DOI: 10.17957/TPMJ/16.3450

UNSTABLE ANGINA

DIRECT TREATMENT COST OF UNSTABLE ANGINA WITH LOW MOLECULAR WEIGHT HEPARIN IN CONSERVATIVE MANAGEMENT gr8shazz@yahoo.com

Dr. Shazia Alam¹, Prof. Dr. Syed Baqir Syum Naqvi², Dr. Maqsood Ahmed³

ABSTRACT... Objective: To determine the direct treatment cost of unstable angina (UA) with low molecular weight heparin (LMWH) in conservative management. Study design: Prospective study. Settings: Government cardiovascular hospital and private tertiary care hospital, Karachi. Study period: One year. Method: All 487 patients with either sex having cardiac history of ischemic heart disease, presenting chest pain diagnosed to have unstable angina admitted in hospital for 2-8 days were recruited and entered in study. The current prospective study was designed to analyze the direct treatment cost of UA with LMWH. Data was collected through proforma and results were analyzed by SPSS version 20. Results: Results were represented in terms of percentages, frequencies and means of cost contribution of LMWH. All costs values converted from Pakistani currency (PKR) into US dollars (\$) as per exchange rate of 2014. Less number of prescriptions found for fondaparinux (24.85%) than enoxaparin (70%). The estimated mean of drug cost particularly observed in three treatment groups of patients who received enoxaparin, fondaparinux and dalteparin was \$36, \$ 15 and \$ 47 correspondingly. Moreover, 4 days total direct cost of enoxaparin and fondaparinux was \$191, \$84 and 6 days treatment costs \$ 149 with dalteparin to treat a single case of UA. It has been found that fondaparinux significantly lowers the cost of care in comparison to enoxaparin and dalteparin. Conclusion: Current analysis concluded that in the treatment of unstable angina, fondaparinux found to be a dominant strategy that simultaneously lowers the cost of care in conservative management.

 Key words:
 Direct cost, UA treatment, Low molecular weight heparin, Conservative management

Article Citation: Alam S, Naqvi SBS, Ahmed M. Unstable Angina; Direct treatment cost of unstable angina with low molecular weight heparin in conservative management. Professional Med J 2016;23(10):1276-1280. DOI: 10.17957/ TPMJ/16.3450

Unstable angina (UA) is potentially considered as life-threatening disorder requires immediate hospitalization and proper treatment. UA is a leading and expensive health care problem worldwide that usually pressurized the individual to pay against affordability. Patients presenting with UA account for approximately 1.4 million hospital admissions annually in the United States and 2 to 2.5 million worldwide.1 Approximately 25,040 UA cases were reported in Canadian Province and the direct hospitalization cost per UA patient was 4,525 Canadian dollars.² The expected proportion of UA may increase from 14% to around 23% in 2050 among Australian population and the direct cost spent was 577 Australian dollars to treat a single case of UA.3 The projected direct cost for UA \$ 46.8 billion including emergency fee and medical cost in U.S.⁴ The aggressiveness of therapeutic approach must be recognized expeditiously and the key in this decision making is to propose that initial management strategy is conservative, usually refer to management of lowrisk patients for 2-8 days who do not undergo for cardiac procedures.. The conservative strategy initially starts with LMWH such as enoxaparin and fondaparinux soon after clinical confirmation of disease.

The management of UA has been summarized in guidelines such as American College of Cardiology (ACC), American Heart Association (AHA) and European Society of Cardiology (ESC). AHA/ACC guidelines considered enoxaparin (Level of evidence A) or fondaparinux (Level of evidence B) for conservative strategy and when

1. B.Pharm, M.Pharm, Ph.D. Assistant Professor, Department of Pharmaceutics, Faculty of Pharmacy, Ziauddin University, Karachi.

 Ph.D. Professor, Faculty of Pharmacy, Department of Pharmaceutics, Hamdard University, Karachi.
 B.Pharm, M.Pharm, Ph.D. Assistant Professor, Department of Pharmaceutics, Faculty of Pharmacy, Ziauddin University, Karachi.

Correspondence Address:

Dr. Shazia Alam B.Pharm, M.Pharm, Ph.D. Assistant professor, Department of Pharmaceutics, Faculty of Pharmacy, Ziauddin University, Karachi. gr8shazz@yahoo.com

Article received on:

16/05/2016 Accepted for publication: 22/08/2016 Received after proof reading: 07/10/2016

INTRODUCTION:

patients do not undergo for cardiac procedure within 24 hrs.⁵ AHA/ACC thought fondaparinux to be a choice of drug for conservative strategy. However, ESC certified fondaparinux over enoxaparin for conservative approach to reduce major bleeding and mortality.6,7,8 ACCP proposed the use of fondaparinux than enoxaparin at the stage of conservative management for UA.9, 10, ¹¹ To date, several studies have examined the treatment patterns and direct cost for patient with UA and the current study used the real cost data of hospitalized UA patients. Given the considerable disease burden of UA and its economic impact, with particular emphasis in health care sector, the objective of study was to evaluate the direct treatment cost of UA with LMWH.

METHOD

The prospective study of one year was conducted in a government cardiovascular hospital and private tertiary care hospital situated in Karachi, Pakistan. All 487 patients with either sex having cardiac history of ischemic heart disease, presenting chest pain diagnosed to have unstable angina were recruited and entered in study who admitted in hospital for 2-8 days. Patients who have renal insufficiency, bleeding complications and those are at high risk and require cardiac procedures were excluded from study. The present study was designed to analyze the direct treatment cost of unstable angina (UA) with LMWH in conservative management. The relevant information was collected by means of proforma keeping all aspects of study including demographics of respondents and cost analysis of LMWH during treatment phase. Prior to conduct economic research, ethical approval was taken from ethical review board of hospital.

RESULTS

Data was properly arranged and analyzed using SPSS 20. Results were represented in terms of percentages and means of cost contribution of LMWH. All costs values converted from Pakistani currency (PKR) into US dollars (\$) as per exchange rate of 2014. Demographic profiles of all 487 UA patients like age groups and genders are specified in figure 1 and 2 respectively. However,

figure 3 indicates the number of prescriptions of LMWH prescribed and utilized by patients during study course. Fig 4 indicated the drug utilization and socioeconomic status. In comparison of fondaparinux and dalteparin, enoxaparin was the most commonly prescribed low molecular weight heparin in all categories. Majority of UA patients exist in upper and lower class utilized enoxaparin. However, rate of high prescriptions of all three medicines was found in individuals who belonged to lower middle and lower class. Level of enoxaparin prescriptions (66) found in both middle and lower middle class than high frequency of drug utilization (109) in patients of lower class family. All cost data of LMWH, mean of hospital stay and day's ranges are mentioned in table I.





Figure 2. Genders of Respondents





Socioeconomic Class

Figure-4. Frequency of Drug Utilization and Socioeconomic Status

1 Longth of hospitalization		Total drug cost	
1-Length of hospitalization (Days)		Mean (PKR)	Mean (\$)
	≤ 3	2653	26
Day's ranges	4-6	3802	37
	≥ 7	6133	60
Mean	4	3184	31
2-Total drug cost (LMWH) Enoxaparin Fondaparinux Dalteparin	4	3657	36
	4	1525	15
	6	4768	47
3-Total direct cost (LMWH) Enoxaparin Fondaparinux Dalteparin	4	19434	191
	4	8508	84
	6	15188	149
Table-I. Cost	Analysi	is of LMWH	

DISCUSSION

Despite recent advancement. UA continues to present an enormous burden worldwide. In third world countries the cost of healthcare is usually borne through out-of-pocket payments. Determination of treatment cost of unstable angina (UA) is important because it describes the distribution of expenditures across the health care services utilized during hospitalization. Such data is particularly useful for health decision makers who are responsible for medical cost of UA in defined population. Figure 1 demonstrated about (36.76%) admissions of age between 55-64 years and few patients of age above 75 years with preponderance level of male patients than females shown in figure 2. Several guidelines suggested the use of enoxaparin and fondaparinux in conservative treatment of UA and variety of economic researches have been demonstrated the cost of care for UA with LMWH. An investigator suggested that a large health economic data of fondaparinux is not recently available which provide general cost savings but it lowers the cost of care when compared to enoxaparin in conservative management.¹² The results in figure 3 showed less number of prescriptions for fondaparinux (24.85%) than enoxaparin (70%). A study showed 60% of expense with enoxaparin as drug cost although treatment cost per unstable angina patients was US \$494.13 Similarly a study reported the average cost of UA treatment with enoxaparin \$155 in United States.^{14, 15} Moreover. another trial of 936 unstable angina patients evaluated the initial cost of enoxaparin \$75 in U.S. ^{16, 17} Further results found 5 days treatment cost of enoxaparin \$140.18 Table 1 represents the total drug cost according to ranges of hospital stay in days. The mean of total drug cost found \$31 at 4 days but the estimated mean of drug cost particularly observed in three treatment groups of patients who received enoxaparin, fondaparinux and dalteparin was \$36, \$ 15 and \$ 47 correspondingly. The results indicate less cost \$15 with fondaparinux per UA patient. An investigator demonstrated the cost ranges of enoxaparin and fondaparinux for 3-8 days of treatment course and estimated cost contributed by enoxaparin and fondaparinux was £50 and £33 respectively.19 One more study discussed the treatment cost

per patient R\$ 2,768 for fondaparinux and R\$ 2.852 for enoxaparin.²⁰ Moreover, in our study. total direct cost of enoxaparin and fondaparinux was \$191 and \$84 to treat a single case of UA at 4 days. An economic research analyzed high treatment cost with dalteparin £ 525 per patient²¹ and 6 days treatment costs \$ 149 per UA case with dalteparin in recent study. It has been found that fondaparinux significantly lowers the cost of care in comparison to enoxaparin and dalteparin. Treatment recommendations suggest both enoxaparin and fondaparinux as rational for conservative approach but present findings showed that fondaparinux may have developed economical advantages over available therapy. Fondaparinux found to reduce the direct treatment cost incurred by patients as out of pocket. So fondaparinux might be one of the possible choices to minimize the economic load on individual while treating UA patients.

CONCLUSION

The direct health costs of UA produce a large economic burden in health-care system. There are certain limitations of availability of scientific economic researches and meta-analysis or systemic reviews on LMWH particularly in Pakistan. In many instances, pharmacoeconomic informations are unavailable when a decision must be made on including a drug in the formulary. Fondaparinux was available only in government hospital but was not included in hospital formulary of private hospital. Same case was observed with strictly limited use of dalteparin in government sector and unavailability in private units whereas enoxaparin was found in the formulary of both hospitals. So it was difficult to increase the number of patients on either fondaparinux or dalteparin comparative to large number of patients who received enoxaparin. Current analysis concluded that in the treatment of unstable angina, fondaparinux could be one of promising substitute among the dominant strategy of other alternatives that simultaneously lowers the cost of care. In current practice, fondaparinux could be added as alternative choice to enoxaparin in conservative management. Such economic assessment may facilitate the decision makers

in future to modify hospital policies, quantify the interventions and their associated cost. **Copyright© 22 Aug, 2016.**

REFERENCES

- Mahoney EM, Jurkovitz CT, Chu H, Becker ED, Culler S, Kosinski AS, et al. Cost and cost-effectiveness of early invasive vs. conservative strategy for the treatment of unstable angina and non–ST-segment elevation myocardial infarction. JAMA. 2002; 288(15):1851-58.
- Zeneca A, Kanichay R, Wilsdon T, Cannolly S, Sauri L. The economic and societal burden of acute coronary syndrome in Canada. CRA Charles River Associates, Draft Final Methodology Report, 2010 CRA.
- 3. The economic costs of heart attacks and chest pain (Acute Coronary Syndrome) Access Economics, 2009.
- Chen SY, Crivera C, Stokes M, Boulanger L, Schein J. Clinical and economic outcomes among hospitalized patients with acute coronary syndrome: an analysis of a national representative medicare population. Clinico Economics and Outcomes Research. 2013; 5: 181–88.
- Kumar A, Cannon. Acute coronary syndrome: Diagnosis and management, Part I. Mayo Clin Proc. 2009; 84 (10): 917-38.
- Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE, et al. ACC/AHA guideline revision. ACC/AHA 2007 Guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction—Executive summary. J Am Coll Cardiol. 2007; 50 (7): 652-726.
- 7. Bassand JP. The place of fondaparinux in the ESC and ACC/AHA guidelines for anticoagulation in patients with non-ST elevation acute coronary syndromes. EUR Heart J Suppl. 2008; 10: 22-29.
- Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE, et al. ACCF/AHA 2007 guidelines for the management of patients with unstable angina/ non-ST-elevation. Circulation. 2013; 127: 663-828.
- Harrington RA, Becker RC, Cannon CP, Gutterman D, Lincoff AM, Poma JL, et al. Antithrombotic therapy for non-ST-segment elevation acute coronary syndromes. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition) Chest. 2008; 133: 670-707.
- Wong CK, Harvey D. Enoxaparin: A perspective on its use for coronary artery disease. Aging Health. 2008; 4(6): 579-91.

- 11. An ASHP discussion guideline for antithrombotic therapy in the management of acute coronary syndrome and venous thromboembolism in health system supported by sanofi-aventis US.
- 12. Nutescu EA. Easing the economic burden of acute coronary syndromes: Cost effectiveness of emerging therapies. AMJ Mangaed Care. 2006; 12: 444- 50.
- Malhotra S, Grover A, Verma NK, Bhargava VK. A study of drug utilization and cost of treatment in patients hospitalized with unstable angina. Eur J Clin Pharmacol. 2000; 56(9-10):755-61.
- Daniel MB, Patricia CA, Berkowitz D, Ray LD, Delong ER, Turpie AGG, et al. Economic assessment of low-molecular-weight heparin (Enoxaparin) versus unfractionated heparin in acute coronary syndrome patients: Results from the ESSENCE randomized trial. Circulation. 1998; 97: 1702-7.
- Rosito GA, Dasilva OB, Ribeiro JP. Pharmacological and clinical evidence for the use of low-molecularweight heparins in acute coronary syndromes. Arq. Bras. Cardiol. 2001; 77(2): 190-5.
- 16. Mark D. When innovative therapies make economic sense: Economic analysis of enoxaparin versus

unfractionated heparin in the ESSENCE trial--An overview. Efficacy and safety of subcutaneous enoxaparin in non-Q wave coronary events. Can J Cardiol. 1998; (14): 24-27.

- Zed PJ. Low-molecular-weight heparins in the management of acute coronary syndromes. Arch Intern Med. 1999; 159 (16): 1849-57.
- Patel and Sunderji R. Enoxaparin for acute coronary syndromes. Drug & Therapeutics Newsletter. 2000, CSU-Pharmaceutical Sciences.
- 19. Radia H. Fondaparinux for the treatment of unstable angina or NSTEMI. London New Drugs Group 2009 http://www.nelm.nhs.uk/search
- Pepe C, Machado M, Olimpio A, Ramos R. Costeffectiveness of fondaparinux in patients with acute coronary syndrome without ST-segment elevation. Arq. Bras. Cardiol. 2012; 99 (1): 613-22.
- 21. Janzon M, Levin LA, Swahn E, FRISC II Investigators. Cost effectiveness of extended treatment with low molecular weight heparin (dalteparin) in unstable coronary artery disease: results from the FRISC II trial. *Heart.* 2003; 89: 287-92.



"You will never change your life until you change something you do daily."

Mike Murdoch

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Shazia Alam	Data collection, Result & Discission	\$
2	Prof. Dr. S. Baqir Syum Naqvi	Data Analysis	E VE
3	Dr. Maqsood Ahmed ³	Data complication	en la

AUTHORSHIP AND CONTRIBUTION DECLARATION