

FDA Patient Safety News: Show #67, September 2007

Warning on Colistimethate for Inhalation

FDA is investigating a patient death that may be associated with the inhalation of the antibiotic colistimethate, or Coly-Mycin M. This drug is used to treat serious infections due to Gram-negative bacteria, particularly *Pseudomonas aeruginosa*. It is approved only for intravenous or intramuscular injection, but some practitioners prescribe it off-label as a solution to be inhaled from a nebulizer. The solution is prepared by mixing the drug with sterile water or saline just prior to inhalation.

Colistimethate is a pro-drug that is inactive in its dry state. When mixed with water, it undergoes spontaneous hydrolysis to the bioactive form, colistin, which may cause pulmonary inflammation. Storing the pre-mixed colistimethate solution for longer than 24 hours results in increased concentrations of colistin, and this may increase the potential for lung toxicity.

In the case FDA is investigating, a cystic fibrosis patient had a home nebulizer treatment with a colistimethate solution that had been pre-mixed by a pharmacy. The patient developed acute respiratory failure and later died.

There are three important precautions that may help to prevent this kind of toxicity:

- First, if you choose to prescribe colistimethate for inhalation, avoid pre-mixed, ready-to-use solutions.
- Second, instruct patients and caregivers to administer the solution promptly after it's mixed.
- Finally, instruct patients who may have supplies of the pre-mixed form to discard them.

Additional Information:

FDA MedWatch Safety Alert. Colistimethate (marketed as Coly-Mycin M and generic products). June 28, 2007.
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm152109.htm>

Importance of Using Aseptic Technique with propofol (Diprivan)

FDA is alerting healthcare professionals about several clusters of patients who experienced chills, fever, and body aches shortly after receiving propofol for endoscopic procedures. Propofol, which is marketed as Diprivan and also sold generically, is administered IV to induce or maintain general anesthesia and sedation.

The adverse events occurred in several states, and the FDA and CDC are continuing to investigate these reports. To date, there is no evidence that the symptomatic patients had bacterial sepsis, or that the propofol vials or pre-filled syringes were contaminated with endotoxins or bacteria.

Nonetheless, FDA is reemphasizing the importance of handling the drug according to the strict aseptic technique described in the product labeling. Here are several key recommendations:

- Use a vial or pre-filled syringe on only one patient.
- Start giving the propofol immediately after the vial or syringe is opened.
- When using the drug for general anesthesia or monitored anesthesia care sedation, finish administering the drug within six hours after opening the vial or pre-filled syringe. For ICU sedation where propofol is administered directly from a vial, complete administration within 12 hours of spiking the vial. In all cases, discard any remaining drug.
- If a patient develops fever, chills, body aches or other symptoms of acute febrile reactions shortly after receiving

propofol, evaluate the patient for bacterial sepsis and treat if necessary.

- Report any adverse events associated with the use of propofol through FDA's MedWatch program.

Additional Information:

FDA MedWatch Safety Alert. Propofol (marketed as Diprivan and generic products). June 15, 2007.
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm152699.htm>

Preventing Patient Deaths from Fentanyl Patches

A recent report from the Institute for Safe Medication Practices warns about the dangers of misprescribing fentanyl transdermal patches, such as Duragesic. ISMP reminds practitioners that these patches are intended only for patients who are opioid-tolerant, and should not be used for acute pain.

ISMP also pointed out other prescribing errors. In some cases, deaths occurred in patients who were prescribed multiple fentanyl patches, resulting in overdose. In other cases the fentanyl was prescribed in addition to other pain medications, such as oxycodone, or it was prescribed for patients with pre-existing respiratory compromise. ISMP points out that sometimes pharmacists have dispensed these prescriptions without questioning them, and nurses have applied the patches without recognizing the prescribing error.

Here are some of ISMP's recommendations to help avoid these tragic and preventable errors:

- Prescribe fentanyl patches only for patients who are opioid tolerant, and who have chronic pain that is not well-controlled with shorter-acting analgesics. These patches should not be used for postoperative pain, or for pain that's short-term or intermittent. Pharmacists should ensure that the patient is opioid-tolerant and suffering from chronic pain before dispensing the drug, and should question the prescriber if this is not the case.
- Set dosing limits. For example, pharmacy computer systems could be set to flash an alert if more than 25 mcg per hour has been prescribed as a first-time dose. Also, in evaluating whether the dose is appropriate, take into account other opiates or analgesics that may have been prescribed.
- Educate practitioners and patients to know the signs of overdose, which include respiratory distress, shallow breathing, fatigue, sleepiness, confusion, dizziness and fainting.
- Prescribing errors are not the only cause of deaths and injuries from fentanyl patches. They also occur when patients mis-use the patches. Sometimes patients and family members do not understand that heat can increase absorption of the drug to dangerous levels. So patients should be told to avoid heating pads, electric blankets or hot baths while the patch is in place, and let their doctors know if they develop a temperature above 102 degrees.
- There have also been cases where children found used patches in the trash and applied them to their own bodies, and died as a result. And so patients should be warned to dispose of the patches by folding them in half and flushing them down the toilet.

Additional Information:

ISMP Medication Safety Alert! Ongoing, Preventable Fatal Events with Fentanyl Transdermal Patches Are Alarming!
June 28, 2007.
<http://www.ismp.org/Newsletters/acutecare/articles/20070628.asp>

Avoiding Hazards with Intra-aortic Balloons

A recent FDA article in the journal Nursing 2007 warns about unsafe practices using intra-aortic balloon pumps. It cites a case where a patient died after the balloon was allowed to remain in the aorta without pumping (to go dormant) for

an extended period of time. The article cautions that a balloon being dormant for more than 15 minutes is hazardous, not only because the patient loses valuable cardiac support, but because blood becomes trapped in the folds of the deflated balloon, promoting the formation of clots.

The article contains a number of recommendations to prevent this kind of problem. Here are a few of them:

When the pump is in use, frequently check that it is working properly, and monitor the patient's physiologic responses to the therapy.

Replace empty helium tanks within 15 minutes, and keep extra tanks nearby to minimize the time that the balloon is dormant.

If you cannot restore operation of the pump within 15 minutes, you must manually inflate and deflate the balloon. This should be done every five minutes if possible, and at a minimum, several times an hour. Keep this up until a new pump is in place or the balloon has been removed.

Pay immediate attention to a helium leak alarm. If you cannot determine the cause of the alarm right away, switch to another pump. If the alarm continues, this could indicate that the balloon has ruptured, which requires that the physician remove it immediately.

Additional Information:

Weil, K. On Guard for Intra-aortic Balloon Pump Problems. Nursing2007, Volume 37 (July), Issue 7, p. 28.
<http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/TipsandArticlesonDeviceSafety/ucm064547.htm>

Caution on No-Name Drug Patches

Catapres TTS patches deliver the antihypertensive drug clonidine transdermally. The patches are available in several strengths and they are worn for a week at a time and then replaced. The Institute for Safe Medication Practices recently noted that medication errors can occur because the name and strength of the drug are not written on the patch itself.

ISMP points out many different caregivers may be interacting with a patient, particularly in a hospital. By looking at the patch, caregivers can only see that there is something on the skin --- not which drug or which strength, or even whether it is a transdermal medication patch or some sort of bandage.

ISMP says that the cover on the Catapres patch could be mistaken for the actual drug patch and applied directly to the skin. Or a nurse could receive a new order for a clonidine patch or an oral dose of clonidine, and not realize that the patient was already wearing a clonidine patch. Or if the patient is wearing both a clonidine patch and another patch that also does not have a visible drug name, the wrong patch might be removed and replaced with the same kind of patch that's still on the patient. In that case, the patient would receive double the dose of one medication and none of the other.

ISMP says that the patch manufacturer, Boehringer Ingelheim, advises against writing directly on the patch because it is not known whether the volatiles in the ink could affect the delivery of the drug. But, the company did note that the patch cover could be labeled and then placed over the patch to protect it.

There is also a code on each patch that can be used to identify the strength: BI 33 designates a 0.3 mg patch, BI 32 is 0.2 mg, and BI 31 is a 0.1 mg patch. ISMP says to consider noting these dose designations with the inventory items so they appear on the computer-generated medication administration records.

Additional Information:

ISMP Medication Safety Alert! Anonymous patches. Volume 12, Issue 13.

http://www.ismp.org/Newsletters/acutecare/articles/20070628_1.asp

Helping Patients Avoid Counterfeit Drugs over the Internet

FDA has previously warned about the risks of buying drugs and other medical products over the Internet. Products bought on the Internet could be fake, sub-potent, or not approved by the FDA. They could also be counterfeit.

FDA recently discovered two different web sites selling a counterfeit version of the weight-loss drug Xenical. In one case, it actually contained another drug, and other samples contained just starch and talc. And that is just one example of the risks people take if they buy drugs over the internet.

An article in a recent issue of "Family Practice Management" gives several tips that practitioners can give to patients to help avoid counterfeit products. One is to advise patients to use only U.S. sites that are licensed by a State board of pharmacy. Some of these sites display the VIPPS seal, which stands for Verified Internet Pharmacy Practice Site. The National Association of Boards of Pharmacy (NABP) gives the seal to Internet pharmacies that meet State licensure and other criteria.

The article also suggests advising patients to carefully compare the appearance and packaging of the medicines they buy online with the same medicine they may have gotten in the past from a conventional pharmacy. If the Internet product does not match up exactly, the patient should not use it. The suspected counterfeiting should be reported to the drug manufacturer, and to the FDA through the Medwatch system.

The article lists some of the drugs that are most susceptible to counterfeiting and points out that counterfeiters tend to favor expensive drugs that are sold in large volume, e.g., anti-cholesterol medications. The article notes that so-called "embarrassment drugs" are widely counterfeited i.e., drugs for conditions that patients may be reluctant to discuss with their doctors. This would include drug such as Viagra, Cialis and Propecia.

Additional Information:

FDA MedWatch Safety Alert. Warning About Counterfeit Drugs From Multiple Internet Sellers. May 1, 2007.
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm170297.htm>
