



A Biostatistical Analysis of Cardiac Dysfunction with Celebrex

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Abstract

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) inhibit cyclooxygenase (COX) enzymes, and are widely used for treating pain and inflammation. Celecoxib (Celebrex), a selective COX-2 inhibitor, is prescribed as an anti-analgesic and anti-inflammatory agent for treating rheumatoid arthritis and other musculoskeletal conditions because of its reduced gastrointestinal side effects compared to non-selective COX inhibitors.¹ Our previous studies have shown that celecoxib inhibits the voltage-gated delayed rectifier potassium channels (Kv2) independently from COX-2 inhibition. Our recent data show that celecoxib inhibits human potassium channel, hERG, expressed in a human cell line.² This channel is critically involved in human cardiac rhythm. To examine the clinical relevance of this finding, we have analyzed 35 quarters of the FDA (Food and Drug Administration) data on adverse effects (encompassing over 3.5 million case reports). The results showed that the percent of individuals taking celecoxib and experiencing cardiac dysfunction is significantly higher than those not taking the drug.

Methods

- United States Food and Drug Administration (FDA) Adverse Effect Reporting System (AERS) reports analyzed using a software FileMaker Pro® from January 2004 to August 2012.

Figure 1. A sample AERS report filed for Celebrex

- Reports are voluntarily submitted by health care professionals, consumers, and manufacturers. FileMaker Pro® used to link between Demographic, Drug, and Reaction files.
- Relationships established based on ISR number, a unique number for each report.

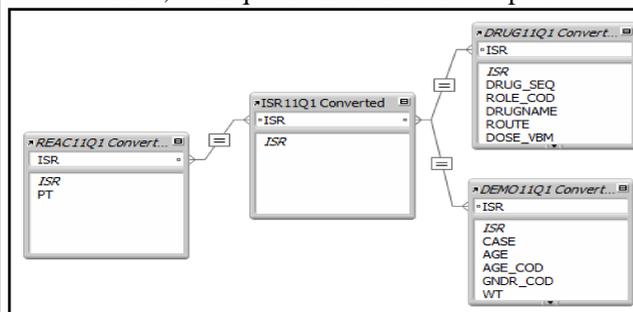


Figure 2. Relationships viewed in FileMaker Pro®

- Data-algorithms used to isolate reports for those individuals taking celecoxib (celebra, celebrex, onsenal) and experiencing cardiac dysfunction.
- Search terms for cardiac dysfunction: arrhythmia, bradycardia, tachycardia, fibrillation, flutter, QT.
- Duplicates removed based on case number.

Results

Table 1. AERS cases from January 2004- August 2012

Isolation Criteria*	Mean OR ^a	Mean PRR ^b	95% CI	p value
Celecoxib	1.517	1.477	1.172 - 2.768	<0.00001
Celecoxib - valdecoxib, arcoxia, and etoricoxib omitted**	1.376	1.406	0.765 - 2.179	<0.001
Celecoxib listed as Primary Suspect***	1.425	1.386	0.647 - 2.635	<0.01

*All isolated reports were compared to reports with celecoxib omitted.
 **Other coxibs omitted include valdecoxib, rofecoxib, etoricoxib.
 ***Primary Suspect determined by person who filed the adverse side effect report.
^a Odds Ratio represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure.
^b Proportional Reporting Ratio represents the frequency of outcome with exposure, compared to frequency of outcome occurring in comparison group.

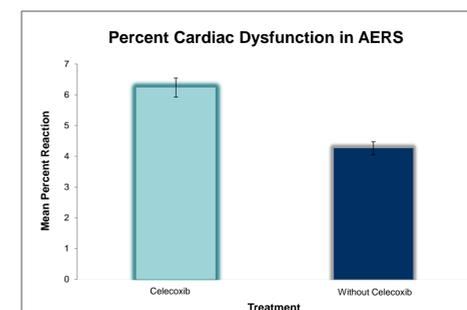


Figure 3. Mean percent cardiac dysfunction in individuals taking celecoxib from January 2004- August 2012 (t=4.9641, p-value=9.436e-06)

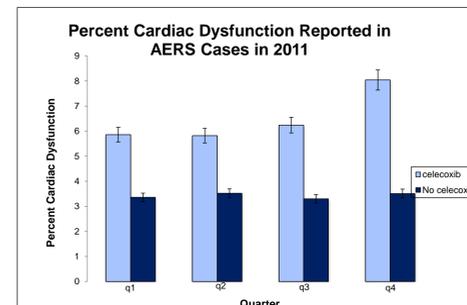


Figure 4. Percent cardiac dysfunction reported for individuals taking celecoxib and those not taking celecoxib for 4 quarters of 2011. Error bars indicate 95% confidence interval (t=5.8084, p-value=0.009567)

Conclusions

- AERS reports analyzed for 35 quarters showed that the percent of individuals taking celecoxib who experienced cardiac dysfunction is significantly higher than those not taking the drug.
- This data can be used to make an informed decision in individuals predisposed to arrhythmias about which NSAID to take when treating pain and inflammation.
- Our work lays the foundation for more rigorous data analysis from multiple databases and clinical research.
- Future studies may include analyzing effect of age, gender, ethnicity in individuals taking Celebrex.

References

- Geis, et al. JAMA, 2000; 284: 1247 - 1255
- Ray, et al. The Lancet, 2005; 365:475-481