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Original Article

# DRUG UTILIZATION AND ECONOMIC IMPACT OF ANTICOAGULANTS IN UNSTABLE ANGINA/ NON- ST ELEVATION MYOCARDIAL INFARCTION IN KARACHI

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**ABSTRACT**

**Objective:** The present study was designed to evaluate drug utilization and the economic impact of anticoagulants for the treatment of unstable angina (UA)/non-ST elevation myocardial infarction (NSTEMI) in Karachi.

**Methods:** A prospective study of prescriptions was conducted in private and public tertiary care hospitals (University of medical education and research) situated in Karachi. The purpose of prescriptions review was to examine the utilization and cost analysis of anticoagulants (enoxaparin, dalteparin and fondaparinux) in hospitalized patients of UA/ NSTEMI during treatment course of 2-8 days. Information of prescribed drugs was obtained from the medical records whereas patient demographics and socioeconomic status were reported through patients/relatives interviews. Data of 487 UA/NSTEMI patients admitted were analyzed during the study period of 2013-2014.

**Results:** Data of 487 UA/NSTEMI hospitalizations demonstrated the increased number of prescriptions for enoxaparin, it was found to be widely used anticoagulant in the public and private organizations in Karachi. Enoxaparin attributed by 70% of drug utilization comparative to 24.8% fondaparinux and 5.1 % dalteparin. Though, economic contribution was in favor of fondaparinux by reducing total drug cost of $ 21 with enoxaparin and $ 32 in contrast of dalteparin on the basis of once daily dose in the conservative management of unstable angina/non-ST elevated myocardial infarction.

**Conclusion:** In patients with unstable angina (UA)/non-ST elevation myocardial infarction (NSTEMI), enoxaparin was found to be most widely prescribed low molecular weight heparin (LMWH) among other available alternatives. However, economic assessment considered fondaparinux as cost saving therapeutic agent for initial conservative management of 2-8 days, added financial benefits over current therapies in the treatment of UA/NSTEMI.

**Keywords:** Drug utilization, Economics, Anticoagulants, Unstable angina/NSTEMI.

## INTRODUCTION

Drug utilization is necessary to recognize the variation among prescribing practice that could support health care professionals to improve clinical outcomes in the healthy society. Such utilizations acts as indicators intended to measure specific aspects of health providers and drug use in a hospital or health care center [1, 2, 16]. Unstable angina (UA)/non-ST elevation myocardial infarction (NSTEMI) referred to acute coronary syndrome (ACS) responsible for unexpected chest pain usually occurs at rest. The most common reason found reduced blood flow to the cardiac muscle associated with narrow coronary arteries caused by fatty depositions (atherosclerosis). Patients with unstable angina have a threefold increased risk of developing myocardial infarction. These life-threatening disorders are main cause of emergency medical care and hospitalization [3, 4]. Drug utilization helps to recognize variability in drug use and to support interventions that improve patient outcomes. Indicators provide information to health care managers concerning drug use, prescribing habits, and important views of patient care. They reflect the status of an important characteristic of the given health care service [2, 16]. Anticoagulants are blood thinners, usually prescribed in hospitalized patients of unstable angina (UA)/non-ST elevation myocardial infarction (NSTEMI) to prevent blockage of coronary arteries. Low molecular weight heparin (enoxaparin and dalteparin) has replaced unfractionated heparin (UFH) during the past decade with the simplicity of subcutaneous administration and eliminate the need of laboratory monitoring [5.

Various guidelines addressed the management of patients with UA/NSTEMI. American Heart Association (AHA), UK National Health Service (NHS) in the year 2000 reported the £80.7 million prescription cost against 634 000 individuals of angina [4]. A study conducted in India (2004), showed 93% prescriptions of low molecular weight heparin (LMWH) and enoxaparin was most widely prescribed drug 76% of the total use of LMWH, trend of enoxaparin found to increased from 17% to 70% [6]. Efficay and safety of subcutaneous enoxaparin in coronary events (ESSENCE) trial compared enoxaparin versus UFH in 3171 unstable angina patients and found the entire treatment costs for early hospitalization $11 857 for enoxaparin and $12 620 for UFH [7]. A study conducted in U. S on 936 UA/NSTEMI patients showed that initial cost of enoxaparin was high US $75 compared to UFH but cost saving observed US $763 at the time of hospital discharge with enoxaparin [8, 9]. Economic trial from the Canadian hospital on the basis of ESSENCE trial demonstrated lower cost of enoxaparin Canadian $848 versus UFH Canadian $892[10].

## MATERIALS AND METHODS

### Study design

This study presented the data on drug utilization and cost assessment of anticoagulants in the conservative management of unstable angina/ NSTEMI in private and government tertiary care hospital with dedicated visits in coronary care units and wards. The inpatient registry was searched to identify the patients who were admitted with UA/NSTEMI after clinical investigations. Total 487 consecutive prescriptions were evaluated during one year study period of 2013- 2014. Demographics detail and socioeconomic status were obtained from patient's interviews. The use of following drugs (enoxaparin, dalteparin and fondaparinux) was recorded through medical profiles. Economic assessment of total drug cost was carried out based on dose frequency.

### Study approval

Mandatory approval from the Institutional Ethics Committee was obtained prior to the initiation of the study.

### Statistical analysis

The data was analyzed using Statistical Package for Social Sciences (SPSS) Version 20.

**Table: 1 Demographic profile among study subjects (n= 487)**

| Patient's profile | Patients (n) | Percentage (%) |
|---|---|---|
| **Age:** | | |
| 35-44 | 35 | (7.2) |
| 45-54 | 118 | (24.2) |
| 55-64 | 179 | (36.8) |
| 65-74 | 122 | (25.1) |
| 75+ | 33 | (6.8) |
| **Mean 59 years** | | |
| Gender: | | |
| Male | 333 | (68.4) |
| Female | 154 | (31.6) |
| **Socioeconomic Status** | | |
| Upper class | 48 | (9.9) |
| Lower upper class | 53 | (10.9) |
| Middle class | 87 | (17.9) |
| Lower middle class | 131 | (26.9) |
| Lower class | 168 | (34.5) |

## RESULTS

The case record files of 487 patients who were admitted with unstable angina/NSTEM were retrieved from the medical records section and properly studied. Prevalence of hospital admissions was described by large number of male patients 68.4% and approximately 31.6% of females with mean age of 59 years old. Furthermore, majority of admitted patients 34.5% indicated their lower socioeconomic status and very fewer 9.9% were from an upper class category. There were no significant difference in the hospital stay and duration of hospital was same among all treatment groups (enoxaparin, fondaparinux and dalteparin) with mean of 4 days. Among 487 hospitalizations, majority of patients were treated with enoxaparin and high number of prescriptions was found in case of enoxaparin70% comparative to 24.8% fondaparinux and very few 5.1% with dalteparin in current local practice. Increased utilization of enoxaparin experienced in both cases of hospitalizations, patients who admitted once or re-hospitalized received 68% and76.3% prescriptions of enoxaparin comparative to other alternatives. Estimated total drug cost found $ 36, $ 15 and $ 47 with enoxaparin, fondaparinux and dalteparin respectively. The cost savings observed in total drug cost with fondaparinux in comparison with other alternatives were $ 21 with enoxaparin and $ 32 with dalteparin. With respect to economic evaluation, patients who treated with fondaparinux showed significant savings in all areas of hospitalization in the conservative management based on a once daily dose.

**Table 2: Frequency of drug utilization (n= 487)**

| Descriptions | Prescriptions (n) | Percentages (%) |
|---|---|---|
| **Anticoagulants** | | |
| Enoxaparin | 341 | (70.0) |
| Fondaparinux | 121 | (24.8) |
| Dalteparin | 25 | (5.1) |
| Length of hospitalization: Mean 4 days | | |

**Table 3: Drug utilization and type of admission (n=487)**

| Anticoagulants | Prescriptions (%) | |
|---|---|---|
| | Re-hospitalized (n) | Admitted once (n) |
| Enoxaparin | 251 (68.0) | 90 (76.3) |
| Fondaparinux | 102 (27.6) | 19 (16.1) |
| Dalteparin | 16 (4.3) | 9 (7.6) |

**Table 4: Cost estimation of anticoagulants (n= 487)**

| Variables | Enoxaparin mean PKR($) | Fondaparinux mean PKR ($) | Dalteparin mean PKR ($) |
|---|---|---|---|
| Drug cost /day | 888(9) | 375(4) | 800(8) |
| CCU drug cost | 529(5) | 211(2) | 672(7) |
| Wards drug cost | 3128(31) | 1315(13) | 4096(40) |
| Total drug cost | 3657(36) | 1525(15) | 4768(47) |

PKR= Pakistani Rupee, USD ($) = US dollar, 1USD= 102.79 PKR, 2014

## DISCUSSION

Based on the results of this study, only patients who received enoxaparin, fondaparinux and dalteparin were evaluated and those who had not received the drug were excluded from this investigation. In accordance with a report of an Indian hospital, enoxaparin was one of the heparin used by 89% of UA/NSTEMI patients. The cost of treatment of a single episode of unstable angina in the hospital was US $494 and enoxaparin accounted 60% of expenditures of drug among other anti-angina agents [11]. Cardiology guidelines recommend both enoxaparin and fondapariniux in the conservative treatment of low risk unstable angina/NSTEMI patients. American College of Cardiology (ACC) recommended the use of enoxaparin and fondaprinux in the conservative management of UA/ NSTEMI [12, 13]. The reason behind the outgrowth in prescriptions and use of LMWH lies in the fact that patients can effectively use it without hospitalization [14]. In our study, one of the reasons of increased drug utilization of enoxaparin was the inclusion of the drug in the hospital formulary of both private and government hospital whereas fondaparinux and dalteparin were added in the formulary of government hospital. A survey of 224 hospitals in U. S reported the inclusion of enoxaparin in 81.1% hospital formulary compared to dalteparin 17.3% [15]. Results of study showed less prescription of dalteparin comparative to enoxaparin. Addition and utilization of fondaparinux in the government hospital was to control the therapy load on admitted UA/NSTEMI patients but still economic analysis must have prime focus and extensive association in favor of those patients who are financially weak or re-hospitalized. Fondaparinux found as cost saving and must be added in hospital formulary to minimize health acre expense. This type of review can alert the physicians in order to monitor the prescribing patterns of medications. The key physicians must then be alerted so that educational programs and protocols can be implemented. Besides all, holding educational programs and implementation of protocols, especially for more expensive and frequently used medications, may be needed in the teaching hospitals to control prescribing patterns in order to decrease economic load on an individual in the healthy society.

## CONCLUSION

Enoxaparin found to be most extensively used and prescribed low molecular weight heparin (LMWH) among private and government hospitals in Karachi. However, fondaparinux remain a choice of drug for the treatment of unstable angina/NSTEMI patients by reducing total drug cost. A variety of low-molecular weight heparins are available for therapy but comparative clinical trials of efficacy and pharmacoeconomic studies comparing the various LMWH still need to be carried out.

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## CONFLICT OF INTEREST

The authors report that there is no conflict of interest

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