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Comparing Different Adverse Effects Among Multiple Drugs Using FAERS Data

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Abstract

US Food and Drug Administration (FDA) Adverse Event (AE) Reporting System (FAERS) is a major source of data for monitoring drug safety. However, there is not general procedure to systematically compare drugs group. We present a statistical method, which can effectively identify significant differences in AE rates among drugs and estimates the differences in age and gender distributions.

Keywords:

Adverse Drug Reaction Reporting Systems; Data Mining.*

Introduction

Post-marketing surveillance is critical to ensure long-term safety, study rare adverse events (AE), and adverse reactions [1]. The US Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) is a post-marketing surveillance program seeking voluntary inputs on AEs to monitor drug safety [2]. We propose an statistical pipeline that provides interpretable results and is convenient to implement. It systematically compares the differences between groups of drugs for specific AEs and can be used to select candidate AEs that are potentially important for future investigation. The method can also be used for other types of reporting systmes. We use FAERS data to compare three Hepatitis C therapies.

Methods

The procedure was carried out in three steps.

Step I: Descriptive Analysis and Visualization

Compare the total number of adverse events distribution between the three therapies using side-by-side histogram plots.

Step II: Difference in AE Rates Among Groups

For each type AE type, compare the reporting rates among the different treatment groups using the chi-squared test and select AEs with significantly different reporting rates by therapy group.

Step III: Quantify and Visualize Risk Factor Effect Size

For each selected AE from step II, investigate whether the difference in reporting rates can be explained by differences in demographics by comparing the effect sizes before and after adjusting for these variables.

Results

The FAERS data contains the top 30 most frequently self-reported AEs of the three Hepatitis C therapies: 28,192 patients were in Therapy A, 5,035 in Therapy B , and 7,820 in Therapy C (Therapy A and B drugs). In step I, we observed that Hepatitis C therapy C caused more AEs than B and C. In step II, the chi-squared test significantly different rates of AEs among the three therapy groups, after Bonferroni correction, except for “arthralgia". In step III, we found that for the 30 most frequently reported AEs, the adjusted odds ratio was less than the unadjusted odds ratio for 15 AEs and was greater than the unadjusted odds ratio for 15 AEs. The difference between the adjusted and unadjusted odds ratio attributable to age and gender ranged from 0.2% to 14.8%.

Conclusion

In this paper, we provided a statistical procedure to compare the difference between AEs among multiple drugs using FAERS data. We are currently developing an R package, “AEtools”, to semi-automate the proposed pipeline for statistical analysis and visualization. Such a procedure, including the R codes, is useful for pharmacoepidemiological studies and will be made publicly available.

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