High-Frequency Oscillatory Ventilation (HFOV) New Patients, New Strategies -- Same Physics

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I dedicate this column to the late Dr. Andrew (Andy) Shennan, the founder of the perinatal program at Women's College Hospital (now at Sunnybrook Health Sciences Centre). To my teacher, my mentor and the man I owe my career as it is to, thank you. You have earned your place where there are no hospitals and no NICUs, where all the babies do is laugh and giggle and sleep.

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While HFOV has been a recognized mode of ventilation in the NICU for 40 years, its application on different patients with different pathologies demands different settings. As the limits of viability are pushed ever lower, our patients have become ever smaller. What all too often has not changed are the HFOV parameters chosen.

For years it has been assumed that smaller patients require higher frequencies (and there are indeed situations where higher frequencies are desirable). There are also situations where this is not the case, and lower frequencies are the more appropriate. Confounding the clinician's selection of frequency are differences between machines, the availability of volume-targeted HFOV, airway resistance (Raw), pulmonary compliance (Cl), achieving proper lung volume (via mean airway pressure (MAP) to ensure an "open lung" approach to ventilation, and surfactant.

Corner frequency (fc) has been identified as the best and appropriate frequency at which to ventilate, while some believe resonant frequency (ω) is the most appropriate. fc is the frequency at which energy passed through the system (airways) decreases instead of passing through. ω, conversely, is the frequency at which response to any given amplitude is greatest (and can even be amplified)(1). The most common example of ω is a glass shattering when a vocalist hits a specific note at sufficient volume. ("Galloping Gertie," otherwise known as the original Tacoma Narrows Bridge, was initially thought to have collapsed due to sustained wind matching the bridge's ω; however, it was an aerodynamic phenomenon known as "flutter" that caused the collapse. More on that later). From an efficiency standpoint, ω gives the most bang for the buck, but, just as the shattering glass, ω has the potential to damage the lung. In the neonatal lung, Fc is usually lower than ω. (1)

While HFOV is generally considered a gentler, lung-protective mode of ventilation, it is hardly foolproof. The most glaring example is the infamous "HIFI" study of the early 1980s terminated early due to bad outcomes, particularly severe brain bleeds, while offering no statistical pulmonary benefit. (2) While the results of this study did not support HFOV, it was not futile; we learned from it the dangers of not ventilating with an adequately recruited lung, now known as the "open lung" approach.

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Underinflation is not the only practice that can lead to undesirable results. The behaviour of the oscillatory waveform itself can also create damage regardless of proper recruitment. During HFOV, gas is pushed into and pulled out of the airways at high frequency and velocity. While we associate shear stress with the lung's relatively large expansion and deflation during conventional ventilation, we assume the small, sub-dead space volumes of HFOV prevent or significantly limit shear stress. This can be true, but high-velocity gas flow creates turbulent flow, which, in turn, causes eddies to form. The more turbulent flow created, the more eddies form. This non-laminar flow is advantageous from the standpoint of gas mixing enhancing ventilation (and indeed is essential for HFO to work); however, localized pressure differences produced by eddies create shear forces that can distort the surface of the airway cell structure and potentially cause damage. Because the gas flow is rapidly changing, these shear forces are potentiated,

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particularly in proximal airways(1). This concept is very similar to aeroelastic flutter. "Flutter is a dynamic instability of an elastic structure in a fluid flow, caused by positive feedback between the body's deflection and the force exerted by the fluid flow. In a linear system, "flutter point" is the point at which the structure is undergoing simple harmonic motion—zero net damping—and so any further decrease in net damping will result in a self-oscillation and eventual failure. «Net damping» can be understood as the sum of the structure›s natural positive damping and the negative damping of the aerodynamic force. Flutter can be classified into two types: *hard flutter*, in which the net damping decreases very suddenly, very close to the flutter point; and *soft flutter*, in which the net damping decreases gradually" .(3) Damping increases as the gas travels further down the airways thus the potential for this phenomenon Is greater in proximal airways. (Damping refers to the reduction, restriction, or prevention of oscillations within or upon that system. Damping in physical systems is a result of a process that dissipates the energy stored within the oscillation. In an overdamped system, the system returns (exponentially decays) to equilibrium without oscillating. (1)

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Oscillatory waveform pressure also behaves differently with varying compliance and resistance. High resistance dampens the waveform and attenuates pressure, whereas low resistance produces less damping and less pressure attenuation. Longer time constants characteristic of high resistance call for lower frequency, resulting in greater pressure transmission, although higher amplitude may still be necessitated. Conversely, low resistance allows for higher frequency. Again, associated lower pressure transmission with higher frequency may be offset by higher pressure transmission due to low resistance. It is important to note that Ra/w increases as flow increases. In order to maintain a given Vt as frequency increases, amplitude must also increase, which, in turn, results in increased flow.

The opposite holds for compliance. Higher oscillatory pressures are transmitted to areas of low compliance (in addition to higher pressure required to ventilate effectively), whereas in areas of high compliance, pressure is rapidly attenuated, although effective ventilation requires a lower pressure. In the presence of low compliance, such as during recruitment, higher frequencies are favourable for two reasons. Firstly, lower compliance results in shorter time constants, and, secondly, the higher pressure transmitted to the distal airways and alveoli may be beneficial in aiding recruitment. A caveat here is that while higher pressure transmission is equal to the critical opening pressure of the lung aids recruitment, pressures above that level may cause barotrauma. As with low resistance, increased pressure attenuation with higher

frequencies may mitigate distal barotrauma.

When considering compliance, one must consider the lungs and the system; oscillatory volume is lost to circuit compliance, and an appropriate low compliance circuit and humidifier should be used. As the water level in the humidifier decreases, system compliance increases. Using an auto-filling humidifier eliminates this problem.

In real life, compliance and resistance do not exist in separate worlds, and lungs and airways rarely are homogeneous in compliance and resistance. Patients may have high airway resistance and high or normal lung compliance or low airway resistance and low compliance. We know that compliance varies between segments of the lung and that airway resistance increases further down the tracheobronchial as diameter decreases. Where resistance and compliance are low lower frequency should be used, whereas where compliance is low, but resistance is normal higher frequency is preferred. What about high resistance coupled with high compliance? Here lower frequency is preferred due to long time constants in both the lung and the airways. Regardless of lung compliance, pressure transmission to the carina is high in the face of high resistance relative to normal/low resistance and must be considered as this may create large airway damage.

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Mean Airway Pressure (MAP)

Perhaps the most inappropriately used parameter in HFOV is MAP. MAP is required to both maintain conducting airway patency and maintain lung volume above functional residual capacity. If MAP is too low, airways may collapse, particularly during the expiratory phase of HFOV, leading to gas trapping. Insufficient MAP results in lower lung compliance and will require higher amplitude to ventilate, which, in turn, potentiates barotrauma. Over time atelectasis may progress to total lung collapse, respiratory and ventilatory failure. Sequelae of lung collapse are increased pulmonary vascular resistance (PVR) and atelectotrauma. The former impedes blood flow and decreases blood pressure, while the latter triggers an inflammatory cascade. If MAP is too high, the result is also a decrease in compliance and increased PVR. In either scenario, FiO_2 will be increased relative to that of a lung maintained in a proper state of inflation. Regular readers of this column will know I believe that the best FiO_2 is the lowest possible, which, it turns out, coincides with optimal compliance resulting from a proper MAP. With HFOV, MAP is the primary regulator of FiO_2.

Because the latest ventilators combine CV and HFOV in a single machine, it is possible to superimpose CV breaths on HFOV and a manual inspiration feature that provides a CV breath on demand. The pressure of the CV breaths is independently adjustable. As the lung develops, MAP may not be sufficient to recruit them; it is, therefore, logical to aid their recruitment with an occasional CV or

manual inspiration. Care must be taken here since the open lung approach to HFOV (and HFJV) maintain lung volume above normal FRC and closer to volumes that may precipitate volutrauma. It is my practice to set CV/manual breath pressures at 5 cmH$_2$O above MAP. This strategy reduces the chance of both volutrauma and barotrauma, and if this setting does not evoke sufficient response, pressure can be increased stepwise until the desired effect is achieved. When superimposing CV breaths on HFOV (HFOV/CMV) CV rate should be set at a minimum. If more CV breaths are required, it probably indicates higher MAP is needed.

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MAP, I:E Ratio, Frequency and Endotracheal Tube (ETT) Size

Intrapulmonary pressure (IP) is not readily directly measurable. It is the pressure transmitted to the lung by MAP and is the pressure that directly affects PVR and venous return. IP is affected by both the I:E ratio, frequency, and ETT diameter. At an I:E ratio of 1:1, IP is closest to set MAP. Increasing I:E ratio results in a decrease in IP. The increasing frequency and decreasing ETT size also reduce IP, and this is accelerated as either frequency is increased or ETT tube size is decreased. While IP is greatest at an I:E of 1:1, since more pressure is transmitted, the risk of barotrauma is increased. Airway lumen is also decreased in the expiratory phase, which increases time constants hence the risk of gas trapping (at least theoretically), especially as frequency is increased. The deeper trough may exacerbate this in the expiratory phase compared to I:E of 1:2. In practice, I submit that if I:E ratio of 1:1 is required, then another mode of ventilation (particularly HFJV) should be considered.

Frequency, Amplitude and Tidal Volume (Vt)

Vt is the primary determinant of ventilation in HFOV. Unlike conventional ventilation (CV), in which CO$_2$ removal is determined equally by rate and peak inspiratory pressure, in HFOV, this is relative to rate (frequency) multiplied by the square of Vt as represented by DCO$_2$, the coefficient of ventilation (DCO$_2$ = f x Vt^2). Increasing amplitude directly increases Vt and hence CO$_2$ clearance. Clinicians must be aware that as the amplitude increases, so does the depth of the expiratory trough. Although we do not think about PEEP when using HFOV, it is the pressure at the lowest point on the oscillatory waveform. Airway instability, gas trapping, and atelectasis may result if the trough is too low. This instability must be compensated for by increasing MAP. In clinical practice,

it is very difficult to determine when this is happening until after the fact since we cannot directly measure distal airway pressure. Increased FiO$_2$ may be the first warning of trouble ahead.

The fixed I:E ratio in HFOV also has implications for Vt. As the frequency is increased, the absolute inspiratory time decreases, as does expiratory time. Since there is less time to deliver volume, Vt will decrease as frequency increases; decreasing frequency has the opposite effect. This relationship must be kept in mind when using first-generation machines such as the Sensormedics 3100A or 3rd generation machines without volume targeting. Time constants lengthen as compliance improves, and frequency should be decreased to reflect this, but the resulting increase in Vt increases ventilation unless amplitude is simultaneously decreased to prevent overventilation.

Ra/w and Gestational Age (GA)

HFOV recommendations are often based on infant weight. However, one study found that GA more than birthweight[4] accurately predicted cricoid ring diameter. Airway diameter increases linearly from 22 weeks GA until eight months post-natal age[5]. Since Ra/w is primarily determined by airway radius, it, therefore, increases exponentially with declining GA. This ratio has implications for time constants and choice of frequency.

This is where I have concerns regarding higher frequencies. While tiny babies should be ventilated with small Vt (whether CV or HFOV is used), this may require higher frequencies with 1st generation machines or without volume-targeted ventilation. This strategy may result in gas trapping and, in my opinion, may be one reason evidence to support the superiority of HFOV over CV has traditionally been inconclusive or lacking. Physics dictates that at some point, Ra/w overtakes lung compliance as the major determinant of time constants and choice of frequency whether using HFOV or HFJV.

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Ventilating the tiniest of babies is a delicate dance at the best of times, while the recency at which we have been offering resuscitation to infants <24 weeks GA severely limits evidence upon which to base our ventilation strategies. To me, the precautionary principle dictates assuming gas trapping exists to a degree (whether globally or regionally) in all micro-premies and ventilating accordingly. Perhaps the nature of HFJV makes it the preferred mode for these babies; indeed, Iowa's outcomes lead credence to this submission. I leave it to clinician-researchers such as Dr. Jane Pillow (whom I have referenced extensively in this column) to provide incontrovertible evidence to guide us.

Volume-targeted HFOV (HFO/VG)

Outside the U.S., HFO/VG has been available on 3rd generation

ventilators for over ten years, and there are now several machines from which to choose. While each machine has its own characteristics, the basic principle is the same; Vt is monitored breath-to-breath, and amplitude is adjusted to maintain an average set Vt.

The ability to control Vt independent of frequency allows clinicians to adjust frequency to match pathology and time constants more closely without worrying about Vt increasing or decreasing. Since the square of Vt times frequency determines DCO_2, small increases in Vt result in much more CO_2 clearance than increasing frequency. In practice, this may result in maintaining adequate ventilation at a lower frequency with less amplitude. In theory, this should reduce gas trapping (should it be present) and may be beneficial for tiny babies.

Like HFOV without using VG, MAP, frequency, and amplitude are set according to patient needs. While frequency is fixed, the amplitude is automatically adjusted to maintain Vt and set amplitude functions as a maximum limit. Should Vt not be reached at this limit, the machine will alarm. Clinicians are cautioned to avoid a "set it and forget it" approach to HFO/VG, and I strongly recommend setting amplitude at 5 cmH_2O above the average used by the machine. Allowing the machine too much latitude will fail to alert the clinician if compliance decreases or if suctioning is required. It is important to note that whether using HVOV or HFO/VG, even a small buildup of secretions in the ETT greatly reduces ventilation. The person suctioning may report removing scant or no secretions; however, if amplitude required to achieve set Vt decreases after suctioning, the need to have done so is self-evident.

As with VG in CV, Vt in HFO/VG is set according to weight and is adjustable in 0.1 ml increments. While volumes of 1-2 ml/kg are usually adequate, more may be required. Vt is measured proximately and how much of it is actually delivered to the lung is not directly measurable at the bedside, but it stands to reason as Vt increases, the lung protectiveness of HFOV is decreased. My personal practice is to limit Vt to 2.5 ml/kg, although I have used 3 ml/kg briefly as required, provided amplitude is not too high. (Please note my patients are primarily micro-prems). If high Vt is consistently needed after optimizing frequency and MAP, I will switch to HFJV.

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ing compliance and Ra/w to provide relatively consistent volumes. This physiology is particularly advantageous during lung recruitment and after surfactant administration, as it prevents inadvertent overventilation as compliance improves. A bench study compared the Sensormedics 3100A, SLE 5000, Drager Babylog VN500, Leoni 8000 +, and the Fabian. (The latter three machines are equipped to provide HFO/VG). Tests were conducted using 5, 10, and 15 Hz.

All 3 HFO/VG capable machines were able to maintain a Vt of 1 ml at 15 Hz under varying test conditions but could not maintain a Vt of 4 ml at the same frequency. The testing was done with a humidifier in line, but it was dry and unheated. I suspect the added compliance of the empty humidifier likely had a greater effect at higher volumes as these machines have limited power available, considerably less than the Sensormedics 3100A and the SLE 5000. At lower frequencies, delivered Vt was higher than indicated at the 1 ml setting(6), and clinicians should be aware of this when ventilating tiny babies. With larger babies, it may be necessary to decrease the frequency with or without VG to achieve adequate Vt.

The HFO/VG adjunct on the Drager Babylog VN500 has had FDA approval pending for quite some time. American clinicians accustomed to using the Sensormedics 3100A must be aware of differences between it and the VN500 once the latter is available. Most notable is that the VN500 (and the other 3 HFO/VG capable machines tested) delivered lower Vt than the 3100A at the same settings, and delivered Vt also varied between the 4(6). In practice, the response should dictates settings, and clinicians should not expect identical performance with different machines.

Hard evidence supporting HFO/VG over standard HFOV is lacking; however, it should, at least in theory, be beneficial, particularly in tiny babies. It is vitally important to understand how the mode works and the difference between the two modes to utilize HFO/VG to its best advantage.

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