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Letter to the Editor

Utility of brain natriuretic peptide in the neonatal pathologies

Sir,

This is with reference to the recently published article titled 'N-terminal pro brain natriuretic peptide as a marker of myocardial dysfunction in newborns with perinatal asphyxia' by Drs. Kariyappa et al.[1]

The authors deserve to be congratulated on the study. The study adds to our understanding and appreciation of hypoxic ischemic encephalopathy (HIE) as well as associated morbidities.

The study primarily focused on understanding the relationship between NT proBNP and hypoxic ischemic encephalopathy. The authors present their findings that the level of NT pro BNP increased with severity of the encephalopathy.

Here, I wanted to emphasize and bring forth some methodology and statistical issues with the study that if addressed, may help further strengthen the study. The authors acknowledge that increasing BNP with the severity of HIE has been previously documented by. Jain et al, as well as by Simović et al.[2,3] From clinicopathologic relation standpoint it would be extremely beneficial to demonstrate if there was an interaction between BNP levels and the pH, bicarbonate level, age of the patient another clinical finding. This would further strength in the study. Relative hypoxia and ensuing acidosis can lead to myocardial depression. Additionally, the brain injury can increase the catecholamine surge significantly leading to further stress on the myocardium. The authors show that pH and bicarbonate levels themselves did correlate with the stage of HIE. Therefore, we need to understand what the added benefit of performing the BNP would be. Using appropriate statistical methods, the authors may be able to demonstrate that the level of BNP elevation is a better predictor of mortality and or other outcomes if supported by data. We would recommend performing a univariate analysis followed by multivariable analysis to ascertain the relationship between BNP level and stage 3 HIE as well as BNP level and mortality. This would demonstrate the superiority of and the value of obtaining BNP levels.

Lack of echocardiogram limits the establishment of clear association between BNP levels and cardiac dysfunction in this particular setup. This is important since BNP has been shown to be elevated in persistent pulmonary hypertension of newborn (PPHN) even in the absence of cardiac dysfunction.[4] Therefore, separation of the source of elevated BNP may be useful. This should be acknowledged in the report. On a minor note, it would also beneficial to clarify that the pH / bicarbonate values reported in the study are from venous blood gas or were obtained separately from other sources. The authors describe obtaining the samples within 3-6 hours of life. Therefore, we would modify the conclusion to suggest that early BNP within first 6 hours of life rather than the stated 48 hours, correlates with the stage of HIE. Similarly, the phrase 'rising BNP' in conclusion implies that there were serial measurements, which they were not.

Lastly, the discussion about therapy is vital. Myocardial depression and more importantly, the cardiovascular derangements in birth asphyxia can be well supported.[5] In fact, in majority of these cases, they may be reversible. Therefore, early recognition of cardiovascular derangement is vital and should trigger appropriate therapies. Elevated BNP at screening along with persistently elevated BNP after 24 hours may be an appropriate adjuvant or surrogate depending on available resources. Therapies could be in the form of interventions to decrease metabolic demand, consideration for therapeutic hypothermia, use of supplemental oxygen, correction of acidosis and lastly inotropic support. Early use of milrinone or dobutamine could be valuable in reversing the cardiac depression and thereby potentially modifying the outcome. Although the outcomes may be dependent on various factors, identifying the modifiable factors such as cardiac dysfunction may be extremely important.

Again, the study represents an opportunity to take the field further and therefore would encourage continued focus on this very important area.

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