pressure (n=802) in Imbulana and colleagues. [12]

Two meta-analyses compared the skin tolerance of the mask to that of prongs: Jasani and colleagues [45] and Imbulana and colleagues, which included 5 papers.[28,46–49] The results showed a reduction in nasal skin lesions, regardless of severity, during mask use. The relative risk was at the limit of significance: 0.80 (95% CI 0.64-1.00). In three randomized control trials, the use of the mask was associated with reduced risk of a moderate to severe nasal lesion: relative risk 0.41 (95% CI 0.24 to 0.72). [32,50,51]

Two studies have been performed since these meta-analyses. In a first one, 75 newborns infants were included: 38 in the mask group, 37 in the prongs group. The study found no difference between skin trauma in the groups, but the duration of treatment was shorter and gestational age higher in the prongs than mask group: 34.4 versus 32.6 weeks of gestational age.[50] In a second study, carried out in India, 175 newborns infants under 30 weeks of gestational age were randomized to three groups: mask, nasal prongs, and rotation of the device twice. The mask group had a significantly lower incidence of nasal lesions than the prongs group, 56.9% vs 91.6%, $p < 0.01$, with less severe lesions, $p < 0.01$ but with identical efficacy. [51]

A meta-analysis [52] looked at both the efficacy and incidence of skin lesions according to the interface, mask *versus* prongs in seven studies.[8,28,46–49,51] This systematic review recommended the preferential use of the mask on the efficacy of the interface and incidence of skin lesions. The authors found a lower incidence of skin lesions in the mask group; relative risk 0.71 [95% CI

0.59 to 0.85] in six studies, n= 665. Since then, a randomized controlled study has been published with the main objective of evaluating the failure of non-invasive ventilation after the placement of a mask (n=90) or prongs (n=88) from the delivery room, for newborn infants born at 26 to 32 weeks of gestational age. This study found less non-invasive ventilation failure (primary objective) and reduced number of nasal trauma cases (secondary objective) in the mask than prongs group: 14 (15.9%) versus 38 (43.2%) nasal injuries; relative risk 0.26 (95% CI 0.12 to 0.52), p=0.0002.[53]

Some studies suggest that a systematic change between two nasal interfaces can reduce pressure points. Thus, among 78 children randomized into three groups according to the continuous positive airway pressure interface used (prongs, n = 21 / mask, n = 35 / rotation every 4 hr, n = 22), the rotation group showed less rate of nasal trauma (erythema p <0.001 and erosion p = 0.007). [8] The pressure points are indeed different between these two types of devices. The mask produces lesions mainly at the level of the nasal dorsum, the prongs at the level of the columella. However, a recent randomized controlled study of 175 newborns infants showed that the mask group had a significantly lower incidence of nasal trauma than the prongs and rotation groups (33.3% vs 91.6% and 56.9%, p < 0.001), and less severe lesions (p< 0.01), with identical efficacy.[51]

However, this strategy remains superior to the use of prongs alone in terms of the incidence of lesions and their severity. The Fischer study alternated prongs and masks every four to six hours.[14] For Xie, the alternation was every six hours when there was a nasal lesion. There is no specific recommendation in the literature; this alternation is often left to the discretion of the caregiver.[29]

Different ointments have been used to prevent or treat nasal injuries. We found the use of epithelial growth spray, hirudoid cream (mucopolysaccharide polysulphate [Heparinoidum MPS]), dexpanthenol (Bepanthène®), lanolin and an anti-infective, mupirocin (Bactroban®).[29,48] Paraffin oil has also been reported for reducing friction between the material and the skin or mucosa before the start of ventilatory support.[29] Scientific evaluation of these strategies is lacking.

Warming and humidification of gases in mechanical ventilation are essential to preserve airway integrity. This is always necessary during invasive and non-invasive ventilation. The use of humidified and warmed air is accompanied by a decrease in nasal mucosal lesions [54,55], improves efficiency by reducing airway resistance and improves the efficiency of the mucociliary layer.[56] The type of humidifier does not seem to be decisive.[57]

Monitoring and care procedure

In the literature, only one paper is aimed at caregivers concerning the implementation and monitoring of nasal continuous positive airway pressure [58]. In addition to the questions of effectiveness, several questions that the caregiver should ask themselves are Is the placement of the continuous positive airway pressure appropriate at the level of the forehead (symmetrical)? Is the size suitable (use of help provided by the manufacturer)? Is it the mask or prongs? Has there been an alternation of the interface? Has the skin color changed at the pressure point? Are the ties not too tight or too loose? Is there pressure from the

mask that could obstruct the nostrils? There is no other paper on strategies of monitoring skin lesions in non-invasive ventilation.

GUIDELINES

In view of the analysis of the literature, several guidelines have been developed.

The grade level as described in Table 1 was added.

The incidence of mucocutaneous lesions related to ventilatory interfaces is high in the newborn population (Level 1). It is higher with birth before 30 weeks of gestational age or birth weight under 1,500 g (Level 3), with immaturity of the skin according to the index of Dubowitz (Level 3), with poor mobility in the newborn (Level 3) and in the first days of ventilation use (Level 3). The time to appearance of skin lesions is two to three days, on average, after the onset of continuous positive airway pressure treatment, even as early as 18 hours (Level 3); intranasal lesions can appear from day eight to nine (Level 3).

Any neonate with a non-invasive ventilation device should receive a screening for mucocutaneous lesions (Grade A). Particular vigilance to the integrity of skin must be provided in particular situations such as immaturity and reduced mobility (Grade C). The skin lesions are mainly located at the nasal localisation, but one should not ignore the other possible sites (Level 4). The integrity of all the other support areas of the interface should be checked (Expert advice).

The clamping tension should be adjusted to achieve maximum efficiency without involving excessive skin stress. This must be checked regularly (Expert advice).

The use of opaque devices increases the incidence of lesions (Level 2). Their use is not recommended (Grade B).

Use of hydrocolloid protection from the beginning of treatment reduces the incidence of mucocutaneous lesions with continuous positive airway pressure

in newborns infants born before 32 weeks of gestational age (Level 1). Its use is recommended in this context (Grade A). The use of a hydrocolloid should not prevent continued monitoring of the underlying skin (Expert advice).

There is no scientific argument validating the use of ointments such as skin protection ointments (Level 4). Their use is not recommended (Expert advice).

Alternating interfaces is less traumatic for the skin than using only prongs (Level 1). When using prongs, the rotation of interfaces is recommended rather than the use of only prongs (Grade A).

The use of the mask compared to prongs reduces the incidence of skin lesions and their severity in preterm infants (Level 1). Preferential use of the mask is recommended (Grade A) for preventing skin lesions.

In case of nasal trauma, high-flow cannula can be considered as an alternative (Level 1, Grade A).

Administration of warmed and humidified air decreases nasal mucosal damage (Level 3). Humidifying and warming the air is recommended (Grade C).

STRATEGIES TO IMPLEMENT THE GUIDELINES

The different strategies for applying these guidelines are as follows.

At the institutional level, professionals should be involved in the choice of ventilation interfaces during the institutional selection process; the skin tolerance criteria should be an important part of the choice.

At the healthcare team level, the strategy should focus on improving the quality of care. First, this should rely on the information and training given to caregivers on the ventilation mode and its usefulness in relation to respiratory physiology, the identification of situations at risk of skin lesions and the nursing procedures to display good practices, as well as the sensitization of parents to the risk of occurrence of skin lesions and information on the signs of well-being or discomfort in the child. Moreover, implementing strategies for systematic nursing documentation of skin and skin lesions appears important to improve the quality of care.

At the individual level, good practices should be established, which could include the following points. Health care practitioners should identify and trace skin and mucosal integrity. The adhesion and position of skin protection and tightening should be verified. The size of the interface should be adapted regarding the by manufacturing size guides. The good positioning of the interface should be verified. The integrity of the other support areas of the interface (absence of pressure, accuracy of tightening, absence of plication of the ears) should be done.

This monitoring is important for all newborns infants, especially those with gestational age under 30 weeks and those weighting less than 1,500 g,

during the first days of ventilation, and those with signs of unexplained discomfort or pain.

If a lesion appears, it should be noted on a specific monitoring document allowing the monitoring of the gradation and severity of the lesion. In practice, a hydrocolloid-type skin protection can be applied as soon as the onset of non-invasive ventilation, with adequate size, and allowing relief of pressure zones of the various existing interfaces while preserving the passage of air through the nostrils. If a mask is used, the hydrocolloid must be applied to the root of the nose and the philtrum. With the use of prongs, the protection must be applied in the shape of an “8” to cover the columella and the lower part of the wings of the nose while leaving the nostril orifices free. This must be balanced against the problem of the use of adhesive on the skin.

The interface mask should be favoured for the beginning of the non-invasive ventilation. The size must be chosen with the help of charts provided by manufacturers. In case of warning signs, a possible change of ventilation interface should be discussed with careful alternating between prongs and mask to vary the pressure points. The implementation of an interface ventilation that does not apply a pressure point at the level of the lesion is desirable for the following hours. Possibly, a change of ventilatory support such as the use of another ventilation interface of high-flow canulae type less prone to nasal lesions could be discussed according to the clinician's judgment. The water heater should be set to 31-33°, with physiological temperature at the level of the oropharynx. A higher temperature can lead to excessive humidification and relative flooding of the pipes.

CLINICAL AND RESEARCH PERSPECTIVES

Partnerships with manufacturers to develop pre-cut means of protection could be beneficial for all. The optimal duration and localisation of hydrocolloids in terms of the type of interface used and the benefit of using a mask with different sizes are unresolved for the moment. Little is known about the long-term sequelae of these lesions and more specifically those that should benefit from subsequent monitoring. Despite some unresolved points, this study has real clinical interest and provides guidance to caregivers.

STRENGTHS AND LIMITATIONS

The literature review was exhaustive. The guidelines were discussed in view of the literature and graded according to the quality of the studies. These guidelines were discussed within the group but were also reviewed by outside experts. The guidelines were validated in January 2020. Other papers have been published since then. Their results are in line with previous studies and are in accordance with our guidelines. [53,59–64] Nevertheless, certain clinical problems must be studied specifically to be able to better handle them.

CONCLUSION

Skin lesions related to ventilation interfaces are frequent, particularly in the population of the most immature infants and those with the lowest birth weight.

The nursing team must be attentive to these lesions that need particular and specific attention from trained caregivers. Parents more aware of this problem could provide help. The use of a hydrocolloid, the preferential use of a mask and alternating ventilation interfaces seem to be the most effective preventive strategies. The exact modalities of the application of these strategies remain to be defined.

Conflict of interest

None

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APPENDIX 1 Group for Reflection and Evaluation of the Environment of Newborns of the French Society of Neonatology

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TABLE

TABLE 1: Level of scientific evidence and grading of the guidelines.

Level of scientific evidence and type of study	Grade of recommendation
Level 1 <ul style="list-style-type: none">- High-powered randomized controlled trial- Meta-analysis of randomized controlled trials	A: Established scientific evidence
Level 2 <ul style="list-style-type: none">- Low-powered randomized comparative studies- Well-conceived non-randomized comparative studies- Cohort studies	B: Scientific presumption
Level 3 <ul style="list-style-type: none">- Case control studies	C: Low scientific evidence
Level 4 <ul style="list-style-type: none">- Comparative studies with major biases- Retrospective studies and case series- Descriptive epidemiological studies	

Table 2: Studies of the incidence of lesions, presence of risk factors and time of appearance of skin and mucous membrane injuries

Authors	Type of study	Population	Country	Practice care	Results
Fischer et al., 2010a	Prospective observational	N= 989 Mean 34 weeks of GA	Switzerland	Rotation mask and prongs every 4/6 hr with rubbing of point of pressure If it is a trauma: rubbing and dexpanthenolum If it persists: barrier with hydrocolloid Skin monitoring every 30-60 min, ventilation interface taken off every 2-4 hr	420 nasal injuries (42.5%). More frequent the 6 first days (90%) Stage 1: 88.3%, Stage 2: 11%; Stage 3: 0.7% Increase with the small GA and the duration of CPAP requirement 90% if newborns were < 28 weeks of GA, 77% at 32 weeks of GA, 28% > 32 weeks of GA and 11% term newborns Risk factors: <32 weeks of GA: OR 2.48; birth weight < 1500 g, OR 2.28; > 5 days of treatment OR 5.36; > 14 days hospitalised in NICU OR 1.67
Do Nascimento et al., 2009	Descriptive observational	N= 147 NN (< 37 SA, n=123)	Brazil	Reusable prongs Skin protection in 96% with "home made" protection (no hydrocolloids)	100% nasal injuries after 2 days of use. Stage 1: 79.6%; stage 2: 19.7%; stage 3: 0.7% Risks factors: 80.3% of the newborns have a ventilation support with unsuitable size (too small)
Fujii et al., 2010	Multicentre Prospective	N= 81 NN Mean 32.5 weeks of GA	Japan	The practices are not detailed (center dependant?)	Study on ulcerations on the whole body. 13 children presented an ulceration. Mainly on the nose. 6/13 had CPAP ventilation support Mainly related to skin maturity (Dubowitz score) and use of the tracheal tube
Ota et al., 2013	Prospective observational	N= 18 <37 weeks of GA <29 days of life <1500 grams	Brazil	Preventive hydrocolloids Choice of tips according to size (3 choices)	Epidemiological study during the first 3 days of treatment, collection of the data 3 times a day Lesions in 12 newborns Skin lesions visible around 18 hr after the start of use Stage 1: 82%; stage 2: 9%; stage 3: 9%

Bonfim et al., 2014	RCT	N= 70 NN < 37 SA	Brazil	Hydrocolloids applied preventively in both groups	56% to 72% nasal injuries depending on the material (n=39 sterilisable material and n= 31 new material) Stage 1: 52%; stage 2: 36%; stage 3: 11% Risk factor for a lesion: duration of treatment Risk factors for the severity of the lesion: small gestational age and duration of treatment No difference in term in material used
Rego and Martinez, 2002	RCT	N= 99 NN, Birth weight <_2500 grams	Brazil	Randomisation: Argyl et Hudson prongs	71 newborns need CPAP support More injuries with Argyle because it is opaque (p = 0.03)
Jatana et al., 2010		N = 200 infants < 1 year ≥ 7 days of non-invasive ventilation support	USA	CPAP and high-flow canula	13% nasal complications in the CPAP group 5% Intranasal complications (ulcerations / granulomas / vestibular stenosis) in the CPAP group occurs from day 8-9 of treatment No skin complications in the other group
Robertson et al., 1996a	Case report	N= 7 NN < 1500 grams	UK		Incidence of nasal lesions: 20% in those weighing less than 1500 g, mainly in the first 3 days of treatment
Ottinger et al., 2016	Case report	N=1 23 weeks of GA, 530 grams	USA		Development of deep ulceration in the columella and septum
Shanmugananda and Rawal, 2007	Case report	N=1 Very preterm infants	UK		Laceration of the ala of the nose after 1 week of treatment
Carlisle et al., 2010	Case report	N= 1 < 26 weeks of gestational age Birth weight: 575 g	Australia		Severe lesion: alternative modification of a tracheal tube

FIGURE LEGENDS

Figure 1: Flow chart of study selection

Figure 2: Part of the nose that can be damaged

A, B, C, D : Wings

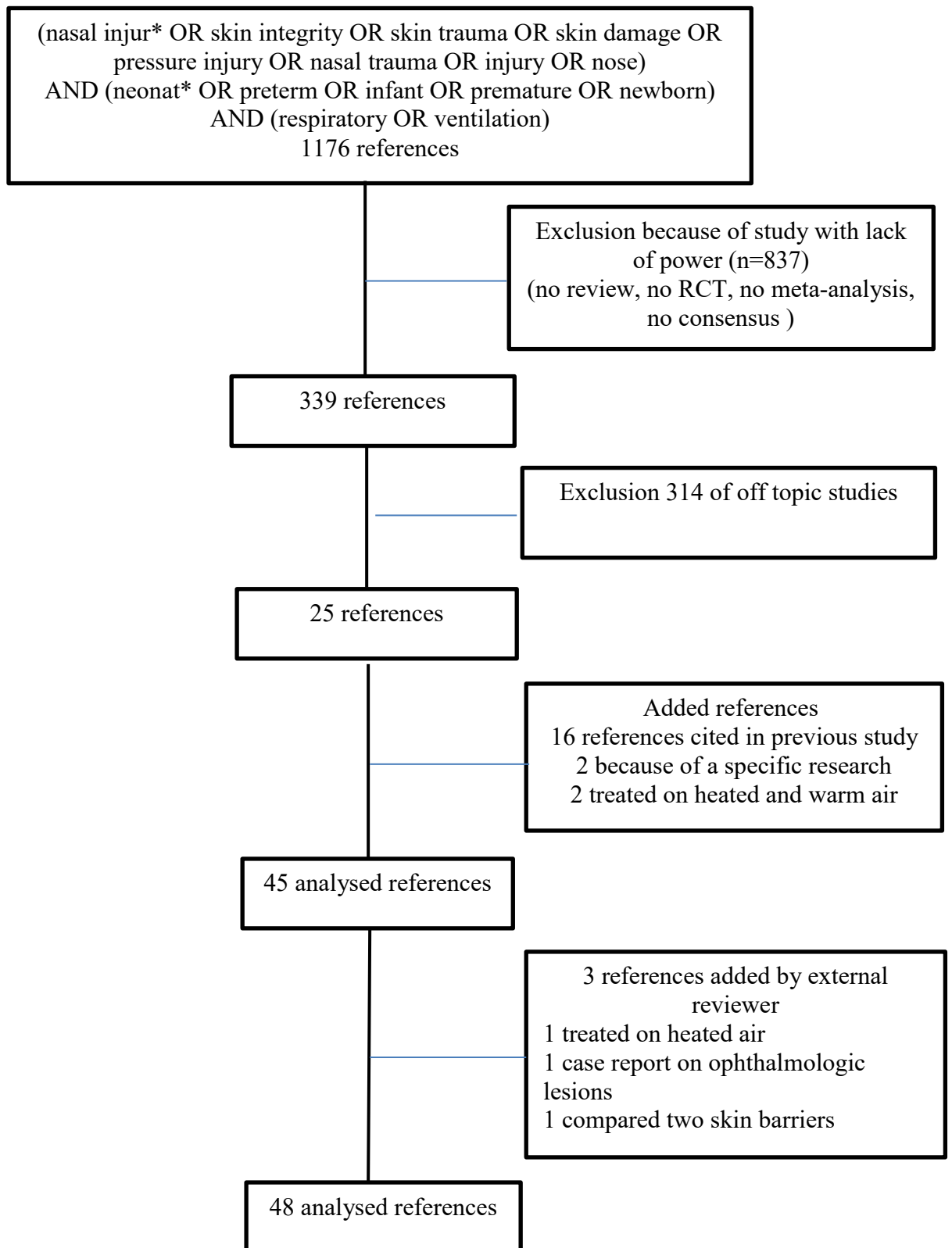
E : Philtrum

F : Columella

G : Dorsum cartilaginum

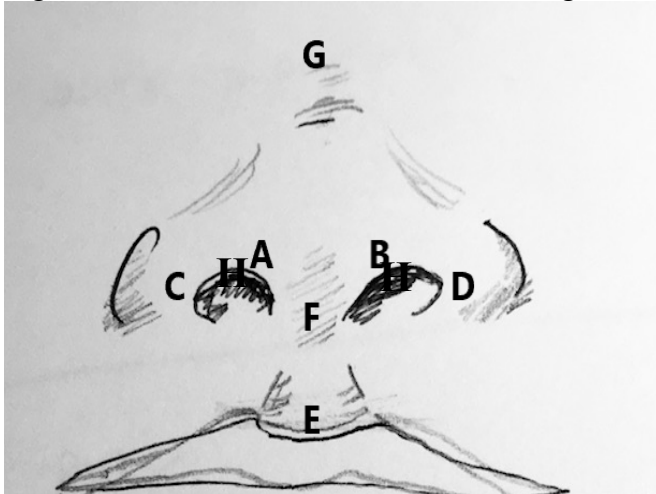
H : Anterior nasal cavities

Figure 1 : Flow chart of study selection



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Figure 2 : Part of the nose that can be damaged



A, B, C, D : Wings

E : Philtrum

F : Columella

G : Dorsum cartilaginum

H : Anterior nasal cavities