

## Question report: June 23rd , 2020

### **1. Can we generate adequate PIP with mouth open in NIPPV?**

Mouth open during NIPPV may decrease the delivered PIP. Owen and co-workers investigated and quantified delivered peak pressures during non-synchronised ventilator-generated NIPPV. They found that during NIPPV delivered PIP was variable and frequently lower than set PIP. (*Owen LS, Arch Dis Child Fetal Neonatal Ed. 2010 Sep;95(5):F359-64*).

**See also the answer to questions 8 and 25.**

### **2. Si no tengo sincronizada, seria mejor usar entonces CPAP en lugar de no sincronizada?**

Recent meta-analyses of studies where NIPPV (synchronized or not) has been used as an alternative to NCPAP after birth (as primary mode) or after extubation (as secondary mode) show that it reduces both the need for intubation and the extubation failure (*Lemyre B. Cochrane Database Syst Rev. 2016 Dec 15 and Lemyre B. Cochrane Database Syst Rev. 2017*). So, the answer to your question is NO, because non-synchronized NIPPV offers some clinical advantages over CPAP.

### **3. The nHFOV does not induce glottal constrictor muscle. This may be an additional advantage of nHFOV relative to NIPPV?**

Even if this could be an advantage, clinical trials with NHFOV have been inconclusive to date (*Sweet DG, Neonatology 2019*) and side effects as increased oxygen requirements and higher heart rates have been also reported (*Ruegger CM, J Pediatr 2018*). However, a recent meta-analysis concluded that this approach may significantly remove carbon dioxide and reduce the risk of intubation compared with NCPAP/BiPAP, but further evidence is required. (*Jing Li, Respir Res 2019*).

### **4. Which sizes of NAVA canula are available? And how can the position be verified?**

Do you mean sizes of NAVA Edi catheters? Literature data show that they can be used in infants as preterm as 26 weeks and with a BW even <750 g. Correct position is verified following the instruction of the manufacturer: initial placement is determined by standard N/G nose-ear-xiphoid distance minus 4 cm. The catheter is then advanced and correct placement confirmed by ECG patterns seen on the Servo-n Maquet ventilator - NAVA Edi catheter positioning screen.

### **5. Are there problems of high resistance with double-loop cannula due to the length and the diameter?**

The approach with double-inspiratory loop cannula has several advantages over short binasal prongs, including reduced incidence of nasal trauma, increased infant comfort, improved mother and child bonding, and high popularity among parents and nursing staff. However, one of the main problems with this device is its higher intrinsic resistance. In this device the highest resistance is at the level of the two nasal prongs, as in short binasal prongs, however its resistance increases in proportion to the length and diameter of the two long connecting tubes. For an effective clinical use of the double-inspiratory loop cannulas choose the ones with the lowest resistance.

**See also the answer to questions 8, 25 and 32.**

### **6. Are there differences in pneumothorax rates when nasal CPAP is compared to synchronised IPPV?**

Recent meta-analyses of studies where NIPPV (synchronized or not) has been used as an alternative to NCPAP after birth (as primary mode) or after extubation (as secondary mode) show no difference in the incidence of pneumothorax between infants randomized to NIPPV and those randomized to NCPAP. (*Lemyre B. Cochrane Database Syst Rev. 2016 Dec 15 and Lemyre B. Cochrane Database Syst Rev. 2017*). Contrariwise, a more recent meta-analysis seems to indicate that when compared to NCPAP, SNIPPV results in lesser incidences of air leak (*Ramaswamy, Ped Pulmonol 2020*)

### **7. What's the safe PEEP that can be achieved?**

2019 European guidelines indicate that pressures conveyed to the nasopharynx are typically kept between 5 and 9 cmH<sub>2</sub>O providing several theoretical benefits including splinting the upper airway, maintaining lung expansion and preventing end-expiratory alveolar collapse. Higher pressures may improve oxygenation but potentially increase risk of air leak (*Sweet, Neonatology 2019;115:432–450*).

### **8. Is a chin strap necessary to reduce leakage for a more effective ventilation via NIPPV?**

A chin strap applied during NIPPV performed by short binasal prongs connected to a standard circuit probably has the main effect of increasing the MAP. I suppose there are no data demonstrating the real efficacy of this (uncomfortable and difficult to apply for a long time) solution in order to improve ventilation. A pacifier may be useful to reduce the leaks from the mouth but this solution must be assessed from case to case. By contrast, using double-inspiratory loop cannulas connected to a standard circuit, we have to consider that the main characteristic of this device is that both the long tubes between the Y-piece and the nasal prongs only conduct inspiratory flow. For this reason, is absolutely not advisable to seal the baby's mouth completely because during NIPPV the expiratory tidal volume leaves the airways mostly through the mouth and a sealed mouth may cause rebreathing and increase of WOB.

Remember that using double-inspiratory loop cannulas connected to a standard circuit, the prongs must fit well because PIP and PEEP levels are controlled by the pressure valves of the ventilator. This differs from HHHFNC, during which double-inspiratory loop cannulas are recommended for use with 50–60% occlusion of the nares, as the bulk of exhaled gas must travel through the non-occluded nostrils.

With synchronized NIPPV, when a ventilator cycle is triggered, there is a negative pressure in the upper airways of the patient produced by his spontaneous inspiratory effort and the problem of the leaks is minimized. In any case, also in this circumstance the use of a pacifier can be considered.

### **9. How to reconcile the presentation with results from US centres like Columbia in NYC claiming excellent outcomes with just CPAP? Maybe experience or technique?**

Despite early NCPAP and early selective surfactant many neonates develop respiratory failure and need invasive mechanical ventilation. NCPAP failure is associated with increased risk of adverse outcomes and prolonged hospitalization. Recent meta-analyses of studies where NIPPV has been used as an alternative to NCPAP after birth (primary mode) or after extubation (secondary mode) show that it reduces both need for intubation and extubation failure (*Lemyre B. Cochrane Database Syst Rev. 2016 Dec 15 and Lemyre B. Cochrane Database Syst Rev. 2017*). The proven greater clinical efficacy of NIPPV over CPAP is probably due to the higher MAP. Synchronized NIPPV is also more effective than non-synchronized NIPPV due to his physiological positive effects: it reduces WOB, respiratory rate, thoraco-abdominal asynchrony, the incidence of desaturation and bradycardias, and improves ventilation.

### **10. When you're applying flow-synchronized NIPPV to preterm infants, how do you adjust the flow rate?**

I usually adjust the flow rate in order to obtain the desired PIP using a sinusoidal/square pressure waveform.

### **11. What clinical factors influence on ventilator setting? It seems that it's more difficult to control the setting compared to pressure-based sNIPPV**

Ventilator parameters during NIPPV synchronized or not (i.e. PIP/PEEP - Ti/Te - Rate, FiO<sub>2</sub>, etc) are similar and depend on severity of RDS. During flow-synchronized NIPPV, performed by Giulia ventilator, the trigger level should be optimized in order to let the ventilator detect all infant's spontaneous breaths while avoiding autotriggering. We suggest to start with a trigger level of 0.1 in preterm infants and of 0.2 in term or near-term infants.

### **12. Do you encounter the same level of abdominal distension with synchronized NIPPV vs non-synchronized?**

With SNIPPV this problem is reduced because with synchronization positive pressure is delivered when the glottis is opening and is transmitted effectively to the lungs.

**13. What kind of flow sensor is suitable for SNIPPV?**

As far as we know, the only flow-sensor currently tested on preterm infants for SNIPPV is the Giulia fixed-orifice pneumotach, a very simple differential pressure transducer.

**14. Un parere sulla ventilazione non invasiva in modalità DUOPAP (bipap)?**

Although popular, there is no evidence that BiPAP confers any advantage over NCPAP (*Sweet DG Neonatology 2019*) and any clinical differences may simply reflect a higher overall mean airway pressure (MAP).

**15. Any benefit of NHFOV over SNIPPV**

Clinical trials with NHFOV have been inconclusive until to date (*Sweet DG Neonatology 2019*) and side effects as increased oxygen requirements and higher heart rates were also reported (*Ruegger CM, J Pediatr 2018*), but a recent meta-analysis concluded that this approach significantly removes carbon dioxide and reduce the risk of intubation compared with NCPAP/BiPAP, but further evidence is required (*Jing Li, Respir Res 2019*).

**16. E' possibile e proficuo utilizzare la NSIPPV nella MAS?**

Currently no clinical data are available on this topic.

**17. What should be the length of nasal cannula for NIPPV, is it single or double prongs?**

Short binasal prongs are more suitable for NIPPV because they are less resistive than the single nasopharyngeal prong, the long nasal prongs and the RAM cannulas. Moreover, by occluding both nostrils, binasal prongs may increase the pressure delivered to the lungs comparing with the single prong.

**18. Any Standardised interfaces available commercially...for nSIPPV**

We tested our flow-synchronized NIPPV only with Giulia manufacturer's Short Binasal Prongs or double-inspiratory loop cannula.

**19. How much resp.rate prefer for NIPPV?**

In non-synchronized NIPPV we use to start with a RR of 40 bpm, then adjust up to 60 bpm if needed or decrease to 20-30 bpm if the infant is doing well. During SNIPPV we prefer the A/C mode (i.e. the ventilator assist each spontaneous breath) setting a back-up rate of 40 bpm. We wean infants from SNIPPV mostly by progressively decreasing PIP rather than decreasing the number of supported breaths (SIMV).

**20. How do you synchronize the mode NIPPV in your hospital?**

We use the Giulia flow-sensor.

**21. After LISA, which mode of ventilation is better: NIPPV or Flow synchronised NIPPV.**

An in vivo model of RDS performed with surfactant depleted adult rabbits demonstrated that SNIPPV applied immediately after surfactant instillation may maximize the effects of surfactant therapy compared to other NIV modalities (NCPAP, NIPPV). Synchronization probably helps spreading of surfactant with a better pulmonary distribution and efficacy and it is also associated with significantly better histological outcomes and lowest injury scores (*Ricci F. PLOS ONE, July 12, 2018*).

**22. In an 800gmer infant, what is safe and maximum PIP when on NIPPV?**

In these tiny infants we use a maximum PIP of 25 cmH<sub>2</sub>O.

**23. Can you comment on incidence of spontaneous intestinal perforation and NEC in NIPPV vs CPAP?**

Recent meta-analyses of studies where NIPPV (synchronized or not) has been used as an alternative to NCPAP after birth (as primary mode) or after extubation (as secondary mode) showed no significant differences between groups in the incidence of gastrointestinal perforation and NEC. (*Lemyre B. Cochrane Database Syst Rev. 2016 Dec 15 and Lemyre B. Cochrane Database Syst Rev. 2017*).

**24. Have you any experience with Benveniste-Ventile using in the delivery room.**

No experience, sorry.

**25. I wish to ask that can we close neonatal mouth to increase the effectiveness of NCPAP.**

A chin strap applied during NCPAP, performed by short binasal prongs connected to a standard circuit, probably has the effect to better stabilize the applied pressure, but I suppose there are no data demonstrating that this (uncomfortable and difficult to apply for a long time) solution may really improve the efficacy of NCPAP.

A pacifier may be useful to reduce the leaks from the mouth, but must be assessed from case to case.

By contrast, using double-inspiratory loop cannulas connected to a standard circuit, we have to consider that the main characteristic of this device is that both the long tubes between the Y-piece and the nasal prongs only conduct inspiratory flow. In this case, in my opinion, is absolutely not advisable to seal the baby's mouth completely because during NCPAP applied with this device the expiratory tidal volume leaves the airways mostly through the mouth and a sealed mouth may cause rebreathing and increase of WOB.

**See also the answer to question 8 and 32.**

**26. How can baby-ventilator synchrony be optimally achieved?**

Currently there are three different methods to perform SNIPPV: Grasby Capsule, NAVA and Giulia flow-sensor.

**27. Can conventional ventilator deliver NIPPV effectively compared against one dedicated ventilator?**

Absolutely YES, most of the trials in preterm infants were conducted using a conventional ventilator for non-synchronized NIPPV.

**28. Does non synchronized NIV is better than CPAP for BPD prevention?**

While BPD seems to be prevented by SNIPPV, this effect is less evident for non-synchronized NIPPV. Literature data show that SNIPPV after extubation reduces the incidence of BPD by 36% by reducing time spent under invasive ventilation by 75% (Lemyre B. Cochrane Database Syst Rev. 2017).

**29. Can the double loop cannula work on any ventilator.**

Yes, it is possible to perform non-synchronized NIPPV with double-inspiratory loop cannula and standard ventilators. Some models of this device are designed to interface easily with commonly available dual-limb circuits for NCPAP and NIPPV.

**30. Do you have any problems with condensation on nasal cannula?**

As expected, condensation may affect the performance of the flow-sensor and cause failure to trigger or autotriggering. For this reason, care should be taken in order to keep sensor and circuit clean from water.

**31. Do you think the double tube cannula is increasing the resistance and making spontaneous breaths more difficult, is the resistance for spontaneous breathing.**

This is particularly true during respiratory support (NCPAP), because during non-invasive ventilation (NIPPV or SNIPPV), when the expiratory valve of the ventilator closes during the inspiratory time, the flow is forced from the main circuit through the two inspiratory limbs towards the patient.

In the double-inspiratory loop cannula the highest resistance is at the level of the two nasal prongs, as in short binasal prongs, however its resistance increases in proportion to the length and diameter of the two long connecting tubes. For an effective clinical use of the double-inspiratory loop cannulas choose the ones with the lowest resistance.

**See also the answer to question 8 and 25.**