conscious animals. The MAP values as well as left ventricular dP/dt observed by Sun et al. using intermittent intravenous pentobarbital anesthesia are, in fact, excessive when compared to values reported in the literature for swine anesthetized with pentobarbital (3). This suggests that the “control” values reported by Sun et al. are supranormal, possibly reflecting enhanced sympathetic tone of uncertain etiology. We would therefore agree with Sun et al. that these differences of concern to them are due to differences in experimental procedures between our laboratories. However, they are not reflective of inadequate technical skills in our laboratory used in the acquisition and interpretation of hemodynamic data.

Our data do, in fact, support the observations of Sun et al. In a prior publication (4), they reported no differences between defibrillation waveform groups with respect to first shock success or clinically important indexes of postresuscitation cardiac function after a 4-min period of ventricular fibrillation (VF). Observed differences appear to resolve rather than evolve during extended observation. Sun et al. have previously acknowledged the effect of prolonged pentobarbital anesthesia on cardiac mechanics (5). We likewise observed no differences during observation after a 5-min VF period. It would appear that the “best” defibrillation waveform for the treatment of VF of 4- to 5-min duration would be the one that is first available.

We have not systematically investigated the differences between defibrillation waveforms in the management of VF of >5-min duration. It is very likely that if we administered monophasic waveform energy doses similar to those used by Sun et al. in their 7-min swine model (4), an average dose approximating 57 J/kg, we would observe results similar to what they have reported. In our hospital’s recent six-year clinical experience with out-of-hospital sudden cardiac death, the largest energy dose used in any patient has been approximately 33 J/kg delivered with seven countershocks. Since the energy doses reported by Sun et al. far exceed what is encountered in BiPAP treatments with EPAPs of 8 to 10 cm H₂O. Patients begun on regimens of any lower pressures are titrated up to a level of ≥10 cm within 1 min of placement of the nasal mask. In the study of Sharon et al., patients were begun with EPAPs of 3 cm H₂O and increased by 1 cm every 3 to 4 min to a maximum of 5 cm H₂O. Given these parameters, we are surprised that the authors experienced any success at all. These pressures are far too low and titration is far too slow for patients with acute respiratory distress. When applied at the higher pressures, BiPAP-treated patients demonstrate marked improvements within a few breaths and are clinically out of danger for ETI within 2 to 3 min.

The presence of positive creatine phosphokinase (CK) markers in BiPAP-treated patients is an artifact of the rapid drop in left ventricular wall pressures that occurs when the BiPAP is applied. There is a washout effect that produces a narrow spike in CK that exceeds normal thresholds for acute myocardial infarctions, although the total amount of CK is the same as that which is slowly washed out over an extended period of time with conventional therapy.

In summary, we believe that the poor outcomes described in the article by Sharon et al. (1) comparing bilevel positive airway pressure (BiPAP) ventilation with intravenous isosorbide-dinitrate in patients with severe pulmonary edema. These findings are in marked contrast to our own research and experience with this modality (2–4). We routinely use BiPAP ventilatory support in those patients with severe pulmonary edema with acute respiratory failure and imminent need of endotracheal intubation (ETI). Our success rate at avoiding ETI is generally >90% in patients more severely ill than those described in the study by Sharon et al. Our patients receive sublingual nitroglycerin (0.25 mg) along with sublingual captopril (25 mg) to supplement their respiratory support. Although intravenous nitrates may be ideal, we find use of the sublingual route can frequently reverse a patient’s respiratory distress before intravenous access is even established.

The fact that two dramatically different outcomes are described for the same intervention may be explained by variations in the overall treatment of the two populations. Our research has shown that an independent predictor of BiPAP failure and subsequent ETI is the use of morphine sulfate. Even moderate amounts such as those used in the study of Sharon et al. seem to be enough to interfere with a patient’s abilities to successfully use the BiPAP system.

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In treating acute pulmonary edema, high expiratory positive airway pressures (EPAPs) are required, and we routinely begin our BiPAP treatments with EPAPs of 8 to 10 cm H₂O. Patients begun on regimens of any lower pressures are titrated up to a level of ≥10 cm within 1 min of placement of the nasal mask. In the study of Sharon et al., patients were begun with EPAPs of 3 cm H₂O and increased by 1 cm every 3 to 4 min to a maximum of 5 cm H₂O. Given these parameters, we are surprised that the authors experienced any success at all. These pressures are far too low and titration is far too slow for patients with acute respiratory distress. When applied at the higher pressures, BiPAP-treated patients demonstrate marked improvements within a few breaths and are clinically out of danger for ETI within 2 to 3 min.

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In summary, we believe that the poor outcomes described in the article by Sharon et al. reflect more problems with the manner in which the BiPAP was utilized than a failure of the therapy itself.

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Effectiveness of BiPAP for Congestive Heart Failure

We were surprised to read the poor results described in the article by Sharon et al. (1) comparing bilevel positive airway pressure (BiPAP) ventilation with intravenous isosorbide-dinitrate in patients with severe pulmonary edema. These findings are in marked contrast to our own research and experience with this modality (2–4). We routinely use BiPAP ventilatory support in those patients with severe pulmonary edema with acute respiratory failure and imminent need of endotracheal intubation (ETI). Our success rate at avoiding ETI is generally >90% in patients more severely ill than those described in the study by Sharon et al. Our patients receive sublingual nitroglycerin (0.25 mg) along with sublingual captopril (25 mg) to supplement their respiratory support. Although intravenous nitrates may be ideal, we find use of the sublingual route can frequently reverse a patient’s respiratory distress before intravenous access is even established.

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REFERENCES


REPLY

We have read with great interest the letters by Sacchetti et al. and Bellone et al. As stated in the introduction of our article, it was also the impression of all physicians in our institution involved in the care of patients with pulmonary edema that BiPAP is indeed helpful in its treatment. However, as is the case in many other treatment modalities, sometimes the clinical impression does not hold in the face of rigorous randomized studies. Therefore, we have tried in the discussion part of our manuscript to suggest a few mechanisms to explain the failure of BiPAP in our patient population. What was especially alarming to us was that the results in the BiPAP arm were worse than our previous experience with simple medical therapy (without high-dose nitrates). Accordingly, we decided to discontinue the study prematurely.

Regarding the remarks by Sacchetti et al. and Bellone et al.: Firstly, it is possible that some of the harmful effect we observed was due to combination of BiPAP ventilation with morphine (although it will be very hard from an ethical point of view to deny patients this small amount of morphine, which is a proven treatment for pulmonary edema). Secondly, we have chosen BiPAP rather than CPAP for our study because BiPAP has some advantage over CPAP by increasing the tidal volume. Also, it was our subjective impression that patients tolerate BiPAP better than CPAP. Thirdly, regarding the BiPAP pressures used in our protocol, it is possible that the moderate pressures we used in the BiPAP arm were not enough and higher pressures would have produced a better effect. However, from our experience, it seemed to us that patients usually do not tolerate higher pressures. Hence, we started with lower pressures and increased the pressures gradually. Furthermore, again taking into account that these two treatment arms were not compared directly, it seems that the patients in the BiPAP arm of our study fared worse than our historical controls that underwent exactly the same treatment without BiPAP. If the assumption of Sacchetti et al. and Bellone et al. were correct, then we would expect that the results of the BiPAP arm would be the same as conservative treatment (basically, if we administered too little BiPAP it should be the same as administering a lot of oxygen only).

Regarding the pH and PCO2 measurements suggested by Bellone et al., these were not performed, because the treatment was administered at the patients’ homes by paramedic units, which are not equipped for such measurements.

Finally, regarding the early CK peak induced by BiPAP, we are not aware of any randomized study demonstrating this event. However, the negative results in our study included not only high CK but also an increased rate of mechanical ventilation, lower O2 saturation, and increased total events. Furthermore, what we have observed was that in the BiPAP arm more patients had an increase in CK into the MI range. In the others we did not observe a CK increase at all. Therefore, we believe that this cannot be explained by early CK release, because the patients who did not have an MI did not have CK release at all.

Since the publication of our study, another randomized study comparing BiPAP ventilation, with conservative treatment using oxygen, morphine, furosemide and low-dose nitrates, was published (1). In this study, the outcome of patients treated by BiPAP ventilation was better than in the control arm, although the study was small (as was our study) and there were significant inequalities in baseline parameters between the two groups. Therefore, we believe that the resolution of this important issue will need further, larger randomized studies.

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