2-1-2006

Pharmacy & Therapeutics Update: Drug Information for Health Care Professionals

Medical University of South Carolina

Paul W. Bush
Medical University of South Carolina

Nannette M. Berensen
Medical University of South Carolina

Kelli L. Davis
Medical University of South Carolina

Holly M. MacFall
Medical University of South Carolina

See next page for additional authors

Authors

Medical University of South Carolina, Paul W. Bush, Nannette M. Berensen, Kelli L. Davis, Holly M. MacFall, and Krystal L. Moorman

MUSC
MEDICAL UNIVERSITY
OF SOUTH CAROLINA

Drug Information Center
Medical University of South Carolina
Department of Pharmacy Services
Charleston, South Carolina

In This Issue

Pharmacy & Therapeutics

Update

Drug Information for Health Care Professionals

February 2006

Evaluation of Propofol Usage and Selected Adverse Events in Pediatric Patients Medication Use Evaluation Results

Background: Propofol is a sedative-hypnotic agent with a short onset and offset of action. It is often used to provide sedation for patients requiring frequent neurologic evaluations.[1,2,3]

Propofol is approved for continuous sedation in adults in the intensive care unit. However, its use for continuous sedation in pediatric patients is not recommended due to concerns of propofol infusion syndrome.[2] Propofol infusion syndrome is a life-threatening condition that manifests as metabolic acidosis, lipemia, bradycardia, myoglobinuria, cardiac failure, and rhabdomyolysis in pediatric patients who receive high-dose propofol for an extended length of time.[2,4] In an evaluation of studies and case reports of propofol infusion syndrome in the pediatric intensive care unit (PICU), Okamoto and colleagues recommended that caution be used for propofol doses higher than 4 mg/kg/hr or for a treatment duration longer than 48 hours.[2] Conversely, several prospective studies have demonstrated safety and efficacy with the use of propofol in pediatric patients for procedural sedation and sedation in the emergency department.[5-7]

Other adverse effects associated with propofol include hypotension, bradycardia, pain on injection, hyperlipidemia, metabolic acidosis, and line infection. Patients should be monitored for these effects. A slow infusion rate is recommended to reduce the risk of hypotension and apnea.[1]

Pain on injection is a common occurrence, but may be decreased or prevented with an injection of lidocaine 1% prior to propofol administration.[1] Because propofol is a phospholipid emulsion, it may increase the risk of hypertriglyceridemia, which could induce pancreatitis. In order to prevent line infections, lines should be changed every 12 hours.

Purpose: The purpose of this medication use evaluation (MUE) was to assess propofol usage and selected adverse events in pediatric patients, evaluate monitoring practices, and devise methods for improving safety.

Methods: Patients were identified for review based on records from the automated medication dispensing system (AcuDose-Rx®) or the pharmacy order entry system (MSMeds™) from August 2004 to April 2005.

Data collected included patient demographics, admitting diagnosis, attending and prescribing physicians, service, location, indication, dose, method of administration, pharmacist order review status, and selected adverse events. The adverse events assessed included pain on injection, bradycardia, hypotension, hypertriglyceridemia, elevations in amylase and lipase concentrations, and metabolic acidosis. Concomitant sedative medications and documentation of propofol bottle and/or tubing changes were also recorded.

Analysis: There were 69 patients and 78 records included in the analysis. Of the 78 records identified, 6 had no documentation of propofol administration on the given date, and 1 patient's medical record could not be obtained.

Of the 69 cases identified, 41 (59%) were female and 28 (41%) were male. Twenty-seven (38%) patients were African American, 30 (42%) were Caucasian, and 1 (1%) was Hispanic. The average age was 10 years, with a range of 2 months to 33 years. The average weight was 39.9 kilograms, with a range of 3.5 to 137 kilograms. Of note, the weight for 2 patients was not reported.

A written order for propofol was documented in the chart in 47 (66%) cases, and an order was present in MSMeds™ in 9 (13%) cases. Orders for propofol were not documented in the chart 30% (n = 21) of the time, and orders were not found in MSMeds™ 86% (n = 61) of the time. The absence of these records may indicate emergent administration of propofol, transfer of the patient from the operating room to another unit, or lack of documentation. The formulary restriction was met for 100% of the cases.

Propofol was ordered for the following indications: continuous sedation (n = 8, 12%), procedural sedation (n = 56, 79%), surgery (n = 6, 8%), and continuous sedation during surgery (n = 1, 1%). Propofol was administered via intravenous (IV) push in 59 (83%) cases and via continuous infusion (CI) in 11 (15%) cases. One patient received propofol by both methods. Propofol was administered via a peripheral line in 38 (54%) cases and a central line in 29 (41%) cases. The type of IV line used for propofol administration could not be determined in 4 (6%) cases. Of the 38 cases of peripheral administration, topical lidocaine was applied in 25 (66%) cases. A total of 31 (50%) patients received lidocaine.

The average initial dose given via IV push was 1.4 mg/kg (range: 0.4 to 4.3 mg/kg). On average, patients received approximately 3 doses during the procedure to maintain sedation (range: 1 to 11 doses). The average total dose given via IV push was 2.6 mg/kg (range: 0.5 to 7.8 mg/kg).

The average initial dose given via CI was 29.6 micrograms/kg/minute (range: 25 to 50 micrograms/kg/minute). No patients received propofol via CI for greater than 72 hours. The minimum average daily dose required was 24.2 micrograms/kg/minute (range: 0.83 to 50 micrograms/kg/minute) and the maximum average daily dose required was 33.7 micrograms/kg/minute (range: 25 to 50 micrograms/kg/minute).

Adverse events (AEs) that were evaluated included pain on injection, bradycardia, hypotension, hypertriglyceridemia, elevations in amylase and lipase, and metabolic acidosis. Documentation of appropriate monitoring for AEs was also assessed. Since propofol was not administered for greater than 72 hours via CI, hypertrigylceridemia and elevations in amylase and lipase were not monitored.

Pain on injection was monitored in 21 (30%) cases. In 2 (10%) cases, pain on injection was reported. One of the 2 patients received lidocaine prior to propofol administration. Blood pressure was monitored in 68 (96%) cases, and hypotension was documented in 26 (38.%) of the monitored cases. The systolic blood pressure decreased an average of 16%, with a range from a 13% increase to 32% decrease. Diastolic blood pressure decreased an average of 25%, with a range from a 58% increase to a 54% decrease. Heart rate was monitored in 66 (95%)

cases, and bradycardia was documented in 5 (8%) of the monitored cases. On average, the heart rate decreased by 25% (range: 10 to 42%).

Metabolic acidosis was defined as an anion gap of greater than 12. Metabolic acidosis was monitored in 14 (19%) cases. Metabolic acidosis was documented in 2 (3%) of the monitored cases. In 1 of the cases, the patient's condition may have contributed to the acidosis. Propofol was administered via CI for greater than 12 hours in 4 patients. In 3 (75%) cases, the propofol bottle and/or tubing changes were documented every 12 hours.

Of the 71 cases of propofol administration, 49 (69%) required other sedatives to be administered. However, the type and dose of medication required was not documented during this evaluation.

Conclusion: These data support that propofol is primarily used in the intensive care units and in the operating room. Doses used are similar to the required doses reported in the literature. Practitioners should be educated regarding appropriate dosing, duration of therapy, monitoring parameters, and adverse events.

Process Improvements: Inservices were provided by clinical pharmacy staff to review proper dosing, and to re-educate the house staff regarding monitoring parameters and pertinent laboratory measures (ie, triglycerides, amylase and lipase concentrations, and arterial blood gases). An entry will be placed on the medication administration record to enhance documentation of bottle and tubing changes.

MUE Team: This MUE was conducted by Dawn Niedermeier, Susan Staggs, Maggie Thomson, Jill Thompson, Nannette Berensen, Kelli Davis, and Holly MacFall.

References are available upon request.

MED•U•WAY Conference to Focus on Hospital Acquired Pneumonia

The next MED•U•WAY Conference will focus on hospital acquired pneumonia. The program will be held on Thursday, March 16, 2006, at 12:00 PM, in 2 West Amphitheater.

The featured speakers will be Patrick Flume, MD, Department of Pulmonary and Critical Care Medicine, Allergy, and Clinical Immunology; Cathy Worrall, BSN, PharmD, BCPS, BCNSP; and Janet Byrne, RN.

Attendees will receive 1 credit hour of continuing education, and lunch is provided. MED•U•WAY is sponsored by the Pharmacy and Therapeutics Committee.

Did You Know...

FDA issued a public health advisory on February 8, 2006, notifying physicians that aprotinin injection (Trasylol®) has been linked to a higher risk of serious adverse events including renal problems, myocardial infarction, and stroke in patients who have undergone coronary artery bypass graft surgery. Physicians who use aprotinin should monitor for the occurrence of toxicity, particularly to the kidneys, heart, or central nervous system. In addition, physicians should consider limiting the use of aprotinin to those cases where the clinical benefit of reduced blood loss is essential to the medical management of the patients and the benefit outweighs potential risks.

FDA issued a public health advisory regarding potential liver toxicity associated with telithromycin (Ketek®) following MedWatch reports and a case review in the *Annals of Internal Medicine* that reported 3 cases of jaundice and abnormal liver function following administration of telithromycin. One patient recovered, 1 required a liver transplant, and 1 patient died. When the livers of the latter 2 patients were examined in the pathology laboratory, massive tissue death was present. These 2 patients had reported some alcohol use. All 3 patients had previously been healthy and were not using other prescription drugs. FDA is also aware that these patients were treated by physicians in the same geographic area. The significance of this observation is not clear at this time.

FDA recently approved human insulin (rDNA origin) inhalation powder (Exubera®) for the treatment of adult patients with type 1 or type 2 diabetes mellitus for control of hyperglycemia. The product is expected to be commercially available by mid-2006.

Formulary Update

The Pharmacy and Therapeutics Committee recently approved the following formulary changes:

Additions:
Effective February 15, 2006
Histrelin acetate implant (Vantas®)

Additions with Restrictions:
Effective February 15, 2006
Caspofungin (Cancidas®) will be restricted to physicians on the hematology/oncology and infectious diseases services.

Iloprost (Ventavis®) will be restricted to attending physicians or fellows on the pulmonary and critical care services.

Automatic Therapeutic Substitutions (ATSs):
Effective March 15, 2006
In adult patients, orders written for benazepril, enalapril, fosinopril, moexipril, perindopril, quinapril, ramipril, and trandolapril will be converted to lisinopril unless "dispense as written" is specified.

Effective February 15, 2006
In adult patients, orders written for ProMod® will be converted to Pro-Stat 64™ unless "dispense as written" is specified.

Changes in Restrictions:
Effective February 15, 2006
Liposomal amphotericin B (AmBisome®) will be available on an unrestricted basis.

Linezolid (Zyvox®) will be restricted per infectious diseases service approval, as per clinical guidelines, or as specified on the hospital acquired pneumonia preprinted order forms.

Line Extensions:
Effective February 15, 2006
Activated charcoal (EZ CHAR®)
25-gram pellets

Dipyridamole (various)
75-mg tablets

Deletions:
Effective February 15, 2006
Bethanechol (Urecholine®)
5-mg/mL vials

Diethylstilbestrol (Stilphostrol®)
50-mg/mL vials

Tetramune®
0.5-mL vials

Activated charcoal (Actidose-Aqua®)
25-gram/120-mL liquid

Adderall®
12.5- and 15-mg tablets

Dibucaine (Nupercainal®)
suppositories

Dipyridamole (various)
5-mg/mL injection

Echothiophate (Phospholine Iodide®)
0.03%, 0.06%, 0.125%, and 0.25% ophthalmic solutions

Epinephrine (various®)
0.5%, 1%, and 2% ophthalmic solutions

Hydroxyprogesterone caproate injection (various)
250-mg/mL injection

Interferon alfa-2b (Intron A®)
5- and 3-mu/mL injection

Leflunomide (Arava®)
100-mg tablets

Lunelle®
50-mg/mL injection

Menotropins (Pergonal®)
75-unit/mL injection

Methotrexate (various)
50-mg/mL injection

Methylprednisolone (Medrol®)
24-mg tablets

Methyltestosterone (Metandren®)
25-mg tablets

Nilutamide (Nilandron®)
50-mg tablets

Nitroglycerin (Nitrobid®)
9-mg extended-release capsules

Oral poliovirus vaccine (Orimune®)
disposable pipettes

Perphenazine (various)
16-mg tablets

Promethazine/codeine (various)
5-mL elixir

Remifentanil (Ultiva®)
1- and 2-mg vials

Rivastigmine (Exelon®)
1.5-, 3-, and 4.5-mg capsules

Theophylline (Slo-Phyllin®)
125-mg extended-release capsules

Ticarcillin disodium (Ticar®)
3- and 20-g injection

Tocainide (Tonocard®)
600-mg tablets

Triamcinolone acetate (various®)
3-mg/mL injection

Triple sulfa (Sultrin®)
vaginal cream and tablets

Urokinase (Abbokinase®)
5000-unit/mL injection

Ramipril (Altace®)
1.25-, 2.5-, 5-, and 10-mg tablets

Cefotetan (Cefotan®)
200-mg/mL injection