toms in another patient that were believed to be a result of exposure to propylene glycol from the use of high-dose continuous lorazepam. This prompted a MEDLINE search. Although no published data were found regarding lorazepam and this effect, several reports confirmed that a similar constellation of symptoms was believed to be secondary to the propylene glycol content of etomidate, nitroglycerin, and silver sulfadiazine. Each milliliter of lorazepam 2 mg/mL was found to contain 0.18 mL of propylene glycol in the formulation. Therefore, the patient was receiving 2.25 mL of propylene glycol per hour. We considered switching the infusion to diazepam as reported by Watling et al., but we found that each milliliter of diazepam 5 mg/mL contained even more propylene glycol, at 0.4 mL. We therefore opted to discontinue the lorazepam infusion over 2 hours after replacing it with continuous midazolam at 12 mg/h. Midazolam 5 mg/mL was found to have no propylene glycol in its formulation, but does have benzyl alcohol 1% as a preservative. Subsequently, the continuous midazolam was increased to as much as 45 mg/h and the morphine was increased to 35 mg/h. The patient’s hyperosmolality resolved within 24 hours, which was consistent with other case reports. Vasopressor and PRBC requirements decreased and the knee effusions resolved over the next several days.

Discussion. This case illustrated to us the importance of monitoring therapies previously reported as safe, especially when doses are escalated. Such increases put the patient at risk of adverse reactions from the parent product, or in this case, an additive in the product formulation. Because the patient was 15 years of age, we did not consider the benzyl alcohol content of the midazolam product to be a problem, although for a neonatal patient this may not have been a desirable alternative. We were unable to determine whether the symptomatology in the reported patient developed as a result of duration or extent of exposure to propylene glycol. However, future continuous lorazepam recipients will be carefully monitored for osmolality, osmolal gap, hypotension, and other symptoms potentially related to propylene glycol toxicity.

We also laud the availability of on-line information, in this case PICUNET. An on-line report of a similar occurrence was discussed with another pediatric intensivist, who confirmed a similar experience. This is a growing means of rapidly providing and obtaining interesting and helpful reports of experience from other healthcare practitioners.

REFERENCES


AUTHORS’ REPLY: We are pleased to see the letter from Seay and Graves. The reason we wrote the article concerning sedation in the intensive care unit with high-dose benzodiazepines and narcotics was for exactly the reasons they cite. It is our impression that the use of high-dose benzodiazepines and narcotics has become a common practice for sedation to facilitate mechanical ventilation. Our concern was and is that too little is known about the use of these agents in high dosages for prolonged periods of time. We believe the approach we described was and is the best available, but certainly one that is not adequately studied or without risk.

We have been concerned about the possibility of propylene glycol toxicity. We agree with Seay and Graves that the reported cases of propylene glycol toxicity may not actually be attributable to this agent. This problem is inherent in the patients receiving this type of sedation because of their multiple problems and the numerous treatments they are receiving. However, propylene glycol toxicity should be considered. We have taken several steps to minimize and monitor patients for the problem: (1) When high dosages of benzodiazepines are needed, the use of diazepam rather than lorazepam reduces the total amount of propylene glycol delivered if smaller dosages of diazepam produce the same level of sedation, which is our experience. (2) In patients receiving high dosages of drug, we monitor for metabolic acidosis and check serum osmolality periodically. Our toxicology laboratory has set up a propylene glycol assay, and in patients at risk we monitor the concentrations. This is especially true of patients with renal failure. (3) The use of oral solutions, as described in our article, may also help by reducing the amount of propylene glycol absorbed, but the extent of gut absorption is not clear.

We hope that similar reports concerning the use of high-dose benzodiazepines and narcotics as a method to facilitate long-term mechanical ventilation will be forthcoming.

JOHN YANOS MD

Correction: RSV immune globulin intravenous

TO THE EDITOR: Concerning the recent article on respiratory syncytial virus immune globulin intravenous (RSV–IGIV), a reader has questioned the information provided about coadministration of RSV–IGIV and measles, mumps, and rubella (MMR) vaccine. On review of the article, I realize the material may have been misleading. Specifically, the sentence being questioned reads: “If the MMR vaccine is given before RSV–IGIV, a 1-month separation period between the two products is recommended.” The manufacturer’s information recommends that if
MMR vaccine is given during or within 10 months after RSV-IGIV administra­tion, then reimmunization is recommended. The report by the Advisory Committee on Immunization Practices recommends that with simultaneous administration of MMR vaccine and an immunoglobulin product, the patient should be revaccinated with MMR vaccine 3–11 months after the immunoglobulin product is given. For example, if the MMR vaccine is administered and the immunoglobulin product is subsequently administered with 14 days of the vaccine, revaccination is recommended.2

Currently, no clinical data are available in the literature that specifically address the interaction of RSV-IGIV and live vaccines. However, since RSV-IGIV may interfere with vaccine effectiveness, I recommend that the above guidelines be considered appropriate and prudent.

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