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Pharmacoeconomics of Apixaban against Warfarin – A Review

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Abstract

Atrial fibrillation, an irregular heartbeat, is a risk factor for various heart-related complications. Its prevalence increases with age and is expected to rise dramatically by 2030. Warfarin is traditionally prescribed to prevent strokes in atrial fibrillation patients, although it has its limits. Apixaban, a newer oral antithrombotic therapy, is effective in reducing strokes and bleeding. Several studies have examined the cost-effectiveness or value for money of Apixaban compared to Warfarin in different countries. In a study conducted in Japan, Apixaban was found to reduce strokes and bleeding events, leading to improved life years gained. Apixaban's total cost per patient was higher, but it was still considered cost-effective. In a study from China, Apixaban also reduced strokes and bleeding compared to Warfarin. The expected life-years gained and quality-adjusted life-years gained were slightly lower compared to the Japanese study, but apixaban was still considered cost-effective. A study from Argentina showed similar results, with Apixaban reducing strokes and bleeding. The cost of Apixaban was higher than Warfarin, but Apixaban was still considered cost-effective based on incremental value-for-money ratios. Overall, the trials show that Apixaban offers better value for money than Warfarin for stroke prevention in atrial fibrillation patients. However, there were variations in the specific outcomes and costs among the countries studied. In Japan, the cost of Apixaban was higher and the life-years gained were greater compared to China and Argentina. Despite these variations, all three studies supported the fact that Apixaban was more value for money as compared to Warfarin.

Keywords: Apixaban, Atrial Fibrillation, Cost-Effectiveness, Warfarin

1. Introduction

Atrial fibrillation is a shaky or irregular heartbeat or arrhythmia. It increases the risk of blood clots, strokes, cardiac disease and other cardiovascular conditions[1]. The prevalence of atrial fibrillation is 0.4% to 1% and this number increases with age (about 8% in patients over 80 years of age). Atrial fibrillation affects many and is one of the persistent arrhythmias in clinical practice. Its prevalence appears to rise as patients develop more severe heart failure, from 4% in people with asymptomatic New York Heart Association (NYHA) class I heart failure to 50% in patients with NYHA class IV heart failure.

Due to several factors, such as ageing and the improved survival rate for patients with hypertension, Coronary Artery Disease (CAD) and Heart Failure (HF), it is expected that the prevalence will go up dramatically reaching 12-15 million by the year 2030[2]. Warfarin has traditionally been employed to treat people with Atrial Fibrillation (AF) who have a moderate to high risk of stroke based on the CHA2DS2-VASc score. Because of several limitations associated with Warfarin use, such as a narrow therapeutic window, the need for routine monitoring, food and drug interactions and pharmacogenetic changes, the Food and Drug Administration (FDA) has approved several oral antithrombotic therapies for stroke

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prevention in patients with nonvalvular AF who are at moderate to high risk for stroke.

Apixaban, an orally active factor Xa inhibitor, has been extensively researched compared to dose-adjusted Warfarin in patients with Nonvalvular Atrial Fibrillation (NVAF). Apixaban has shown a significant reduction in the occurrence of stroke, systemic embolism and significant bleeding in the patients compared to the Warfarin control group. However, being new, Apixaban is expected to be costly. Hence many studies were conducted on the cost-effectiveness of Apixaban as compared to Warfarin in non-valvular AF patients for stroke prevention. The current article reviews some of those studies from various countries and prepares a narrative review.

2. Methodology

A comprehensive search was conducted in the databases using keywords like Apixaban, Warfarin and cost-effectiveness. Many research articles from PubMed and Cochran databases were reviewed. Three articles which compared the value for money of Apixaban with Warfarin in nonvalvular AF patients were selected. These articles are from Japan, China and Argentina, respectively. They were published between 2015-2016. These articles were thoroughly researched and a short review of the value for money of these medicines in the three countries was prepared.

3. Discussions

In the first study conducted in Japan in 2015[3,4], the researcher utilised a modified version of an earlier established approach for health economic evaluation, the Markov model. They compared the cost-effectiveness of the drug Apixaban against Warfarin in Japan. They included major cardiovascular problems including ischemic and hemorrhagic stroke and bleeding issues, etc.

After a thorough evaluation of the study, the base case analysis revealed that Apixaban reduced the incidence of strokes by seventeen out of one thousand patients compared to Warfarin. Furthermore, the number of bleeding incidences, including significant bleeding, stroke and Clinically Relevant Non-Major Bleeding (CRNM), decreased by 85 instances among individuals who received Apixaban. The estimated life-years gained throughout the average course of life treatment per patient was 10.285 in the Warfarin group and 10.516 in the Apixaban group. As a result, Apixaban was predicted to increase life expectancy by 0.231 years and enhance the quality of life of patients, resulting in a gain of 0.240 quality-adjusted life years. On the other hand, the lifetime horizon exhibited that the total cost per patient was (US $51,440) for Warfarin, while the total cost for Apixaban was (US $56,557). As a result, the incremental cost was US$5117. Consequently, the calculated Incremental Cost-Effectiveness Ratio (ICER) was (US$21,357) per QUALITY ADJUSTED LIFE YEARS gained[5]. From the standpoint of the payer, Apixaban is deemed to be more cost-effective.

In the second research that was conducted in China in 2016[6], the researchers here also used a Markov model for the economic evaluation of health problems and included 12 cardiovascular health problems and deaths. Clinical Event Risks were set according to the published trial[3].

This study depicts that, the total number of stroke patients is reduced by 27 per thousand patients in the study group compared to Warfarin, and the total bleeding episodes apart from hemorrhagic stroke also reduced by 74 cases. In comparison to Warfarin, the years gained due to the therapy were 6.67 years for the Warfarin-received patients and 6.84 years for the Apixaban-received patients. Thus, Apixaban was estimated to extend 0.17 life years and improve the quality of life of patients, which led to 0.18 QUALITY ADJUSTED LIFE YEARS gained. The analysis of the cost was based on a public institutional perspective in Hong Kong and because of that, the only direct medical costs were measured. Overall, this study also accepted the value for money of Apixaban.

The last research was conducted in Argentina in the year 2015[7]. Again, the Markov model was used but here 18 health states were included. The model health state consists of stroke in both types, systemic embolism, bleeding in all forms and death. The expected changes between health states were taken from the ARISTOTLE trial. This study indicates that the using of Apixaban contributes to a decrease in stroke cases by 24 compared to Warfarin. Additionally, the bleeding event cases dropped by 41 patients per 1000 in the Apixaban group. Furthermore, the use of Apixaban grew the life year by 0.164 and the quality-adjusted life years by 0.172. On the other hand, the treatment cost for Apixaban was greater than Warfarin by USD 135.06. Corresponding to this result, the increment cost per life year gained is

USD 135.06, and the increment cost per stroke avoided was USD 5422.01. Additionally, the increment cost per quality-adjusted life years gained is USD 786.06, and the incremental cost per bleeding event avoided was USD 3268.66. Apixaban was considered cost-effective in Argentina compared to Warfarin, as its Willingness to Pay (WTP) ranges from USD 11,558 to 34,674 per incremental quality-adjusted life year, surpassing the thresholds of 90% and 95% respectively.

4. Conclusion

According to the results presented by the three researchers, there is a variation in the rated item among examined countries. The net cost of Apixaban used in the treatment of patients with NVAF compared to Warfarin per patient is deemed quite costly in Japan at approximately 5117 USD, while the price of the treatment in Argentina per patient is approximately USD 135.06. Furthermore, the Japanese study found that patients who received Apixaban acquired approximately 0.231 more life years, but the Chinese and Argentina studies found 0.17 and 0.164, respectively. Furthermore, the quality-adjusted life years gained was 0.240 in Japan, 0.18 in China, and 0.172 in Argentina. Finally, according to the reviewed studies, Apixaban is considered more cost-effective than Warfarin in NVAF patients.

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