EDITORIAL

Withdraw Sedation Gently or Face Withdrawal Syndrome!

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Critically ill children and neonates were often cared for without sedation and analgesia until the early 1990s.[1] Studies done at this time demonstrated that postoperative and ICU sedation and analgesia were important not only for humane care but also to decrease morbidity and even mortality. From these studies emerged the awareness that sedation and analgesia are important while caring for sick neonates and children.[2]

Today, sedation and analgesia are among the most important supportive therapies given to critically ill children, especially those on mechanical ventilation. However, like all other therapies, these therapies are not without ill effects. Children are unique as far as adverse effects of sedation–analgesia are concerned as they often encounter tolerance and withdrawal syndrome.[3,4]

Withdrawal was first described in the adult literature (opioid addiction related) and among neonates (when they were born to opioid-addicted mothers), but the recognition that this syndrome could be seen in pediatric patients was in the 1990s.[5] Arnold et al. have given the first description of this entity in neonates and noted that the same could occur in infants too. Tobias et al. reported a protocol to prevent and treat opioid withdrawal.[6,7]

Iatrogenic withdrawal syndrome (IWS) is a clinical syndrome that manifests after stopping a sedative–opioid drug after prolonged exposure.[5,8] The manifestations include autonomic dysfunction, gastrointestinal disturbances, and neurologic and motor abnormalities.[4] Studies assessing the risk factors for the syndrome have found younger age (especially those under six months of age), those with preexisting cognitive impairment, higher severity of illness, and higher nursing workload to be important risk factors. Lack of a sedative weaning protocol has also been considered as one of the risk factors.

In this issue of the journal, Tiacharoen et al. report the withdrawal syndrome in children assigned to a sedation weaning protocol and compared this to usual care in a pilot randomized controlled study in critically ill children.[9] Most of the intensivists do wean sedation and analgesia, but there is no fixed protocol for the same. The sedation weaning protocol used in this study is fairly well worked out and is derived from previous studies and includes inputs from clinical pharmacists. The authors have shown that it is feasible to implement such a sedation weaning protocol and the strength of the study lies in this protocol. Further validation of this protocol would require larger numbers to be studied and use by other units.

Unfortunately, the study has several limitations. While the authors did calculate a required sample size, they excluded many patients for rather flimsy reasons and the ultimate number studied is very small, and hence, no definitive results have been shown. The number of exclusions for probable drug interactions with methadone (n = 36) and exclusion of five patients for suspected allergies to sedative medications are definitely too large a number, especially since the sample size determined was 46 (23 in each group) and the final number studied was only 30 (19 and 11 in intervention and control groups, respectively).

The tools used for assessment of sedation (State Behavioral Scale) and IWS (Withdrawal Assessment Tool 1 or WAT 1) were appropriate, though it is not clear whether the nurses assessing the WAT 1 scores were blinded to the sedation weaning group. Iatrogenic withdrawal syndrome was seen in 83% of the patients and was no different between the intervention and control groups. The prevalence of IWS in this study is quite high, even if we consider that the median duration of sedation infusion was 10 days. Most of the studies would suggest IWS prevalence rates of 35–57% after five or more days of the infusion of benzodiazepine and/or opioids.[10,11] It is not clear from the study whether the sedation was interrupted every morning to titrate the further need, as has been recommended.[12] Moreover, randomization started after a particular dose of fentanyl and midazolam infusions was reached; it is not clear how the sedation was weaned until this level. Also, the patients were classified into high risk and low risk for IWS, but numbers are so small that this did not influence the prevalence of IWS.

In spite of these limitations, the authors have demonstrated small benefits in terms of reduction in the number of days that the children demonstrated withdrawal symptoms ("withdrawal days"), rescue medications given for withdrawal symptoms, and the length of pediatric intensive care unit (PICU) stay. However, it should be noted that the control group had a higher PRISM III score which could have influenced the longer duration of the PICU stay. The duration of mechanical ventilation and sedation infusions also seem longer than necessary for the given severity of illness.

The PICU is often manned by trainees at different levels of experience and some of them may be unfamiliar with weaning of sedation/analgesia. In such circumstances, the weaning protocol is a welcome addition and may streamline this otherwise difficult process.

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