EDITORIAL

Can Anyone Spare A Little Indigo Carmine? The Drug Shortage Crisis

As part of our intraoperative routine during a recent radical retropubic prostatectomy, I asked for indigo carmine to be given to aid in identification of the ureteral orifices. In this patient with a large median lobe and a heavily trabeculated bladder, surgical experience could not trump the comfort of seeing the blue jet streaming from the ureteral orifices. I was unceremoniously informed by the circulator that the hospital was out of stock. The hospital pharmacy had attempted to obtain the indigo carmine from several distributors without success. There was no time estimate when it would be available again as there was there was a nationwide shortage of indigo carmine. I had officially experienced my first "drug shortage". We fell back on the best alternative available, methylene blue, with less than acceptable results. Everyone in the OR that day was aware of the high profile shortage of critical chemotherapy agents. But how can something as pedestrian as indigo carmine be unavailable?

It turns out that over the last year shortages have included other relatively common urologic medications such as mitomycin C and IV levofloxin. There was even an interruption in the availability of intravesical BCG this spring. Staples such as sodium bicarbonate, lidocaine, morphine and midazolam have recently experienced supply problems. Until the shortage of several critical chemotherapeutic agents hit the media late last year, the growing drug shortage problem had not received much attention.

A consequence of the drug shortages beyond simply the lack of a key medication is patient safety. The Institute for Safe Medication Practices has noted that when medications are in short supply, there is an increase in the use of less desirable and unfamiliar alternative drugs or dosing forms. Hospital pharmacies will often repackage and redistribute agents to meet critical patient needs. All of these increase the potential for dosing and administration errors. Even worse, shortages have led to a flurry of counterfeit medications hitting the market such as the oncology medication Avastin that contained no active ingredient.

The shortage of approved medications has been a growing problem over the last few years. In 2005, the Food and Drug Administration (FDA) reported a shortage of about 61 drugs. By 2010, the number had tripled to 178 and in 2011 the American Society of Health System Pharmacists reported 267 medication shortages.

So why are we suddenly experiencing all of these shortages? The reasons cited by the experts are multiple and complex. These include increased oversight of drug production by the FDA, delays in raw materials, safety concerns over the integrity of the supply chain and discontinuations of product lines by manufacturers. Many of the medications with supply issues are sterile and older injectable generic formulations that are more difficult to manufacture. Quality control problems, including glass shards and metal filings in drugs and fungal contamination, are also leading causes of drug shortages according to the FDA.

Pundits debate whether federal regulation is the cause or solution to this public health problem. Some editorialists point to the 2003 Medicare Modernization Act as one reason for the shortage in generic forms of intravenous chemotherapy. This key legislation changed the formula for how drug costs are reimbursed and may have impacted the ability of drug prices to freely fluctuate based on manufacturing costs. Current government mandated pricing policies have made intravenously administered generic oncology drugs an area that manufacturers are not rushing into.

Companies may discontinue older medications in favor of newer, more profitable drugs. Many medications on the FDA's shortage list are supplied by only a few manufacturers. With a production problem due to component shortages or when a facility fails a safety inspection, there is limited capacity for other manufacturers to quickly ramp up production.

Reporting manufacturing delays and shortages to the FDA have been voluntarily thus far. Currently, the FDA cannot mandate reporting of the reason, duration or specific details of the shortage. The President's recent executive order instructed the FDA to broaden reporting of potential shortages by manufacturers. It also accelerated the review process for companies interested in producing generics, and improved reporting of medication price fixing to the Justice Department. Congress is also considering further legislation in this area.

Everyone should be alarmed by the ever-increasing number of important medication shortages. Time will tell if these new government regulations will improve the situation. Until that time, we have stockpiled a few extra vials of indigo carmine in our operating room for the next radical prostatectomy just in case.

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