Where Did All Our Drugs Go? Drug Shortages: What is the Current Situation?
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Objectives
- Identify common medications affected by current drug shortages
- Delineate impact of drug shortages on anesthesia services
- List resources to identify up-to-date drug shortage information and resolution dates
- Discuss recent governmental actions to address the drug shortage crisis
- Discuss alternative therapies being used in clinical practice as a result of drug shortages

What is a Drug Shortage?
- American Society of Health-System Pharmacists
  - A supply issue that affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent

Disclosure Statement – no financial relationships to disclose
- Clark Lyda, PharmD

FDA Shortage list: http://www.fda.gov/drugs/drugsafety/drugshortages/ucm050792.htm

Examples of shortages

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How are Drug Shortages Reported?

- drugshortages@fda.hhs.gov
- “Report a Drug Shortage to ASHP” link
- University of Utah Drug Information Services

Why Drug Shortages?

- Government- FDA, DEA
- Materials
- Manufacturing
- Distributors
- Business Decisions
- Inventory
- Recalls

Role of DEA

- Limits of yearly production of controlled medications, C-II – C-V
- Fill their allocated quantity of controlled drugs.
- Not able to make any more until the next January
- Recent shortages of fentanyl, morphine, hydromorphone

Supply Chain

A Drug Supply Chain Example

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New FDA Commissioner, 2009

- Margaret Hamburg, MD
- Aggressive campaign to increase the FDA inspections
- Contaminated Heparin 2008
- 1st year, FDA warning letters to MFR companies increased 42%
- Second year (2010), the letters increased 158%
- Spring 2012, generic production had decreased 30%

FDA Inspections

- From the US House of Representatives, Committee on Oversight and Government Reform report on the FDA’s contribution to the drug shortage crisis, June 2012,
- “the FDA field force does not believe that it is within the scope of their authority to worry about the implications of their actions, even if means a manufacturer closing a manufacturing line or facility.”

FDA Findings

- Teva- Endotoxin in propofol (2009)
- Bedford Labs- lack of sterility, glass and stainless steel particles (2011)
- Hospira- stainless steel particle contamination propofol, morphine vials overfilled up to 2x volume (2009, 2010 and 2011)
- Sandoz – crystal formation in solutions, contaminated opioids (2011 and 2012)

Drug Shortages by Primary Reason

Medicare Modernization Act 2003

- Prescription benefit for seniors
- Government price cap for generic medications
- Changed the reimbursement rate for injectable drugs delivered in outpatient settings
- Limits price increases to 6% per year
- Low profit margins of generic injectables (6%)
  - change production lines to a more lucrative drug
Group Purchasing Organizations

- Increased purchasing power
- 98% of US hospitals use GPO contracts
- Six GPO's have 90% of market, 2 have 60%
- Intense competition, prices driven down
  - Intended goal
- Ultimately limits production to 1 or 2 companies
  - Contract losers, quit making the generic drug

Hospital Inventory Control

- “Just In Time Ordering”
- Order enough product for 2 or 3 days
- Delivery 1 to 2 times every day
- Limit inventory costs
- Maximize turnover and profits
- Limits ability to respond to any drug shortage

National Survey

- University of Michigan Health System (UMHS) distributed an online survey to directors of pharmacy
- Collected data from four domains
  - Demographics
  - Impact of drug shortages
  - Resource utilization to manage shortages
  - Adequacy of current resources

Is Everyone Affected?

- 99% of hospitals were affected by at least one drug shortage

Less Drugs, More Frustrations

- Drug shortages have lead to increased:
  - Time spent managing shortages
  - Labor costs
  - Frustration
- Estimated annual labor cost of $216 million for all health systems nationwide

A Change in Practice

- Alternatives
  - Using different or unfamiliar agents
  - Temporary guidelines/policies
- Assessment of inventory
  - Changing dispense location of medications
  - Changing strengths or concentrations stocked in Pyxis
Impact on Medication Safety

- ISMP released a special issue addressing the effects of drug shortages
- Drug shortages have lead to an increase in medication errors
  - One in three reported having a near miss
  - One in four reported having an actual error
  - One in five reported adverse patient outcomes

Alternative Therapy

- Problems with alternatives
  - Less effective
  - Increase side effects
  - Unfamiliar with alternative agent
- Hydromorphone 2 mg IV ordered by MD, verified by pharmacy and given by RN.
  - Patient to ICU after Naloxone

Unfamiliar Agents: A Patient Case

- A 47 year old female is admitted for an elective procedure
- Propofol shortage
- Unfamiliarity with Brevital® Sodium
- Serious dilution error, massive overdose
- Patient died despite resuscitation efforts

Compounding Error

- Shortage of Bupivacaine 0.5% w/epinephrine 1:200,000
- Pharmacy mixed small amount for anesthesia
- Added too much epinephrine
- Two patients: HTN, V-Fib, Pulmonary edema, extended stay in SICU

Changes in Supply

- Drug shortages have lead to changes in current supply
  - Different strengths
  - Different concentrations
  - Different packaging

Obama Becomes Involved

- On October 31, 2011 Obama issued an executive order
Executive Order

- Executive Order 13588
  - Required drug companies to report to the FDA when critical supplies were threatened
  - Required FDA to expedite regulatory reviews and increase staffing in its Drug Shortage Program

Obama Administration Acts

- Continued efforts by the Obama administration included
  - A letter to drug manufacturers reminding them of their legal responsibilities to report the discontinuation of certain drugs to the FDA
  - Encouraged manufacturers to voluntarily report potential shortages when not required by law

FDA’s Role

- Has taken multiple steps to help prevent drug shortages
  - Asking other firms to increase production
  - Working with manufacturers to identify steps to prevent the dangers of manufacturing products with quality issues
  - Expediting review of regulatory submissions
  - Approved Import of propofol from Europe

FDA’s Actions to Prevent Shortages

- FDA has helped prevent several drug shortages
  - In 2010, prevented 38 drug shortages
  - In 2011, prevented 99 drug shortages
  - In 2012, prevented 128 drug shortages

A review of FDA’s approach to medical product shortages. Available at: www.fda.gov/DrugShortageReport
FDA Provides Resources

- Increased resources provided on their website regarding drug shortages
  - List of drugs on shortage
  - Report of the FDA’s actions in decreasing the number or shortages
  - Links to actions by the Obama administration on drug shortages

ASHP Provides Resources

- Increased resources provided on their website regarding drug shortages
  - List of drugs on shortage and the reason behind the shortages
  - ASHP’s actions involving drug shortages
  - Guidelines to managing drug shortages
  - Links to articles and news on drug shortages
- [http://www.ashp.org/shortages](http://www.ashp.org/shortages)

ASHP’s Website

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ASHP’s Website

- Nalbuphine Injection
- [21 January 2013]
- Products Affected - Description
  - Nalbuphine injection, Hospira
    - 10 mg/mL, 1 mL ampules (NDC 00409-1463-01)
    - 10 mg/mL, 10 mL vials (NDC 00409-1464-01)
  - 20 mg/mL, 1 mL ampules (NDC 00409-1465-01)
  - 20 mg/mL, 1 mL Novaphas ampule (NDC 00409-1465-49) - discontinued
- Reason for the Shortage
  - Teva discontinued all nalbuphine injections in July, 2010.
  - Hospira has nalbuphine on shortage due to manufacturing delays. Hospira discontinued the 20 mg/mL 1 mL Novaphas ampules in December 2012.

Actions to Implement

- Partner with other institutions
  - Different wholesale distributor
- Social media
- Collegial networks with professional organizations
- Professional list-serves and discussion groups
- Group Purchasing Organizations

Hospital Action

- Hospital developed Policy
  - 1. Transparent and open for review.
  - 2. Relevant to population of patients affected
  - 3. System by which patient can appeal a decision
  - 4. Institution implement policy so that everyone follows the rules

Hospital Action

- 5. Allocation must be fair, similar patients always treated similarly, no special people, physicians or patients
- 6. No gray market drugs
- 7. Prohibit use of drugs in short supply to be used in research studies.
- 8. Close inventory management and control

Hospital Action

- 9. Schedule patients to avoid waste of partial vials
- 10. Coin toss to decide between two equal patients
- 11. Protocol to update information systems, electronic POE systems

Resources

- ASHP http://www.ashp.org/DrugShortages/Current/
- ASA - Link to Drug shortages
  - http://www.ashq.org/
- AANA – Link to FDA
Propofol Shortage: Teva to Restart Production

- Continue Importation of Propoven
  - Fresnius/APP increased production & shipment
- Domestic production improved
- Teva expected to release product February 2013
  - Discontinued in 2010, now reentering market
- Etomidate production increasing

Trends in Drug Shortages

- Significantly increasing
- Generic, sterile injectables
- Critical drugs
- Older drugs
- Generic Pharmaceutical Association
- May Improve in 2014?

Conclusion

- Drug shortages caused by multiple factors
- FDA implemented some actions that may help
- Resources for information presented
- Future of drug shortages….
  - Politics, Medicare Modernization Act, Obama Care, etc.

Thank You

- Questions?