

Before Diagnosing Paroxysmal Sympathetic Hyperactivity in PICU Patients Alternative Conditions must be Considered

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Keywords: Paroxysmal sympathetic hyperactivity, Pediatric, PICU, Sympathetic overactivity, Vegetative nervous system.

Indian Journal of Critical Care Medicine (2024): 10.5005/jp-journals-10071-24645

We read with interest Agrwal et al.'s article on a study of five pediatric patients with definite and 30 patients with incomplete paroxysmal sympathetic hyperactivity (PSH) syndrome.¹ Patients with definite PSH had a longer duration of mechanical ventilation, a longer PICU stay, and higher PRISMIII scores compared with patients with incomplete PSH.¹ It was concluded that PSH is common in children with neurological diseases admitted to the PICU, and that these children had higher disease severity scores, longer duration of mechanical ventilation, and longer PICU stay than controls.¹ The study is excellent, but some points should be discussed.

A limitation of the study is that parameters, such as T4/T4, basal cortisol levels, or the serum catecholamine levels were not analyzed in patients with PSH or in patients with incomplete PSH. Since PSH is believed to be due to hyperstimulation of the sympathetic nervous system, various causes, such as hyperthyroidism, hypercorticism, or hyperadrenalism should be excluded.

A second limitation is that cardiac causes of sympathetic overactivity have not completely been ruled out. Did any of the patients with PSH or incomplete PSH suffer from heart failure, malignant ventricular arrhythmias, atrial fibrillation, myocardial infarction, Takotsubo syndrome (TTS), or pulmonary hypertension? Stress cardiomyopathy must be sufficiently ruled out, especially in patients with central nervous system (CNS) disease.

A third limitation of the study is that cerebral imaging results were not reported. Since four of five patients with definite PSH and nine of the 30 patients with incomplete PSH had CNS disease, provision of cerebral imaging results is mandatory. It would be also interesting to know how many patients had lesions of the hypothalamus, pituitary gland, or CNS sympathetic tract lesions, that is, structures which can be responsible for sympathetic overactivity.

A fourth limitation is that the medications the included patients took during PICU stay were not reported. Of particular interest is to know how many of the patients received adrenergic medications to maintain cardiac output and blood flow and how many received cholinergic drugs to maintain cognitive functions, digestion, heart rate control, and blood pressure control.

A fifth limitation is that there is no mention of blood gas analysis results or electrolyte imbalances. We should know how many of the patients had acidosis, alkalosis, or electrolyte imbalances. It is also important to know how many of them had severe kidney failure.

We disagree that incidence figures for PSH have been calculated. Incidence is defined as number of patients/100,000/

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How to cite this article: Finsterer J. Before Diagnosing Paroxysmal Sympathetic Hyperactivity in PICU Patients, Alternative Conditions must be Considered. *Indian J Crit Care Med* 2024;28(5):516–517.

Source of support: Nil

Conflict of interest: None

Completing interests: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Availability of data and material: All data are available from the corresponding author.

year. The authors calculated the frequency for only a single center, which does not mean "incidence" per definition.

In the discussion, it is stated that four patients suffered from viral meningoencephalitis, but in the results section, it is mentioned that only two patients suffered from viral meningoencephalitis, one from bacterial meningitis, and one from tuberculous meningitis. This discrepancy should be resolved.

There is also a discrepancy between the "Data collection" section and the "Outcome variables" section.¹ In the "Data collection" section, the outcome was defined as "improvement or death" while in the "Outcome variables" section, the primary outcome was defined as "incidence of PSH" and secondary outcome was defined as "association of PSH with mortality and morbidity, such as requirement of mechanical ventilation, length of PICU stay, and ventilation".¹ This discrepancy should be resolved.

In summary, the excellent study has limitations that should be addressed before drawing final conclusions. Clarifying the weaknesses would strengthen the conclusions and could improve the study. In patients with definite or incomplete PSH, alternative causes of sympathetic hyperstimulation must be excluded.

AUTHOR CONTRIBUTION

JF was responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave

final approval. SM: contributed to literature search, discussion, correction, and final approval.

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