Asking the correct questions of push dose vasopressors

Dear Editor,

I read with interest the article published by Rotando and colleagues entitled "Push dose pressors: Experience in critically ill patients outside of the operating room" [1]. Research regarding the efficacy of bolus or "push dose" vasopressors is important and more research is necessary. The results of trial merit further discussion, particularly those pertaining to push dose phenylephrine.

The article reported a much higher rates of adverse events (11.6%) compared to other trials. The authors attributed this to the expanded definition of adverse events that was used. One of the adverse event criteria was heart rate increase by >30%, which occurred in 5.8% of patients that were administered phenylephrine. Phenylephrine does not have activity at β_1 receptors and has been associated with reflex bradycardia in prior reports due to α_1 receptor activity [2,3]. Administration of phenylephrine is very unlikely to cause an increase in heart rate. The heart rate increases observed in this study were likely due to pain, anxiety, other interventions, or underlying illness and this outcome should not have been reported as an adverse effect of phenylephrine. On a similar note, dysrhythmia is also unlikely to develop following phenylephrine administration due to lack of β_1 activity. Unfortunately, the case of dysrhythmia is not described in detail in the article. However, it is quite likely that this developed as a result of the patient's underlying illness or stress response as opposed to phenylephrine. If the tachycardia and dysrhythmia adverse events are eliminated from the results, the phenylephrine adverse event rate from this trial is similar to the event rate observed in prior studies [4,5].

The article also reported that medication errors, in particular dosing protocol violations, occurred in 10.3% of patients receiving push dose phenylephrine. The protocolized maximum dosing threshold of >200 μg was chosen based off of intraoperative data. However, the appropriate push dose of phenylephrine to administer in critically ill patients is unknown. Swenson and colleagues reported that phenylephrine doses of <200 μg were only associated with moderate increases in blood pressure and that a doses >200 μg were more likely to yield a significant increase in blood pressure [4]. It is possible that providers in the article by Rotando violated the protocol because they did not believe that the recommended dose was appropriate. Also it was not reported if adverse events were more common in patients receiving doses above 200 μg. With no clear threshold established for safety and efficacy of push dose phenylephrine, the clinical significance of these medication errors is unclear.

Administration of push dose vasopressors carries important safety risks. Medication errors have been reported and the drugs can cause adverse effects through their own mechanisms [6]. However, push dose vasopressors have the ability to provide great value to the care of critically ill patients. They can be stored in automated dispensing cabinets, can be safely administered peripherally, and can readily restore hemodynamic stability. Use of push dose vasopressors may also prevent the need to initiate a vasopressor infusion, an outcome that was reported in the article by Rotando (28% of patients were started on continuous infusion vasopressors following administration of push dose vasopressors) [1]. In order to gain an appreciation for the relative risks and benefits of push dose vasopressors, future trials should report on safety outcomes that are attributable to pharmacologic activity of the medication being administered and clinically relevant.

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