safely and efficiently and that such systems must meet the needs of different ventilatory modes and peak inspiratory flow rates.

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References


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In Reply: — We wish to thank Troncy et al. for their interest in our work and welcome the opportunity to make the following clarifications.

As we stated in our published paper,1 our lung model produced negligible breath-to-breath variation. With no variability, inferential statistical analysis becomes meaningless. In our opinion, such analysis would be misleading and add nothing to our results.

Table 2 of our paper shows that, with the exception of the premixing system, the inspired nitric oxide concentration was affected by changes in tidal volume, inspiratory time, and inspiratory flow pattern. The methods that injected NO only during the inspiratory phase performed well with constant flow ventilation, but were not acceptable with pressure-controlled ventilation. This is explained by the fact that the NO injection was at a constant flow, whereas the flow from the ventilator was decelerating. Thus, the delivered NO concentration increased as the flow from the ventilator decreased. With the continuous injection method, the spikes in NO concentration were greater with a shorter inspiratory time, which allowed more NO to flow into the inspiratory circuit during the expiratory phase, which can be best appreciated from figure 2 in our article. The spikes in NO concentration were also greater with a higher tidal volume resulting from the higher inspiratory flow and thus less time for mixing.

We do not agree with the interpretation of Troncy et al. of figure 5 of our paper. We believe that it is obvious that the delivered NO patterns are different between the premixing system and the inspiratory injection system during pressure support ventilation. When tidal volume varies breath-by-breath such as can occur with synchronized intermittent mandatory ventilation, NO accumulates in the inspiratory limb of the circuit with the inspiratory injection system. The smaller the tidal volume and the longer the inspiratory time, the more NO accumulates in the inspiratory circuit. Thus, when a mandatory breath follows a spontaneous breath, a large spike of NO can be delivered.

Troncy et al. suggest that premixing systems were only used in the early stages of inhaled NO therapy. We believe that these systems are still commonly used. We use this system regularly in our practice, and it is the system used in the phase 2 and phase 3 clinical trials of inhaled NO for the acute respiratory distress syndrome in the United States. We have used the premixing system on about 150 patients and for thousands of hours over the past 5 yr without incident. We have noted no deterioration of ventilator or blender components. Although the NO concentration changes when the ventilator FiO2 setting is changed with the premixing system, the desired NO concentration can be maintained by adjusting the external blender setting. With the inspiratory injection system favored by Troncy et al., the NO concentration is affected by changes in the inspiratory flow setting of the ventilator and changes in the inspiratory flow pattern. We have successfully used nomograms to adjust the NO dilution with our premixing system for years.5 Regardless of the system used or the validity of nomograms, the delivered NO dose should be measured. As our data show, the analyzed dose can be deceptive when the NO concentration varies during the inspiratory phase and when a slow response analyzer is used. It should be noted that most commercially available electrochemical and chemiluminescence analyzers have a response time too slow to detect

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changes in NO concentration that may occur during the inspiratory phase.

The FiO₂ is limited by all NO delivery systems. With the premixing system, the FiO₂ setting on the ventilator cannot be set at 1.0 because NO enters the system through the high pressure air inlet. With the inspiratory injection system, the ventilator can be set at an FiO₂ of 1.0, but the oxygen concentration delivered to the patient will be less than 100%. For example, an inspiratory injection system that delivers a NO concentration of 20 ppm from a 400 ppm source gas cylinder must reduce the FiO₂ by 5%. Thus, even though the ventilator is set at an FiO₂ of 1.0, the patient only receives an FiO₂ of 0.95. It should also be noted that the inspiratory injection system will increase the tidal volume delivered from the ventilator by 5% under these conditions.

Like Troncy et al., we have been concerned by the generation of NO₂ in premixing systems. However, published data from our laboratory show that this is not problematic at the NO doses currently used (usually ≤ 20 ppm). This is consistent with data by Dubé et al., who have shown similar and acceptable NO₂ concentrations (≤ 1 ppm) for either the premixing system or inspiratory injection system.

It is important to note that the inspiratory injection system favored by Troncy et al. differs from systems that are being developed by industry. One of the systems, the Ohmeda INOvent Delivery System (Ohmeda, Madison, WI) is now available in the United States. This is an inspiratory injection system that is much more sophisticated than that described by us¹ or Dubé et al.¹ The INOvent Delivery System measures the inspiratory flow from the ventilator and precisely injects NO into the inspiratory limb proportional to the ventilator flow to achieve the desired NO concentration. In that way, the delivered NO concentration is constant, regardless of changes in the flow pattern from the ventilator. Preliminary testing in our laboratory shows this system to be precise regardless of ventilatory pattern. It bears emphasis, however, that this system differs from previously described inspiratory injection systems because those systems (unlike the INOvent Delivery System) do not vary the injection of NO with changes in ventilatory pattern.

It is important that NO delivery systems provide a precise and predictable NO concentration to avoid complications resulting from inaccurate dosing. The delivered NO dose should not change with changes in ventilatory pattern. Dose-response studies of inhaled NO can only be compared if they deliver a constant NO concentration. The only system that we evaluated that met these criteria was the premixing system. Inspiratory injection systems that vary the NO injection with changes in ventilatory pattern may be desirable, pending laboratory and clinical evaluation of such systems as they become commercially available.

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References


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An Algorithm for Quantifying Blood Pressure Lability

To the Editor—Reich et al.¹ have developed and preliminarily validated an algorithm for quantifying blood pressure lability. The problem is clinically significant, and the authors' use of receiver-operating characteristic curves to finetune their system for optimal results seems meritorious.

However, the authors' system does not appear to be an expert system by the conventional use of the term. Consequently, the keyword classification of the article appears incorrect. Further, the first sentence of the conclusion from the abstract, which reads, "One potential application of expert systems to anesthesia practice is a smart alarm to detect blood pressure lability," is a nonsequitur because of this.

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