Economic Aspects of Antibacterial Adverse Effects

Paul M. Beringer,1 Annie Wong-Beringer2 and Jay P. Rho3

1 Department of Clinical Pharmacy, USC School of Pharmacy, Los Angeles, California, USA
2 Western University of Health Sciences, College of Pharmacy, Pomona, California, USA
3 Departments of Clinical Pharmacy and Family Medicine, USC Schools of Pharmacy and Medicine, Los Angeles, California, USA

Contents

Summary ........................................................................................................ 35
1. Economic Considerations ........................................................................ 36
2. Adverse Effects of Antibacterial Agents .............................................. 37
   2.1 β-Lactams ....................................................................................... 37
   2.2 Aminoglycosides ........................................................................... 39
   2.3 Vancomycin ................................................................................... 41
   2.4 Macrolides ...................................................................................... 43
   2.5 Fluoroquinolones ........................................................................... 44
3. Conclusion ................................................................................................ 46

Summary

The economic impact of adverse effects is often understated. Increased hospitalisations attributed to adverse drug reactions alone account for billions of dollars each year within the US healthcare system. Although most classes of antibacterials are well tolerated, severe reactions do occur and can add significantly to the cost of care. Among hospitalised patients, antibacterial adverse effects account for nearly 25% of adverse drug reactions. Published pharmacoeconomic data on direct and indirect costs of antibacterial adverse effects are lacking.

The importance of determining the most cost-effective treatment regimen is becoming more apparent due to limited resources available within the healthcare system. When considering the cost of new antibacterials, a simple comparison of acquisition costs may not accurately reflect the true costs of treatment. A drug with a lower acquisition cost may be more toxic and/or less effective, resulting in higher complication rates and/or treatment failures, thus leading to a higher overall treatment cost. In addition, nephrotoxic agents such as aminoglycosides and vancomycin often require close monitoring of serum drug concentrations and creatinine levels, which also contributes to the total cost of therapy. Indirect costs as a result of reduced quality of life or loss of productivity are certainly not reflected in the acquisition costs of antimicrobials. Institutions must evaluate a drug’s potential for causing an adverse event, among various other factors, when considering drugs for inclusion on their formularies. Drugs with good safety profiles may minimise hospitalisation or facilitate early discharge.
Thus, the adverse effect profile of an antimicrobial agent can contribute significantly to its overall direct costs, primarily as a result of higher monitoring costs and additional days of hospitalisation. For example, in the US, the cost associated with adverse effects, such as nephrotoxicity, observed with aminoglycosides and vancomycin, may add approximately $US2500 per patient with nephrotoxicity (1990 values). Indirect costs can also be substantial as a result of reduced productivity. Many adverse effects of antibacterial agents are predictable and may be minimised with appropriate monitoring and care. This article reviews the pharmacoeconomic aspects of adverse effects associated with some of the more important antibacterial classes such as the \(\beta\)-lactams, aminoglycosides, vancomycin, macrolides and fluoroquinolones.

An adverse drug reaction, as defined by the World Health Organization, is any response to a drug ‘which is noxious and unintended and which occurs at doses used in man for prophylaxis, diagnosis or therapy’.\(^1\) Although most reactions are relatively minor and reversible upon discontinuation, in rare instances, adverse effects of antibacterials can be fatal (anaphylaxis) or severely debilitating (e.g. hepatic injury, ototoxicity) and can have a significant impact on the health of the patient. The elderly are particularly at risk for development of adverse reactions due to underlying comorbidities, age-related changes in the metabolism and excretion of drugs, and greater medication use. Beyond a resultant increase in morbidity and mortality, the financial implications of adverse drug effects can be quite substantial. Just taking into consideration the increased number of hospitalisations attributed to adverse drug reactions, the financial burden on the US healthcare system will reach well into the billions of dollars each year. Furthermore, a high percentage of adverse reactions go unreported, making the true economic impact even higher.

The purpose of this article is to: (i) provide an overview of the adverse effects of the more commonly prescribed antibacterial agents; (ii) review and evaluate studies reporting costs associated with the occurrence of antibacterial adverse effects; and (iii) discuss the economic impact of antibacterial adverse effects.

A MEDLINE search was performed to identify all English-language studies published since 1980 containing relevant information on the economic impact of adverse effects associated with the following classes of antibacterials: \(\beta\)-lactams, aminoglycosides, vancomycin, macrolides and fluoroquinolones.

Additional studies were identified from reference lists of the initial articles.

1. Economic Considerations

Unfortunately, published pharmacoeconomic data on the direct cost of antibacterial adverse effects are rather sparse. Indirect costs as related to productivity, quality of life, and time spent by families and patients receiving medical care, were not uniformly addressed in available studies. Some have suggested the use of instruments, such as tables used in compensation or court proceedings relating to accidents at work or on the highway, to quantify the economic impact of adverse drug events such as the loss of a limb due to thrombosis.\(^2\) Most pharmacoeconomic studies involving antibacterials have focused on overall cost effectiveness, describing in minimal detail the financial impact of antibacterial adverse effects. For example, in a study utilising a concurrent adverse drug reporting programme, antibacterials were the second leading cause accounting for 23.3\% of identified reactions in hospitalised patients; however, no attributable costs were estimated in this study.\(^3\) In a more recent study conducted in the US, on average an adverse drug event in a hospitalised patient was associated with an excess of 1.9 days in the length of stay, extra costs of $US2262 (1990-1993 values), and an almost 2-fold increase in the risk of death.\(^4\)