The role of magnesium sulphate in the treatment of persistent pulmonary hypertension of the newborn

To the Editor

Daffa and Milaat[1] presented a clinical study highlighting the role of magnesium sulphate ($MgSO_4$) in the treatment of persistent pulmonary hypertension of the newborn (PPHN). We were quite interested to know in details the initial therapeutic measures those babies received before the use of $MgSO_4$, as the majority of them have underline pulmonary disorders. Furthermore, there was no mention of the ventilatory management strategies adopted by the treating team. Recently, the gentle ventilation technique has received a lot of attention and hyperventilation modality has been avoided mostly to prevent further lung damage and hypocarbia with it's adverse neurological sequel. Moreover, the role of surfactant replacement therapy (SRT) has not been mentioned in the treatment, particularly as ≥ 90% of the cases have underline pulmonary diseases (meconium aspiration syndrome, congenital pneumonia). Surfactant replacement therapy has been shown to improve oxygenation and ventilation by improving lung compliance and optimizing gas exchange, which may play a major role in the prevention or treatment of PPHN. The authors did not mention the hemodynamic support of their patients although, most of them sustained birth asphyxia which causes compromised myocardial contractility and poor tissue perfusion that worsens the PPHN. The cardiovascular support improves cardiac output, tissue perfusion, and decreases right to left shunting at atrial or ductal levels. The great positive impact of cardiovascular support, either by volume expanders, inotropes or both, on the overall stabilization of these critical patients has been well recognized.[2,3] We would like to share with you our preliminary data about the use of $MgSO_4$ in the treatment of PPHN which was presented in the Pediatric and Neonatal Symposium, 1998, Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia. Eleven newborn infants with respiratory failure and severe PPHN, and a predicted mortality of 100%, based on alveolar-arterial oxygen tension difference (A-aDO2), were included in a clinical trial to determine the efficacy of $MgSO_4$ as a life saving therapy after they failed to improve with the conventional treatment of PPHN (gentle ventilation, hemodynamic support and alkalinization). A loading dose of 200 mg/kg $MgSO_4$ was given over 30 minutes, followed by continuous infusion of 50-100 mg/kg/hour to maintain serum magnesium concentration between 3.5-5.5 mmol/L. No other vasodilator drug was used before or during the treatment with $MgSO_4$ and patients were not hyperventilated. Mean (SD) duration of treatment was 115.2 (20.1) hours. Baseline arterial oxygen tension (PaO_2) and hemoglobin oxygen saturation (SpO2) had mean (SD) values of 42.86 (5.7) mm Hg and 74% (11.2) which started to increase a few hours after $MgSO_4$ infusion with no significant change in pH and PCO^2. Both PaO_2 and SpO_2 increased significantly after 24 hours to 93 (26.8) mm Hg and 96.8% (1.9). Alveolar-arterial oxygen tension difference was significantly lower after 24 hours: 641.5 (11) to 455.7 (56.7) mm Hg. Peaked inspiratory pressure could be significantly reduced from 35.8 (4.4) to 24.4 (3.3) cm H_2O after 72 hours. Mean ventilatory time support and total oxygen dependency were 12.8 and 16 days. Systemic hypotension and bradycardia were frequently noted. Nine infants survived (82%).

To date, there are several clinical studies[4-7] evaluating the effects of $MgSO_4$ therapy in the management of PPHN, but unfortunately, none of the published studies was prospective, randomized, and controlled. Therefore, the question, "What is the exact role of $MgSO_4$ in the treatment of PPHN?" still remains to be answered! Magnesium is a non-specific vasodilator, and while potentially lowering pulmonary vascular resistance, has been shown to cause a fall in systemic blood pressure in neonatal models of hypoxic or septic pulmonary hypertension. Several clinical trials have noted beneficial effects in human newborns, which may have been due to other effects of magnesium (for example sedation, muscle relaxation, bronchodilation and cardioprotection). Furthermore, Ryan et al[8] in an animal study have shown that unlike nitric oxide, $MgSO_4$ is not a selective pulmonary vasodilator and may lead to deleterious effects on systemic pressures in critically ill newborns. Therefore, at this point of time, the management of PPHN remains supportive rather than curative. Indeed, given the wide array of causes of PPHN, it is unlikely that any one therapy will be universally effective.

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