Compounding Errors

Northeastern University

Haochong Wang
Abstract:

Medication safety is always one of the top concerns that people have nowadays, and by the efforts of many organizations put, we do have faith in most of the marketed medications. However, compounded drugs are not as easily controllable as the manufactured drugs, and they did cause some tragic accidents in the past few decades. The most serious accident in the past decade is the New England Compounding Center’s meningitis fungal outbreak that happened in 2012. Hundreds of people became the victims of the lethal injections and over 60 people have died (CDC, 2013). People may wonder, with all the regulations and oversights of FDA, CDC and etc., why can’t we stop people dying from pharmaceutical errors? What went wrong during the production? Why a compounding pharmacy has produced thousands of vials and shipped to over 20 states? What roles did the FDA and the state of pharmacy play in this event? There are many questions being asked and by digging deep to this incident, manufacturing without oversight, lacking of sterility, and failure of regulation are the main three reasons that eventually made this happen.

Introduction:

As a pharmacist, one of the most important missions is to dispense medications to the patients precisely and safely. Pharmacists are the last ones who check the medications before handing them to the patients, and that’s why patients rely on pharmacists. This means that in the pharmacy, any errors made by pharmacists are irreversible, unbearable and they could be lethal to the patients. Recall the arguments of some of the debaters from the "The Debate Rooms" stating that errors are ok apparently do not apply in this field. The definition of "error" in pharmacy can be very hard to determine. One may think that mistakenly typed 2mg to 20mg on a
prescription may be a "typo", but it many kill a patient eventually. Sophomore year, one of the professors told a story that happened few years ago in a hospital in Boston. A patient was prescribed for a certain medication 4 times a day with total doses of 4mg. However, the pharmacist accidentally dispensed 4mg of that drug 4 times a day, which was 16mg total and eventually killed the patient. The responsible pharmacist's license was suspended, but nothing can heal the hurt brought to that patient's family. Besides dispensing medications according to prescriptions, compounding medications is also another part of a pharmacist's job.

Compounding is to prepare a medication in such way to meet the special needs of individual patient. For example, for pediatrics patients, the tablets are usually crushed to fine powder and mixed with oral solutions to make them easy to take; powders sometimes are added to an IV bag to make the medication injectable. During this process, the medications are taken out of their packaging and exposed to open air, giving a greater chance of contamination. Therefore, sterilization of the compounded medications is crucial. Several accidents due to the failure of sterilization of compounded drugs have taken so many lives in the past few decades. In 2007, the Food and Drug Administration (FDA) claimed that since 1990, there are more than 200 adverse events involving compounded drugs, in 2002, five cases of fungal meningitis in North Carolina were reported, and in 2011, nine patients were killed by a supplement that was contaminated by bacteria (Alcorn, 2012). However, that was not the end of the story, one of the most damaging breakdowns of U.S. drug safety in the past decade has been reported in the fall of 2012, NECC fungal meningitis outbreak.

NECC Overview:

In September 2012, the first meningitis case has been reported. The patients have all
received injections from the NECC's steroid methylprednisolone acetate. Later on, more cases scattered across the country have been reported and caught people's attention. The U.S. Centers for Disease Control and Prevention (CDC) confirmed right away that the contaminated injection vials were originated from the New England Compounding Center in Framingham, MA. NECC was licensed by the state of pharmacy as a compounding pharmacy, which prepares specific prescription to meet the needs of individual patients. Beginning on May 2012, three lots of steroid methylprednisolone acetate were shipped to different health-care providers in over 20 states, including unknown amount of contaminated vials (Lancet, 2012). According to the latest update of CDC, there are 64 deaths and over 700 cases in 20 states (CDC, 2013).

Compounding vs. Manufacturing:

Since compounded drug is specially prepared for one patient and one prescription, why there are 17,000 contaminated injection vials sold to over 20 states (CBS, 2013)? Nobody knew what was going on until a former salesman of NECC revealed the secrete on CBS 60 Minute episode. The truth is that NECC was no longer doing what it supposed to be doing, which is compounding, instead, they became a large-scale manufacturer. As mentioned before, for a drug to be compounded, there must be a prescription for each individual patients, and the medication is prepared to meet the special needs of the patient. Whereas manufacturing, prescriptions are not required, the same type of medications can be manufactured with large amount. According to the salesman who refused to give his real name, NECC provides lower price of the same medication than brand name drugs do, so many clinics chose to do business with NECC. In order to comply with the rule “one drug, one patient and one prescription”, NECC asks the clinics to provide them some names. The salesman said that most of the names do not actually exist, such
as Jane Smith, John Smith, Jane Doe, and etc. Some of the sites wouldn’t do business with them because what NECC was doing was obviously illegal, NECC would just move on for the “bigger fish”. A month before the first death of fungal infection, one of the technicians warned the NECC’s supervisor that something is going to happen, they would get shut down, the supervisor just “shrugged” and ignored what he said (CBS, 2013). So even though NECC seems like doing the correct thing, making one injection vial for each individual patient, they are actually manufacturing the vials and sold them without any assurance. Both NECC and their business partners knew they were doing it illegally, but because of their greediness, dozens of people were killed.

Failure of Sterility:

Even if that is so, if NECC could manufacture with sterility, the tragedy might not happen today. The sterility of compounded drugs is the first priority and the reason why the process of making them must be in a sterilized space. Many pharmacies have clean rooms for compounding medications and IV bags, as the name suggests, clean rooms have to be really clean. The injection vials from NECC not only didn’t have any assurance from the regulatory agents, but also didn’t even go through any sterility testing by NECC itself before they were shipped to the sites. Moreover, the clean room I of NECC, where the toxic vials were produced, has been tested positive of contaminations several times over the past few years. One of the NECC’s technicians says that there were approximately a dozen times over the past three years that they would see mold in the clean room (CBS, 2013). Not only the clean room is not clean, their facility is about 100 feet away a recycle site owned by the same owner. Even though the reason why the vials got contaminated is still unknown, but I think it is pretty clear that their sloppiness must have something to with it.
Regulations and Oversights:

The Food and Drug Administration of the U.S. is the most authoritative agency in monitoring the pharmaceutical products, and all prescription drugs must be approved by the FDA for marketing. And for each state, the state of pharmacy also plays a crucial role of regulation, especially for compounding pharmacies. However, people may wonder, with all the regulations from state pharmacy and FDA and etc., why there are still accidents occur once in a while? This brings us the other key difference between manufacturing and compounding, which is the regulation and oversight. In 1998, congress exempted compounding pharmacies from the oversight of the FDA. The theory was that mixing drugs one prescription at a time shouldn’t require the federal inspection. The law passed, and without the FDA supervision, compounding took off, state health departments became responsible for this industry (Outterson, 2012). Since then, compounding pharmacy is being licensed by the state and compounded drugs do not require the assurance from the FDA or the state of pharmacy, usually the pharmacist would be the person who checks the medication. However manufactured medications are required to have the oversight of the FDA and go through a series of complicated quality assurances before they can make it to the market. In 2004, FDA inspected the facility and sent NECC a warning letter. The letter stated “Failure to promptly correct these deviations may result in additional regulatory action without further notice, including seizure or injunction against you and your firm (NEJM, 2012).” However, neither state nor federal regulators in the USA acted against a known negligent drug manufacturer, and hundreds of Americans have died or fallen ill as a result (Alcorn, 2012).

Conclusion:

For more than two decades, the FDA has struggled to regulate industrial-scale
compounding. The law exempted the oversight of the FDA in 1998 passed over the strong objections of then-FDA commissioner David Kessler. He says in the interview that “if you’re not going to have oversight, one day, people are going to die; this should not happen in 2013, maybe at the turn of the previous century, where we didn’t have the institutions like the FDA. There is no reason why people had to die (CBS, 2013)”. The current FDA commissioner Margaret Hamburg also states that she cannot promise that every pharmaceutical drug in the United States is safe to take, especially when it comes to compounded drugs (NEJM, 2012). Compounding pharmacies are essential businesses that produce important products for patients. However, too many patients have suffered and died as a result of compounding errors not only in this NECC case but also in the past few decades. The FDA and the state of pharmacy should reinforce the regulatory systems on compounding medications to make sure that every prescription drugs are safe to use. Every compounding pharmacy should also assure their compounded drugs are sterilized. Patients’ safety should be achieved not only by just one or two parties, but by every agents.
Reference:


http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(12)61864-9/fulltext#


Lethal Medicine Linked to Meningitis Outbreak (2013). *CBS 60 Minutes*. Retrieved from

http://www.cbsnews.com/video/watch/?id=50152765n
