High-frequency oscillatory ventilation in pediatrics and neonatology

Ventilação oscilatória de alta frequência em pediatria e neonatologia

INTRODUCTION

One of the mainstays of intensive care in pediatrics and neonatology is safe control of the ventilatory function achieved by mechanical ventilation (MV). Although a life saving procedure, there is growing evidence that conventional mechanical ventilation (CMV) may worsen pulmonary function and contribute to development of a multiple organ dysfunction in the endeavor to warrant normal gas exchange during acute respiratory failure.(1-4)

Several publications call the attention to ventilator induced lung injury (VILI). The prevailing opinion is that use of high tidal volumes, that generate high inspiratory pressures during MV of patients with acute respiratory distress syndrome (ARDS), cause structural injury in, the un-
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Thus VILI may be defined as a simulation of acute pulmonary injury taking place in patients submitted to MV. Repetitive overdistension of the lungs and subsequent development of atelectasia contribute to pulmonary injury, which is caused by using the ventilator standard for oxygenation and ventilation support. A cyclic change in pulmonary volume may be a significant cause of MVIPI, suggesting that a ventilation strategy avoiding major pulmonary volume variations might be beneficial.

The concept of protective mechanical ventilation emerged from the understanding of VILI. It may be defined as a ventilation that minimizes tidal volume, maintains a low peak inspiratory pressure, offers a sufficient positive end expiratory pressure (PEEP) to maintain alveolar opening, avoids alveolar collapse and cyclic opening and closing of the alveolar units, uses non-toxic concentrations of oxygen and permits hypercapnia.

Although CMV is effective for most children, there is a significant number of patients with severe respiratory failure for whom CMV may not assure oxygenation and ventilation. In such cases, when protective mechanical ventilation is mandatory, high frequency oscillatory ventilation (HFOV) becomes an attractive alternative.

HFOV is a ventilation mode that uses a lower tidal volume than the anatomic dead space volume (1–3 mL/Kg) with a frequency well above the physiological one (5–10 Hertz), that is to say, 300-600 cycles/minute. This ventilation mode has been successfully used to treat patients with severe respiratory failure when CMV fails. Furthermore, reports state that when HFOV is used earlier, together with a protective strategy, a decrease of the acute or chronic pulmonary injury occurs in patients with ARDS.

The 3100A by SensorMedics® ventilator is approved by Food and Drug Administration (FDA) for use in children up to 35 kg. This is a device for mechanical pulmonary ventilation with a continuous flow of gas capable of eliminating CO₂ and keeping airway pressure constant. The ventilator has an electromagnetic piston that generates high frequency oscillation on the air flow, establishing pressure oscillation amplitude. Contrary to the CMV, in HFOV tidal volume is inversely related to frequency and inspiration as well as expiration is active. The amplitude of pressure is greater in the ventilator circuit and in the tracheal proximal portion, progressively decreasing along the airway, resulting in low pressure amplitude in the alveoli.

Literature review and selection of more relevant publications on high frequency ventilation using as database MedLine and SciElo published in the last 15 years was carried out. The following key words were used: high frequency oscillatory ventilation, mechanical ventilation, acute respiratory distress syndrome and newborn.

CLINICAL APPLICATIONS OF HFOV IN PEDIATRICS

Acute pulmonary injury and acute respiratory distress syndrome

The combination of low volume and pressure variation and maintenance of constant mean airway pressure (MAP) make use of HFOV attractive for ARDS. Maintenance of pulmonary volume avoids pulmonary overdistension as well as occurrence of atelectasia in patients with ARDS and the flow standard may improve in relation to ventilation-perfusion.

Successful treatment of ARDS requires a strategy to keep the lungs open, the open lung approach. Recruitment of collapsed alveoli reduces intrapulmonary shunt, reducing the fraction of inspired oxygen (FiO₂) to less toxic concentrations. It was shown that children with ARDS have a significant improvement in oxygenation, lower incidence of barotraumas and better results with use of HFOV, without influencing mortality. In adults with ARDS an immediate and sustained improvement was reported in relation to partial oxygen pressure (PaO₂/FiO₂) when patients were submitted to HFOV combined with alveolar recruitment maneuvers. An additional benefit was shown to be reduction of inflammatory mediators in samples of bronchoalveolar lavage of patients with HFOV when compared to CMV. Further, in these studies with adults, no statistical difference was observed in mortality when comparing HFOV to CMV.

It is noteworthy that these studies call attention to early introduction of HFOV in ARDS when benefits could be more easily demonstrated.

To summarize, in cases of ARDS, the HFOV is an important therapeutic tool and although, decrease of mortality with use of this ventilation mode has not been proven, studies focusing on its early utilization must be implemented.
Air leak syndrome

Pneumothorax, mediastinal emphysema and pulmonary interstitial air are observed in acute pulmonary injury as a result of base disease as well as ventilation therapy. HFOV has been successfully used for these patients\(^{14,15}\) emphasizing that the strategy must encompass low MAP and use of pressure amplitude at lower values, needed to keep adequate alveolar ventilation, resolving the air leak. In such cases a high FiO\(_2\) must be permitted for short periods, accepting arterial oxygen saturation (SaO\(_2\) > 85%) as long as oxygen release is adequate, lactic acidosis does not occur and the patient is hemodynamically stable.\(^{1,12}\) Decrease of MAP and pressure amplitude lead to hypercapnia and, to maintain adequate elimination of carbon dioxide (CO\(_2\)), frequency may be reduced. However, hypercapnia must be accepted, because adjustment of the respiratory rate to normalize CO\(_2\) increases tidal volume, with a worse air leak.\(^{1,14}\)

Obstructive pulmonary disease

Use of HFOV when facing increased resistance of the airways is controversial.\(^{1,12}\) For some years HFOV was contraindicated for obstructive pulmonary disease because of high risk of air trapping and dynamic hyperinflation.\(^{1,16}\) However, successful use of HFOV in children with asthma and bronchiolitis has been reported.\(^{15}\) This is probably due to the unique characteristic of this ventilation mode, active expiration. In this condition, air is actively removed from the lungs without risk of trapping.\(^{16}\) Thus, in the previously described condition, HFOV may be considered as an alternative when facing refractory respiratory acidosis caused by inadequate alveolar ventilation.

In one of the largest studies carried out in a single center, including 53 patients of which 17 presented with obstructive disease, the open airway\(^{17}\) technique was applied by carefully titrating MAP in HFOV to open airways and adjust ventilation,\(^{18}\) a success for this therapy.

In summary, in situations of obstructive pulmonary disease, it is always prudent to evaluate the risk and benefit of introducing HFOV.

CLINICAL APPLICATIONS OF HFOV IN NEONATOLOGY

Since introduction of HFOV in neonatology during the sixties, a dramatic decrease of mortality\(^{3}\) as well as establishment of a new category of disease, ventilator induced injuries\(^{(4)}\) were observed. This included bronchopulmonary displasia (BPD) and occurrence of air leak (pneumothorax, pneumomediastinum, etc.). To reduce occurrence of BPD various modifications in the ventilation strategies were introduced, and the less aggressive MV strategy was implemented. In this aspect, use of HFOV in neonatology as previously described for older children emerged as an important technique for pulmonary protection.

Since its introduction in neonatology in 1981, including 8 new-born with ARDS, various studies have been carried out to evaluate efficacy and safety of HFOV in relation to CMV in prematures. These studies present highly variable results. Since the onset it was well established that, just as in adults and in older children, MAP applied during HFOV had a direct correlation with oxygenation, therefore the high values of MAP permitted ventilation with low FiO\(_2\)\(^{(19)}\) and no major hemodynamic aftermaths were observed. It was noted that in prematures a given MAP needed to achieve and sustain alveolar expansions, could be maintained. The oscillatory drives reopened atelactatic areas more efficiently than the same mean pressure maintained in an static way and that small volumes, generated at a respiratory rate of 10 a 15 Hz, provided a good safety margin to avoid overdistension of the lung normal areas.\(^{20}\)

It must be recalled that benefits of HFOV in prematures became evident after establishing a ventilation strategy based on recovery of the pulmonary volume aiming at early reversion of the atelactatic areas by a more aggressive use of MAP and achieving a decrease of FiO\(_2\) prior to decrease of pressures.\(^{21}\)

A second fundamentally important aspect observed in studies comparing efficacy and safety of HFOV in relation to CMV in neonatology, is the strategy used in CMV, where PEEP used often is relatively low, permitting alveolar collapse at the end of expiration, although MAP remains at somewhat lower levels than those of HFOV. This because the latter modality has the intrinsic advantage of keeping the lung at pressures above the zone of alveolar collapse, in view of the small amplitude of tidal volume utilized. This facilitates maintenance of the lung at pressures above the lower inflection point of the pressure-volume curve, which is almost impossible in CMV. On the contrary, especially in earlier studies, there was no concern about using lower tidal volume values associated to adequate levels of PEEP.\(^{21}\)

After almost twenty studies comparing HFOV to...
CMV in neonatology, it was shown that both treatments are comparable in relation to mortality. Initially, some studies suggested that HFOV was associated to a higher incidence of peri-intraventricular hemorrhage,\(^{(22,23)}\) resulting in some resistance to introduction of HFOV as routine in extreme prematures. However, in the last five years, strong evidence has appeared that HFOV and CMV are equivalent with regard to risk of evolving into intracranial hemorrhage in prematures.\(^{(24,25)}\)

Safety and efficacy of HFOV were reviewed in 2007 in a meta-analysis with 3585 children in 15 studies that compared this ventilation mode with CMV.\(^{(26)}\)

The authors concluded that there is no evidence that HFOV used as initial strategy presented advantages in relation to CMV, regarding efficacy of ventilation or mortality at 28-30 days of age or age equivalent to term. Nevertheless, authors found a small decrease in the incidence of chronic pulmonary disease with 36-37 weeks gestational age, corrected among survivors with use of HFOV. However, this evidence is weakened by inconsistency of results over the 15 studies and the threshold significance (RR 0.89; 95% CI: 0.81-0.99).

Analyses of subgroups showed that there was a decrease of chronic pulmonary disease when HFOV was carried out with a high tidal volume strategy, when piston oscillators were used to perform HFOV, when randomization took place between two to six hours of life and when an inspiration/expiration ratio of 1:2 was used for HFOV. Some of the inconsistency of these results is due to variability of the strategies used for HFOV (high volume our reduced volume) as well as for CMV, over time.

It is noteworthy that currently when the prenatal use of corticoids to induce pulmonary maturity in the premature, exogenous surfactant and use of more protective CMV techniques has become a routine, any benefit from HFOV in relation to CMV, probably will only be proven in new-born with severe pulmonary disease. For instance, Courtney et al.\(^{(24)}\) showed that benefit of using HFOV in relation to CMV was only observed when inclusion was restricted to new-born of very low weight that met criteria of major severity, based upon FiO\(_2\) and MAP after administration of surfactant.

Although the meta-analysis\(^{(26)}\) disclosed increased incidence of intraventricular hemorrhage and of leukoencephalomalacia with HFOV, in some studies these were not significant (intraventricular hemorrhage: RR1.05; 95% C.I. 0.96-1.15 – leukoencephalomalacia: RR1.10; 95% CI 0.85-1.43). Conversely to use of HFOV as a first form of treatment in ARDS, use as a rescue therapy was reported in only two controlled studies,\(^{(27,28)}\) without evidence of improved evolution in the long term of newborn, be it in chronic pulmonary disease, occurrence of neurological complications, or survival.

Finally, HFOV has only shown a better result than CMV during the neonatal period in relation to management of extrapulmonary air. The few studies comparing HFOV to CMV in this situation demonstrate that air leak through the thoracic drain is lower with use of HFOV,\(^{(29,30)}\) a fact confirmed in a case report\(^{(31)}\) and in an experimental study\(^{(32)}\) which disclosed benefit using HFOV in presence of a trachoesophageal or bronchopleural fistula.

To summarize, data currently available in literature confirm that HFOV is a safe ventilation mode for use in neonatology, however there is no evidence proving a clear benefit or advantage of HFOV in relation to CMV in newborn, be as initial or as rescue therapy. The only clinical situation where there is evidence of better results with HFOV is extrapulmonary air, especially in bronchopleural fistula.

**TRANSITION FROM CONVENTIONAL VENTILATION TO HIGH FREQUENCY VENTILATION**

A patient transferred to HFOV must be duly monitored regarding pulse oxymetry, relation PaO\(_2\)/FiO\(_2\) and capnography. From the cardiovascular point of view, an adequate intravascular volume must be assured based upon peripheral perfusion, capillary filling, arterial pressure and heart rate. The endotracheal tube must be correctly positioned and preferably there should be a closed suction system of the tracheal tube. Sedation should be optimized and in some cases curarization may be needed.

As already mentioned, early use of HFOV\(^{(24,33,34)}\) has received considerable attention. As such, for children after the neonatal period and with ARDS, when SaO\(_2\) is below 90%, in FiO\(_2\) higher than 0.6, with inspiratory pressure (Plp) of 30-32 cmH\(_2\)O and PEEP higher than 10-12 cmH\(_2\)O, transfer from conventional to HFOV is recommended.

**Implementation of HFOV**

Initial parameters used in HFOV are:\(^{(1,2)}\)
- sufficient FiO\(_2\) to maintain SaO\(_2\) ≥ 90% (100%
during the transition time from CMV to HFOV;
- inspiratory time, 33% of the oscillatory cycle;
- frequency of 10 Hz for sucklings and from 5 to 8 Hz for older children or according to the patient's weight < 10kg = 6-10Hz; 11-20kg = 8-10Hz; 21-40kg = 6-10Hz; > 40kg = 5-8Hz. For a term newborn = 12 or 15 Hz and for newborn prematures/ very low weight = 15 Hz;
- flow must remain between 15 and 20 L/min, depending upon the patient's size and on the MAP required. In newborn use flow between 8 and 15 L/ min;
- MAP form 2 to 4 cmH$_2$O above that used for CMV. MAP can later be increased to achieve SaO$_2$ ≥ 90% with FiO$_2$ ≤ 0.6. For newborn with diffuse alveolar disease or air leak syndrome use MAP 3-5 cmH$_2$O above CMV. An early rescue intervention may be made in newborn using MAP of 10-14 cmH$_2$O. In newborn as well as in older children, if SaO$_2$ falls quickly below 90%, recruit manual ventilation and gradually increase MAP;
- pressure amplitude (ΔP) will be that sufficient to achieve perceptible movement of the thoracic wall (movement of the thigh root which is easily seen) that may be modified to the desired ventilation levels by evaluating PaCO$_2$. Changes in frequency also define alteration in PaCO$_2$ and, to the contrary of what takes place in CMV, in HFOV there is fall of PaCO$_2$ when FR is diminished. In newborn at term the ΔP can be ≥ 25 cmH$_2$O ands in prematures/ very low weight can be ≥ 16 cmH$_2$O.

**VENTILATION HANDLING**

**Oxygenation**

Criteria to transfer a patient from CMV to HFOV vary according to the team's experience. In general, transfere is based upon clinical judgment, index of oxygenation pressure peak that has been needed in CMV and disease progression.$^{(1,2)}$

Because there is a strict relation between pulmonary volume and surface area of gas exchange, practically all oxygenation in HFOV depends on MAP and FiO$_2$. When MAP is increased the pulmonary volumes are recruited and oxygenation improves up to the optimal point, beyond which the lungs become hyper expanded. If there is superdistension, alveolar capillaries are compressed, thereby reducing the gas exchange area and of the PaO$_2$. Furthermore, a more significant hemodynamic impairment may take place.$^{(1)}$

The ability to achieve adequate oxygenation in non-toxic FiO$_2$ is the main indicator that MAP is adequate. In general, chest radiography must be made to evaluate the level of pulmonary expansion and presence of nine or more intercostal spaces is an indicator of superdistension. MAP may be reduced when alveolar recruitment is considered satisfactory and a lower transpulmonary pressure is required to maintain the lung open. Verification of the level of pulmonary recruitment includes evaluation of gas exchange efficiency (rate of oxygenation) need for oxygen and chest X-ray exam.$^{(1,2)}$

In summary, MAP may be increased from 1 to 2 cmH$_2$O until FiO$_2$ < 0.6 with SaO$_2$ between 88-92% in cases of ARDS. In cases of air leak syndrome, use of a higher FiO$_2$ (between 80% and 100%) is permitted, especially in the first 12-24 hours to minimize MAP, while an adequate SaO$_2$ is achieved.

**Elimination of carbon dioxide**

Ventilation adjustments are achieved by increasing pressure amplitude or by reducing frequency, although elimination of CO$_2$ is more related to amplitude and less with frequency. Change of inspiratory time and flow increase are other maneuvers that may improve ventilation. Amplitude may be changed by a button that controls movement of the electromagnetic piston. Increase of amplitude results in increase of tidal volume. Conversely, decrease of amplitude supplies lower tidal volume e reduces the ventilation minute. Increases of ΔP from 2–5 cmH$_2$O changes PaCO$_2$ by 3–5 mmHg and increase of ΔP of more than 5 cmH$_2$O changes PaCO$_2$ by 5–10 mmHg. It is appropriate to reduce respiratory rate only if carbon dioxide arterial pressure (PaCO$_2$) is refractory to changes of the ΔP.$^{(1,2)}$

Choice of adequate amplitude is essentially result from visual clinical inspection of the level of movement of the patient’s thoracic wall and measurement of blood gases. One characteristic of HFOV is that intensity of the piston movement is inversely related to frequency, that is to say increased frequency diminishes movement of the piston with an effective decrease of pressure amplitude and of released tidal volume. Increase of the inspiratory time leads to increase of tidal volume and may improve elimination of CO$_2$ e oxygenation.$^{(1)}$

Flow is the determinant of MAP and interferes with removal of CO$_2$. Typically, the flow needed to achieve adequate mean airway pressure and maintain adequate minute ventilation ranges from 20 to 40 L/min.
Radiological examination
The exam must be made one or two hours after beginning and as often as 6 or 8 hours until stabilization. Later, chest X-ray must be performed daily and after significant parameter changes. The ideal number of intercostal spaces ranges from eight to nine.[1,2]

Suction of the tracheal tube
Suction of the tracheal tube must be restricted as much as possible, especially in the first 24 hours. This procedure must be considered if PaCO₂ is progressively increasing. Consider recruitment maneuver after.[1,2]

Sedation and neuromuscular blockade
Patients must be deeply sedated at onset of HFOV using an association of benzodiazepines and opioids. Neuromuscular blockade may be necessary and, when used must be interrupted daily to assess if it must be maintained. Remember that small respiratory efforts that alter MAP less than 5 cmH₂O do not require deeper sedation and/or neuromuscular blockade unless oxygenation or ventilation are impaired.[1,2]

Weaning from HFOV
ΔP must be slowly reduced while an adequate PaCO₂ is maintained. MAP might be reduced by 1 to 2 cmH₂O to levels between 15 and 20 cmH₂O with good recovery after suction.[1,2]

In newborn ΔP must also be slowly reduced, remembering that spontaneous breathing may increase tidal volume. Just as in older children, in newborn MAP must be reduced by 1 to 2 cmH₂O. Term newborn and prematures must return to HFOV when MAP is at 10 – 12 cmH₂O.[1,2]

Complications of high frequency oscillatory ventilation
The main complications of HFOV are the following.
- Barotrauma and hemodynamic impairment: complications derived from use of high mean airway pressures. Mehta et al.[35] reported prevalence of 21.8% of pneumothorax and in 26% of patients HFOV had to be discontinued because of hemodynamic problems. However, in two randomized controlled studies[36,37] that compared HFOV with CMV, prevalence of pneumothorax and hypertension were comparable between groups.

It is also noteworthy that it is challenging to recognize pneumothorax in patients under HFOV. Assessment relies on reduction or asymmetry of body vibration in response to the pressure waves or to an increase of the ΔP.[40]

- Increase of central venous pressure and pulmonary artery occlusion pressure: derived from increase of MAP and decrease of venous return. Therefore close attention must be paid to volemic reposition of patients that will go from CMV to HFOV.[1]

- Deep sedation and, sometimes curarization: these conditions may lead to an extended mechanical ventilation time and LOS, in addition to polyneuropathy inherent to curarization.[38,39]

- Obstruction of the airways and tracheal tube by secretions: complications with 4% to 5% incidence[40] it is important to promote adequate humidification due to high flow of gas and minute ventilation.

RESUMO
Este trabalho teve por objetivo rever a literatura e descrever a utilização da ventilação oscilatória de alta frequência em crianças e recém-nascidos. Revisão bibliográfica e seleção de publicações mais relevantes sobre ventilação de alta frequência utilizando as bases de dados MedLine e SciElo publicadas nos últimos 15 anos. As seguintes palavras-chave foram utilizadas: ventilação oscilatória de alta frequência, ventilação mecânica, síndrome do desconforto respiratório agudo, crianças e recém-nascidos. Descreveu-se o emprego da ventilação oscilatória de alta frequência em crianças com síndrome do desconforto respiratório agudo, crianças e recém-nascidos. Descreveu-se o emprego da ventilação oscilatória de alta frequência em recém-nascidos, síndrome do desconforto respiratório agudo, síndrome de escape de ar e doença pulmonar obstructiva. Avaliou em recém-nascidos, síndrome do desconforto respiratório agudo, displasia broncopulmonar, hemorragia peri-intraventricular, leucoencefalomalácia e extravasamento de ar. Também, abordou a transição da ventilação mecânica convencional para a ventilação de alta frequência e o manuseio específico da ventilação de alta frequência quanto à oxigenação, eliminação de gás carbônico, realização de exame radiológico, realização de sucção traqueal e utilização de sedação e bloqueio neuromuscular. Foram abordados o desmame deste modo ventilatório e as complicações. Em crianças maiores a ventilação oscilatória de alta frequência é uma opção terapêutica, principalmente na síndrome do desconforto respiratório agudo, devendo ser empregada precocemente. Também pode ser útil em casos de síndrome de escape de ar e doença pulmonar obstructiva. Em recém-nascidos, não há evidências que demonstrem superioridade da ventilação oscilatória de alta frequência em relação à ventilação convencional, sendo a síndrome de escape de ar a única situação clínica em que há evidência de melhores resultados com este modo ventilatório.

Descritores: Ventilação oscilatória de alta frequência; Ventilação mecânica; Síndrome do desconforto respiratório agudo; Criança; Recém-nascido
REFERÊNCIAS


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