Economic Challenges in Pharmacogenetics

(for intraoperative paralytics, analgesics, antiemetics, and anesthetics)

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Financial Disclosure

- I am employed by the University of Iowa, in part, to consult and analyze data for/with hospitals, anesthesia groups, and companies
  - Current projects: Baxter, Hospira, Merck
- Department of Anesthesia bills for my time
  - I receive no funds other than from the University of Iowa, including no travel reimbursement or honoraria
  - I own no healthcare stocks (other than indirectly through mutual funds)
  - I have tenure with no incentive program

Pseudocholinesterase Deficiency

- Single nucleotide polymorphism
- Occurs in approximately 1 in 2886 individuals

Pseudocholinesterase Deficiency

- Overestimate cost by pretending that PACU nurse, respiratory therapist, and anesthesiologist's time are variable costs

$0.04 = (1/2,886) \times$ mean 2.4 hr $\times$ $169.28 per hour

Dexter F et al. Anesth Analg 2001

Pseudocholinesterase Deficiency

- Overestimate cost by pretending that PACU nurse, respiratory therapist, and anesthesiologist's time are variable costs

$0.04 = (1/2,886) \times$ mean 2.4 hr $\times$ $169.28 per hour

- Rare events are generally unimportant economically unless cause permanent injury

Pseudocholinesterase Deficiency

- Similar conclusions from different analyses
  - Toronto Western Hospital
  - 0.3% = 95% upper CI for % total PACU time attributable to pseudocholinesterase deficiency

Chung F, Mezzei G. Anesth Analg 1999

Pseudocholinesterase Deficiency

- Similar conclusions from different analyses
  - St. Michael's Hospital in Toronto
  - 4.0% = 95% upper CI for % of all PACU nursing workload attributable to "arrived intubated" from any cause

Cohen MM et al. Anesthesiology 1999

Pseudocholinesterase Deficiency

- Small economic impact of rare events can be generalized to other drugs because is a consequence of extra OR and PACU capacity being reasonable from societal perspective
  - Bottleneck = surgeons > anesthesiologists > CRNAs > nurses, capital

Morphine, Methadone, Etc. Extra Pain

- Examples
  - CYP2D6 and IL-1 Receptor antagonist polymorphisms affect morphine consumption
- Maximum economic cost from extra pain is people's willingness to pay for completely effective postoperative pain relief

  $35 The Netherlands, $50 USA

van den Bosch JE et al. Anesthesiology 2006
Gan TJ et al. J Clinical Anesth 2003

Morphine, Methadone, Etc. Respiratory Depression

- APSF funding announcement
  - Winter 2009 newsletter, page 50
- Ashraf S. Habib, MB, BCh, Duke University
- Patients receiving naloxone will be identified using computerized surveillance system
- Controls will be matched by age, gender, ethnicity and type of surgery
- Blood will be collected "for analysis of known genetic polymorphisms involving the opioid mu receptor and the CYP2D6 enzyme"

Morphine, Methadone, Etc. Respiratory Depression

- Economic challenges
  - Incidence and consequences of polymorphisms poorly known currently
  - Incidence of postoperative respiratory depression from narcotics is likely low
- Cost of having test result will likely need to be $20 or less to be cost effective relative to monitoring
- ➢ Unrealistic for genomic testing for anesthesia, but reasonable for information systems to use previously completed tests' results

Ondansetron

- Multiple investigations have shown influence of polymorphisms, variations in promoter regions, etc., on PONV
- You'll know about these studies far more than me, so I won't even try to summarize them
  - Focus on the economics

Ondansetron

- Maximum economic value from identifying non-responders is people's willingness to pay for completely effective antiemetic
  €67 Germany, $17 The Netherlands
  $33 USA, $56 USA

Kerger H et al. Acta Anaesthesiol Scand 2007
van den Bosch JE et al. Anesthesiology 2006
Gan TJ et al. J Clin Anesth 2003
Gan TJ et al. Anesth Analg 2001

Ondansetron

- Genetic testing too costly for inexpensive treatment of non-life threatening condition
- Pharmacogenomics for science of better use of drugs (e.g., not rescue ondansetron failure with another dose of 5-HT3 antagonist)
  – Decision support systems are inexpensive since not a variable cost per patient like testing
- ➢ Principles apply to many anesthesia issues, specifically pharmacogenomics as tool for developing economically sound treatment plan

Ondansetron

- Thank Dr. Candiotti for discussing with me another economically reasonable argument
- Patients with 3 copies of the CYP2D6 gene (ultrarapid metabolism) have higher rates of vomiting despite ondansetron prophylaxis

Candiotti K et al. Anesthesiology 2005

Ondansetron

- Thank Dr. Candiotti for discussing with me another economically reasonable argument
- Patients with 3 copies of the CYP2D6 gene (ultrarapid metabolism) have higher rates of vomiting despite ondansetron prophylaxis
- No rationale for genetic testing of our patients
- ➢ Likely good cost effectiveness for decision-support (informatics tools) to apply already completed genomic testing results to optimize anesthetic plans

Hypothetical Economically Important Examples

- None that I could figure out for this talk for intraoperative anesthetic drugs per se
  – Unless involves application of test results obtained for another (prior) purpose

- ➢ Easily Yes for biomarkers and genetic tests predicting magnitude and time course of acute and chronic pain including labor, since such tests would affect ***whether*** perform procedures at all
  - Cost of anesthesia ≅ time of anesthesia provider

Economic Challenges in Pharmacogenetics

- Prediction (forecast)
  – Principal issue regarding pharmacogenetics in anesthesia will be learning how best to modify preanesthesia evaluation (information systems) so that prior pharmacogenetic test results are known and are incorporated into anesthetics
- ➢ Questions (or email in 10 yr about prediction)
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