Evidence-Based Medicine Analysis of Mechanical Insufflation-Exsufflation Devices

To the Editor:

Evidence-based medicine has become the accepted standard[1] for validating treatments. However, although evidence-based medicine purports to consider the best available evidence, whether that be randomized double-blind placebo-controlled trials or not, treatments not justified by randomized double-blind placebo-controlled trials are largely denigrated, as in the recent paper by Auger et al.[2] Most importantly, however, evidence-based medicine grounded in randomized double-blind placebo-controlled trials is irrelevant when the intervention takes the place of a life-preserving function or vital organ and use of a placebo would result in certain morbidity or death. This would be the case by withdrawing continuous noninvasive ventilatory support from patients who have little to no measurable vital capacity[3,4] or when pulmonary morbidity is otherwise inevitable by not clearing congested airways due to ineffective cough flows.[5] Remarkably, this stark limitation of randomized double-blind placebo-controlled trials has been ignored. For example, for renal failure, no placebo control is possible for dialysis or organ transplantation, nor is one possible for parachutes that essentially substitute for wings.[6] Anyone with profuse airway secretions who cannot generate effective cough flows will develop acute respiratory failure and, if intubated, will fail extubation. Whereas controlled studies can compare different methods of augmenting cough flows, those with placebo controls (augmenting vs nothing) cannot be ethically subject to meta-analysis for high-quality randomized double-blind placebo-controlled trials.

In 2011, we reported 101 continuous noninvasive ventilatory support-dependent subjects with Duchenne muscular dystrophy. They had "… a mean [vital capacity] 176 ± 102 mL, or 3% of predicted normal, which is not compatible with survival without continuous ventilator support … [and] 31 consecutive intubated Duchenne muscular dystrophy subjects who failed extubation at other institutions and/or failed ventilator weaning parameters and spontaneous breathing trials were successfully extubated …" to continuous noninvasive ventilatory support thanks, in large part, to mechanical insufflation-exsufflation, despite vital capacities as low as 80 mL.[5] In the paper by Auger et al,[2] the authors did not even consider the study worth citing, although it is certain that our continuous noninvasive ventilatory support-dependent subjects with respiratory infections could not possibly have survived without a tracheostomy tube without the effective airway clearance by mechanical insufflation-exsufflation.

Randomized double-blind placebo-controlled trials are certainly necessary to demonstrate minor evidence-based medicine-supported improvements on major life-preserving breakthroughs, but they cannot be used when those breakthrough interventions substitute for critical life-preserving functions, as does mechanical insufflation-exsufflation for any population with inadequate strength to clear airways by coughing. It must also be pointed out that in all of the controlled studies cited by Auger et al,[2] mechanical insufflation-exsufflation was used at grossly inadequate pressures, since the 40 cm H_2O of currently available devices is not equivalent to the 40 mm Hg pressures at which mechanical insufflation-exsufflation was studied and used effectively in the 1950s.[3]

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Evidence-Based Medicine Analysis of Mechanical Insufflation-Exsufflation Devices—Reply

In reply:

We thank Dr Bach and colleagues for all of their comments, and we want to take this opportunity to reemphasize a few points of our publication. Evidence-based medicine is often contrasted to the real world of clinical practice. However, in our opinion, they are not contradictory but complementary.

From a methodological point of view, randomized controlled trials are the most rigorous way of determining whether a cause-effect relation exists between a treatment (drugs or medical devices) and a clinical outcome.[1] It is the best way to avoid the risk of bias. The use of placebo groups is still an unresolved debate.[2] Even if proven-therapy trials can be thought ethically preferable to placebo-controlled trials, the reality is more complex.

Robust published studies on treatments used in current practice regularly reflect the lack of demonstration of their effectiveness. The use of adaptive servo ventilation based on limited data is a good example.[3-5] It was only after the SERVE-HF study was conducted that the cardiovascular risk in treated

patients was discovered.[6] The mortality rate in the intervention group was statistically higher than in the control group (10%/y vs 7.5%/y). These results have surprised the medical community and led to a safety alert. Although the SERVE-HF study was also criticized, it had the merit of formally highlighting the lack of evidence-based knowledge in this field.

Another example is chest physiotherapy, which was commonly used for bronchiolitis in infants. The available evidence now demonstrate that it is not effective. Its risk/benefit seems even unfavorable. A Cochrane review of 9 studies, carried out on 891 infants hospitalized for bronchiolitis, demonstrated no difference between children treated with or without physiotherapy,[7] neither in terms of clinical outcome nor considering blood oxygenation, breathing frequency, duration of illness, and duration of hospitalization. Many adverse effects of physiotherapy, such as vomiting, pain, and even rib fractures (one fracture per 1,000 treated infants) are highlighted in these 9 studies. The 2016 update confirms the need for clinical evidence to adapt clinical practice.[8]

We pointed out in our discussion that designing a randomized study with a treated group versus an untreated group is sometimes difficult to consider due to ethical considerations.[9] However, different experimental designs are available when conventional trials cannot be applied to the clinical development of medical devices.[10] Aware of the difficulties of conducting randomized controlled studies, we decided to also consider observational studies to collect information on safety data in our systematic review.

The work of Bach et al[11] in 2011, dealing with continuous noninvasive ventilatory support in subjects with Duchenne muscular dystrophy, is clearly interesting in that it provides descriptive information on the impact of noninvasive ventilation associated with mechanical in-exsufflation on patient survival. However, we wish to emphasize that the aim of our work was to evaluate the current level of evidence available for the use of mechanical in-exsufflation devices for airway clearance in patients with neuromuscular diseases.[9] The purpose of this evidence-based evaluation is to provide the basis for health-care professionals' working group discussions to make public health recommendations.

To conclude, we believe that patients, caregivers, and health-care professionals need evidence-based data to be able to benefit from factual information so that they can take or deliver treatments in an informed manner.

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