Heart, Lung and Circulation (2015) **24,** 860–868
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2015.02.018

ORIGINAL ARTICLE

Cost-Effectiveness Analysis of Fondaparinux vs Enoxaparin in Non-ST Elevation Acute Coronary Syndrome in Thailand☆

Unchalee Permsuwan, PhD [a*], Nathorn Chaiyakunapruk, PharmD, PhD [b,c,d,e], Surakit Nathisuwan, PharmD, BCPS [f], Apichard Sukonthasarn, MD [g]

[a]Faculty of Pharmacy, Chiang Mai University, Chiang Mai, Thailand
[b]School of Pharmacy, Monash University Malaysia, Malaysia
[c]Center of Pharmaceutical Outcomes Research (CPOR), Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok, Thailand
[d]School of Population Health, University of Queensland, Brisbane, Australia
[e]School of Pharmacy, University of Wisconsin-Madison, Madison, WI, USA
[f]Faculty of Pharmacy, Mahidol University, Bangkok, Thailand
[g]Department of Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Received 27 August 2014; received in revised form 2 February 2015; accepted 20 February 2015; online published-ahead-of-print 14 March 2015

Background Non-ST elevation acute coronary syndrome (NSTE-ACS) imposes a significant health and economic burden on a society. Anticoagulants are recommended as standard therapy by various clinical practice guidelines. Fondaparinux was introduced and evaluated in a number of large randomised, controlled trials. This study therefore aimed to determine the cost-effectiveness of fondaparinux versus enoxaparin in the treatment of NSTE-ACS in Thailand.

Methods A two-part construct model comprising a one-year decision tree and a Markov model was developed to capture short and long-term costs and outcomes from the perspective of provider and society. Effectiveness data were derived from OASIS-5 trial while bleeding rates were derived from the Thai Acute Coronary Syndrome Registry (TACSR). Costs data were based on a Thai database and presented in the year of 2013. Both costs and outcomes were discounted by 3% annually. A series of sensitivity analyses were performed.

Results The results showed that compared with enoxaparin, fondaparinux was a cost-saving strategy (lower cost with slightly higher effectiveness). Cost of revascularisation with major bleeding had a greater impact on the amount of cost saved both from societal and provider perspectives. With a threshold of 160,000 THB ((4,857.3 USD) per QALY in Thailand, fondaparinux was about 99% more cost-effective compared with enoxaparin.

Conclusion Fondaparinux should be considered as a cost-effective alternative when compared to enoxaparin for NSTE-ACS based on Thailand's context, especially in the era of limited healthcare resources.

Keywords Fondaparinux • Enoxaparin • NSTE-ACS • Cost-Effectiveness • Thailand

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

*Corresponding author at: Department of Pharmaceutical Care, Faculty of Pharmacy, Chiang Mai University, Chiang Mai 50200, Thailand. Tel.: +66 54944355; fax: +66 53222741, Email: unchalee.permsuwan@gmail.com

Introduction

Acute coronary syndrome (ACS) encompasses a range of conditions from unstable angina (UA) to ST-segment-elevation myocardial infarction (STEMI). ACS associated with non-ST segment elevation includes UA and non-ST segment elevation MI (NSTEMI). ACS presents a unique challenge to clinicians due to the high rate of mortality and morbidity associated with these conditions [1]. UA and NSTEMI share similar pathophysiology and clinical presentations, but NSTEMI is characterised by an increase in the biochemical markers of myocardial injury; hence, non-ST elevation acute coronary syndrome (NSTE-ACS) has become the preferred diagnosis for UA/NSTEMI [2]. NSTE-ACS imposes a health and economic burden on society. Patients with NSTE-ACS are also at high risk of death. According to the NICE clinical guideline 2010 for NSTE-ACS [3], treatment with anticoagulants in addition to anti-platelet agents such as aspirin and clopidogrel is recommended. Although low-molecular-weight heparins (LMWHs) have been demonstrated to reduce coronary events, they are associated with an increased risk of bleeding, which can be associated with an increased risk of death [1,4–6]. Appropriate management of NSTE-ACS is challenging, as the benefit of treatments in reducing cardiovascular associated mortality must be balanced against a risk of bleeding.

Fondaparinux is a synthetic pentasaccharide that can inhibit Factor Xa leading to inhibition of thrombin generation [7]. Compared to LMWHs, this new agent possesses favourable pharmacokinetic and pharmacodynamic profiles including high selectivity and specificity against Factor Xa, complete absorption through subcutaneous injection and long half-life allowing simple once daily fix dosing. This agent has been tested and approved in a variety of conditions such as prevention and treatment of venous thromboembolism and acute coronary syndrome. Clinical effectiveness data for fondaparinux in acute coronary syndrome is primarily based on a large multi-centre pivotal trial (OASIS-5) [8] which compared fondaparinux with enoxaparin for the treatment of NSTE-ACS. Fondaparinux was demonstrated to be non-inferior to enoxaparin in preventing death, MI, and refractory ischaemia at nine days. Importantly, fondaparinux was associated with a significant reduction in the rate of major bleeding over both short- and longer term. The short-term efficacy and the reduction in the number of cases of bleeding with fondaparinux, translated to a reduction in the longer-term mortality and morbidity of patients.

For Thailand, LMWHs have been the anticoagulant of choice in the ACS setting especially enoxaparin. Enoxaparin has to be administered twice daily and requires dose adjustment for weight of individual patients. This not only increases the cost of drug administration but also requires diligent effort by clinicians to measure the patient's weight and monitor the drug dose accordingly. With limited healthcare resources in Thailand, such issues can lead to problems in care of patients. In addition, a reduction of bleeding associated with enoxaparin would provide a large cost saving to a developing healthcare system. While data on cost-effectiveness of fondaparinux exists, such studies were done in the countries that have vast differences in healthcare environment from Thailand; hence, the application of data might be limited. Therefore, the aim of our study was to conduct a cost-effectiveness analysis comparing fondaparinux and enoxaparin in patients with NSTE-ACS in Thailand using parameters and data that reflect the local context, when available.

Methods

Overall Description

We used a Markov model to simulate NSTE-ACS patients receiving fondaparinux compared to enoxaparin, which was a standard treatment. We performed a cost-utility analysis with incremental cost per quality-adjusted life year (QALY) gained. The model simulated the life-time horizon to capture long-term costs and effectiveness incurred. As recommended by Thailand's health technology assessment guidelines, the study applied an annual discount rate of 3.0% to costs and benefits [9] and was undertaken from a societal perspective [10]. Costs included drug cost, cost of major bleeding, cost of ACS first year after hospitalisation, cost of ACS in second and subsequent years, and direct non-medical costs such as transportation, care-giver time. Indirect cost was excluded to avoid double-counting since QALY already counted morbidity and mortality effect as a recommendation of Thailand's health technology assessment guidelines [11]. We also performed analysis based on provider perspective, in which only direct medical costs were included. All above costs were adjusted with CPI [12] and presented in the year 2013. The costs were converted at a rate of 32.94 baht per USD as the average rate for 2013 [13].

Intervention and Comparators

We compared fondaparinux (at a dose of 2.5 mg once daily) with enoxaparin (at a dose of 1 mg/kg body weight twice daily) for six days in the treatment of patients with NSTE-ACS. Due to the report from the OASIS-5 trial [8] regarding a few cases of coronary and catheter-related thrombosis in patients who underwent PCI, patients receiving fondaparinux who underwent revascularisation would receive 100 IU/kg of unfractionated heparin (UFH) to flush the catheters. Enoxaparin is the most commonly prescribed LMWH in Thailand. It is therefore considered to be the most appropriate comparator as the treatment most likely to be displaced by fondaparinux.

Study Cohort

The study cohort included only patients with NSTE-ACS. The mean age of patients recruited in the OASIS-5 trial [8] was 66.6 years so that we assumed our study cohort with age started at 60 years and older. We also excluded the patients with creatinine clearance (CrCl) < 30 ml/min. The dose of medications was calculated based on 60 kg body weight for our Thai patients.