Practice sting Mix-up amphotericin B

Mix-ups between the various amphotericin B products can have very serious consequences. In 2008 and 2013, a predecessor of VMI issued an alert about a mix-up three times. VMI has received two notifications in the past year regarding the interchange between amphotericin B in liposomes (Ambisome®) and conventional amphotericin B (Fungizone®). In a notification from the spring of 2020, a concurrence of circumstances caused the incident. The notification shows that despite a number of precautions, an incident can still occur.

Notification

A critically ill COVID-19 patient in the ICU with aspergillosis has to switch to Ambisome® due to liver enzyme elevations caused by voriconazole. In the daily multidisciplinary consultation (MDC) of the ICU, the hospital pharmacist explicitly indicates to prescribe Ambisome® and not Fungizone® because of fatal mix-ups in the past. During the consultation, the resident physician mentions in the disease notes: start Ambisome®: dose 300 mg (3 mg/kg).

Subsequently, the resident physician searches the Patient Data Management System (PDMS) of the ICU for a medication prescription for Ambisome® using the generic name. She finds an prescription for amphotericin B without the addition of Ambisome® or Fungizone® although this addition is present in the hospital's electronic prescribing system (EPS). In contrast to the hospital's EPS – managed by the hospital pharmacy – a physician can convert in the PDMS the prescription to Ambisome® for inflow rate and volume. However, the label text remains Amphotericin B 300 mg. If the resident physician had searched the PDMS for Ambisome®, she would have found the correct prescription. The resident physician does not receive a medication monitoring signal that the dose is too high, because the PDMS does not have a medication monitoring module. Such a module was not purchased due to financial reasons. Besides this module was not considered necessary because a hospital pharmacist is present in the daily MDC. Furthermore, the scan module for checking the correct medicine had not been implemented at the time of the incident.

To prevent the Ambisome® ampoules from having to be delivered during working times, a pharmacy assistant delivers the Ambisome® ampoules to the patient's room in the ICU before the prescription is received at the pharmacy, on the instructions of the hospital pharmacist, for the first administration at 6 p.m. The nurse prepares and administers the first 2 doses of Ambisome®. Due to the hectic pace in the ICU and the scarcity of protective equipment and the clothing change procedure due to Covid-19, the nurses do not put the ampoules in the medication room of the ICU but in the patient's room.

During the first Covid-19 wave, the ICU asked the pharmacy whether it could support the preparation of intravenous medications. The pharmacy prepares these medications seven days a week from 8 a.m. to 5 p.m. based on a work list daily provided by the ICU.

Based on the work list of the ICU - which states Amphotericin B 300 mg - the pharmacist's assistants prepare the third dose in the medication room of the ICU. The pharmacy assistants are not familiar with the two different presentations of amphotericin B, which differ in dosage and inflow rate. Since ampoules of conventional amphotericin B (Fungizone®) are kept in the medication refrigerator in the medication room of the ICU, the pharmacist's assistants take Fungizone® ampoules from the refrigerator and prepare the infusion. The warning on the label in the refrigerator Attention: Amphotericin B (Fungizone®) non-liposomal does not raise any questions for the pharmacy assistants. The Parenteralia Handbook - which contains warnings about a possible mix-up - is currently unavailable due to a malfunction in the ICU. The pharmacy assistants therefore consult the duty hospital pharmacist. The hospital pharmacist explains how to

prepare the infusion solution. He assumes that the pharmacy assistants mean Ambisome® ampoules because Ambisome® ampoules were delivered to the ICU two days earlier.

The pharmacy assistant delivers the prepared medication to the nurse who administers the medication to the patient in 30 minutes. Shortly after administration, the patient develops severe hyperkalaemia leading to cardiac arrhythmias. The next day, the patient's condition deteriorates and the patient dies.

Differences between Fungizone® and Ambisome®

The indications of both amphotericin B products are similar, but they differ greatly in dosage, inflow rate and toxicity. For example, in systemic mycoses, the dose of Fungizone® is up to 1 mg/kg body weight per day with an infusion time of 2 to 6 hours and of Ambisome® up to 5 mg/kg body weight per day with an infusion time of 30 to 60 minutes. Using the wrong form of amphotericin B when preparing an infusion can lead to a seriously too high or too low dose, as this notification shows.

Recommendations

For the medicines committee

- Preferably work in the hospital with an integrated or linked EPS-PDMS.
- Make sure that the management of medication prescriptions within the EPS and PDMS is the responsibility of a hospital pharmacist.
- Make sure that every prescribing system has an up-to-date drug monitoring and scanning module.

For prescribers

- Select the correct medicine in the EPS or PDMS. Check that the correct product is selected.
- Consult the pharmacy if an intended drug is not available in the EPS or PDMS.

For hospital pharmacists

- If you have questions from pharmacy assistants and other healthcare workers about preparing a medicine for administration, verify that the correct medicine is used.
- Treat amphotericin B products as high-risk medications.
- Draw the attention of physicians, nurses and pharmacy assistants to the fact that the different amphotericin B products are not interchangeable. Also check if this is stated in the Parenteralia Handbook and the hospital's antibiotic policy. And whether this is reported when the medicine is 'clicked on' in the electronic prescription systems used in the hospital.
- Only use the brand names of amphotericin B products in the hospital. Implement this consistently in the information sources and systems.
- Discuss in the antibiotics committee of the hospital whether Fungizone® intravenously still has a place in the treatment given the potential dangers of mix-ups.
- Preferably deliver all amphotericin B products from the pharmacy in the patient's name. If products are in stock, add a warning such as CAUTION: Do not confuse with liposomal amphotericin B (Ambisome®), amphotericin B lipid complex (Abelcet®) or conventional amphotericin B (Fungizone®) in the hospital emergency/wake/bedside cabinet.
- Preferably prepare amphotericin B for administration in the pharmacy.

For nurses and pharmacy assistants preparing amphotericin B for administration

- Always check the presentation and dosage before preparation. Even if it was previously checked by a colleague.
- Get yourself checked by a colleague.