Pak Heart J

EFFECT OF GENDER ON EFFICACY OF STREPTOKINASE IN ACUTE ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

Ahmad Hasan[1], Shahzad Tawab[2], Muhammad Arif[3], Muhammad Muzamil[4], Aqib Javed[5], Muhammad Aslam[6]

[1,2,4-6]Cardiology Department, Allama Iqbal Medical College, Lahore, Pakistan.
[3]Medical Department Allama Iqbal Medical College, Lahore, Pakistan.

Address for Correspondence:

Ahmad Hasan

Cardiology Department, Allama Iqbal Medical College Lahore, Lahore, Pakistan

Email: ahnmalik@hotmail.com

Date Received: March 26, 2019

Date Revised: April 25, 2019

Date Accepted: May 22, 2019

Contribution

AJ and ST conceived the idea and designed the study. Data collection was done by MA, MM and AJ. Final review was done by MA. All authors contributed equally to the submitted manuscript.

All authors declare no conflict of interest.

This article may be cited as: Hasan A, Tawab S, Arif M, Muzamil M, Javed A, Aslam M. Effect of gender on efficacy of streptokinase in acute ST segment elevation myocardial infarction. Pak Heart J 2019; 52 (03):254-7

ABSTRACT

Objective: To study the relation of gender with the efficacy of thrombolytic therapy.

Methodology: It is a cross sectional study conducted from December 2017 to July 2018 at Jinnah Hospital Lahore. Patients from single center fulfilling the eligibility criteria for thrombolytic therapy and receiving the therapy were included and were followed during their hospital stay and their hospital outcome was recorded SPSS version 22 was used for analysis.

Results: Among 780 patients 52.6% (n = 410) were males. The resolution of chest pain within 90 mins occurred more in males (69.5%) as compared to females (49.7%)(p =.000), wash-out phenomenon was more in males (72.9%) as compared to females (51.6%) (p = .000), ST resolution (22.4% in males 21.6% in females) (p=.783) and reperfusion arrhythmias (18.3% in males vs 16.2% in females) (p 0.444). Cardiac failure [15.9% in females vs 9.3% males (p = 0.005)], reduction in LV ejection fraction (LVEF) [(10.8% in females vs 5.6% in males (p = 0.008)], sudden cardiac death during hospital stay [females (8.6%) vs males (4.4%) (p = 0.015)], immediate hypotension [females 27.3% vs 24.9% (p = 0.442)], malignant arrhythmias requiring intervention [females (10%) than in males (6.6%) (p = 0.83)] were more in females as compared to males.

Conclusion: Female gender is more prone to complications with less beneficial clinical response to thrombolytic therapy as compared to their counterpart gender.

Key Words: Thrombolytic therapy, Gender, Efficacy.

INTRODUCTION

It has already been established by available data that gender differences do exist in the incidence and clinical presentation of cardiovascular diseases, and also the response to antithrombotic therapy between the two genders differ in both terms of safety and efficacy.

The pathophysiological mechanisms underlying these differences in genders are not fully understood, and may be of multiple reasons. Some characteristics relating to female hormonal changes, pregnancy associated hemodynamics might explain the differences in the risk of bleeding and thrombosis related to antithrombotic therapies, causing the net clinical benefit of these therapies less efficacious than the counter-part of the same age.

Coronary artery disease is the leading cause of mortality and morbidity in both men and women which accounts for over one third of total deaths.[1] The worldwide INTERHEART Study, a large cohort study of more than 52000 individuals with myocardial infarction, has shown that women present at least 10 years later than men as having ACS, mostly after menopause[2]. Despite this delay in onset, mortality is increasing more rapidly amongst women than men.[3]

Fibrinolytic therapy has been a major advance in the treatment of acute STEMI since >90% of STEMI is due to plaque rupture and subsequent thrombus formation which has led to about decrease to about 46% mortality in vascular death shown by ISIS 2 trial. Cardiovascular disease (CVD) remains still the leading cause of death in women and, and according to a recently released United States statistics, it accounted for around 0.4 million female deaths in 2013.[3]

Both gender differ in the anatomy and physiology of the cardiovascular system (body make up, female hormonal changes during menstrual cycle), pregnancy, menopausal response of body and also in risk factors, prevalence, symptoms, management, and outcomes of CVD.[4,5] There are also sex-related differences in the pharmacokinetics (PK) of the drugs administered and pharmacodynamics (PD), which is the relationship between the drug effect and its concentration at the point of action, of the most commonly used cardiovascular drugs[4,5] So, it would not be a surprise that efficacy and safety of the most of the cardiac drugs can differ between two gender.[6,7]

The current study was carried out to see whether there is difference in the effect of the thrombolytic therapy among females and males with acute STEMI, both in terms of its effect and complications.

METHODOLOGY

This cross sectional study was conducted at Jinnah Hospital Lahore including 780 patients from Dec 2017 to Jul 2018.All the patients eligible for thrombolytic therapy were included in the study. The door-to-needle time was average of 42 minutes. After ruling out the contraindications for thrombolysis, 1.5 million units were administered with standard protocol, the time of administration of streptokinase for every patient varied depending upon the response. ECG of all the patients was taken before the administration of streptokinase and 90 mins after giving the streptokinase by a single operator and was interpreted by two experts independently and blindly to each other as well as all other study characteristics and outcomes. The patients were continuously monitored through the electronic monitors for any change in rhythm or reperfusion arrhythmias. Perception of pain was recorded by using Numerical Pain Rating Scale both before and 90 minutes after administration of streptokinase. Two set of serial cardiac enzymes were done one within 24hours of the infarction and second on the 2nd post admission day. Echocardiography was done on Vivid 7 (GE Systems) one day before discharge measuring Ejection Fraction (by parasternal long axis, parasternal short axis, Simpson`s method and taking the average). Computed tomography of brain, if indicated, was done when required. All the data was entered in Microsoft Excel and analyzed for statistical significance in SPSS version 22.

RESULTS

About 780 patients were included. Age distribution of the patients was done which shows that 57.1% (n = 445) were less than 50 years of age while 42.9% (n = 335) were above 60 years of age, with mean age of 49.78 ± 7.69 years (Table 1).

Patients were distributed according to gender showing that 52.6% (n = 410) were males while 47.4% (n = 370) were females (Table 1).

Table 1: Gender Distribution of Study Population (n= 780)

Variables	Frequency (n)	Percentage (%)
Age		
Mean=49.7846 SD=7.69,		
< 50 years	445	57.1
> 50 years	335	42.9
Gender		
Males	410	52.6
Females	370	47.4

The frequency of efficacy of thrombolytic therapy among the two genders is shown in figure 1. The resolution of chest pain within 90mins occurred more in males (69.5%) as compared to females (49.7%)(p =.000). The wash-out phenomenon (rapid rise and rapid fall of CKMB) was also more in males (72.9%) as compared to females (51.6%) (p = .000) (Figure 1)

There was also a difference, betweenthe two sexes of ST resolution (22.4% in males 21.6% in females) (p=.783)and reperfusion arrhythmias (18.3% in males vs 16.2% in females) (p = 0.444)

Regarding complications, Females were more prone to complication such as cardiac failure 15.9% females vs 9.3% males (p = 0.005), more reduction in LV ejection fraction (LVEF) in females as compared to males (10.8% vs 5.6% (p = 0.008), more incidence of sudden cardiac death during hospital stay in females (8.6%) vs males (4.4%) (p = 0.015), the females experienced more episode of immediate hypotension during streptokinase administration 27.3% vs 24.9% (p = 0.442). There were 05 out of 370 patients who got intracerebral bleed during or after the streptokinase administration with females more prone to get this complication against their counterpart 1.4% vs 0.2% (p = 0.77). Malignant arrhythmias requiring intervention were also more common in females (10%) than in males (6.6%) (p = 0.83) (Figure 2).

Figure 1: Frequency of efficacy of thrombolytic therapy among genders.

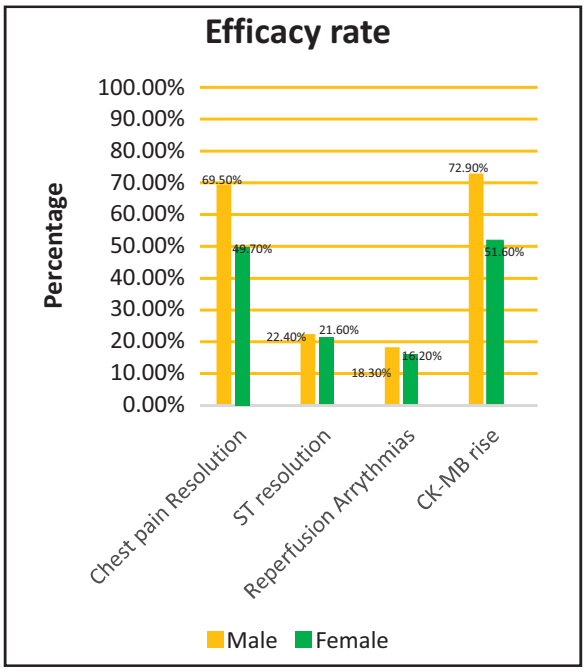
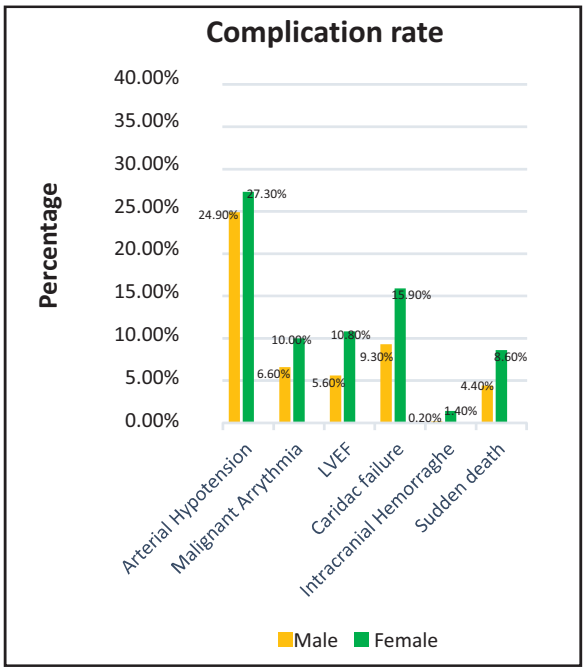


Figure 2: Frequency of complication of thrombolytic therapy among genders.



DISCUSSION

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in both sexes.[8,9] In the past, the risk of coronary artery disease(CAD) was underestimated in females due to a misconception that women were protected against this disease. But, even when women during the fertile period have a less risk of developing cardiovascular events, this benefit of having less events decreases after menopause, so that CAD becomes the major cause of mortality in women older than 65 years of age.[10-13] In Europe, CVD causes a greater proportion of deaths among females (51%) as compared to men (42%), i.e. meaning by leading to double deaths as from all forms of cancer combined.[8,9]

Numerous randomized clinical trials have revealed a sex-related difference in the efficacy and safety of many widely used cardiovascular drugs both in emergency and cardiology departments as well.[14,15] Women with IHD having a higher mortality, and poorer CVD outcomes compared to men.[16,17]

Our study also showed that there does exit a difference in both the beneficial effect of the thrombolytic therapy in both genders as well as the complication rates. The men benefit more from this therapy achieving early relief of chest pain, ST segment resolution. This is in contrast to a review by J. Tamargoet. al. while in favor to a study of 1012 patients showing the results in consistence with our study that the females respond less to thrombolytic therapy as compared to men.[18,19] The complication rates and side effects of the thrombolytic therapy were high in female, with immediate hypotension being the most common.[20-21] Various other studies have also shown that Women show a greater, almost 1.7-fold incidence of adverse reactions which are severe in intensity than in men even requiring longer hospital stays.[22,23] Our study also showed that women are more prone to have side effects and complications of thrombolytic therapy as compared to their counterpart ranging from arterial hypotension, malignant arrhythmias, depressed LV function to even the most grave one, the sudden cardiac death.

The reasons for these differences are widely unclear but may be due to sex-related differences in pharmacodynamics, different

drug dose requirements, immunological and hormonal factors.[24]

CONCLUSION

It may be concluded that the two genders do vary significantly in their response to thrombolytic therapy and special attention with vigilance to females while administering the therapy is needed.

REFERENCES

1. Kreatsoulas C, Sloane D, Pogue J, Velianou JL, Anand SS. Referrals in acute coronary events for CARdiac catheterization: The RACE CAR Trial. Can J Cardiol 2010;26(8):290-6.
2. Yusuf S, Hawken S, Ounpuu S. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004;364:937.
3. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics-2015 update: a report from the American Heart Association. Circulation 2015;131:e 29-322.
4. Jochmann N, Stangl K, Garbe E, Baumann G, Stangl V. Female-specific aspects in the pharmacotherapy of chronic cardiovascular diseases. Eur Heart J 2005;26:1585-95.
5. Rosano GM, Lewis B, Agewall S, Wassmann S, Vitale C, Schmidt H, et al. Gender differences in the effect of cardiovascular drugs: a position document of the Working Group on Pharmacology and Drug Therapy of the ESC. Eur Heart J 2015;36:2677-80.)
6. Soldin OP, Mattison DR. Sex differences in pharmacokinetics and pharmacodynamics. ClinPharmacokinet 2009;48:143-58.
7. Regitz-Zagrosek V, Oertelt-Prigione S, Prescott E, Franconi F, Gerdts E, Foryst-Ludwig A, et al. Gender in cardiovascular diseases: impact on clinical manifestations, management, and outcomes. Eur Heart J 2016;37:24-34.
8. Stramba-Badiale M, Fox KM, Priori SG, Collins P, Daly C, Graham I, et al. Cardiovascular diseases in women: a statement from the Policy Conference of the European Society of Cardiology. Eur Heart J 2006;27:994-1005.
9. Maas AH, van der Schouw YT, Regitz-Zagrosek V, Swahn E, Appelman YE, Pasterkamp G, et al. Red alert for women's heart: the urgent need for more research and knowledge on cardiovascular disease in women: proceedings of the workshop held in Brussels on gender differences in cardiovascular disease, 29 September 2010. Eur Heart J 2011;32(11):1362-8.
10. Garcıa M, Mulvagh SL, Merz NB, Buring JE, Manson JE. Cardiovascular disease in women: clinical perspectives. CircRes 2016;118:1273-93.
11. Mosca L, Benjamin EJ, Berra K, Bezanson JL, Dolor RJ, Lloyd-Jones DM, et al.Outcome of stable angina. Circulation2006;113:490-8.
12. Vaccarino V, Parsons L, Peterson ED, Rogers WJ, Kiefe CI, Canto J. Sex differences in mortality after acute myocardial infarction: changes from 1994 to 2006. Arch Intern Med 2009;169:1767-74.
13. Tamargo J, Rosano G, Walther T, Duarte J, Niessner A, Kaski JC,et al. Gender differences in the effects of cardiovascular drugs. EurHeart JCardiovascPharmacother2017;3(3):163-82.
14. Capodanno D, Angiolillo DJ. Impact of race and gender on antithrombotic therapy. ThrombHaemost 2012;104:471-84.
15. Razakjr OA, Tan HC, Yip WL, Lim YT. Predictors of bleeding complications and thrombocytopenia with the use of abciximab during percutaneous coronary intervention. J IntervCardiol 2005;18:33-37.
16. Regitz-Zagrosek V. Therapeutic implications of the gender-specific aspects of cardiovascular disease. Nat Rev Drug Discov 2006;5(5):425-38.
17. Parekh A, Fadiran EO, Uhl K, Throckmorton DC. Adverse effects in women: implications for drug development and regulatory policies. Expert Rev ClinPharmacol 2011;4:453-66.
18. Franconi F, Campese I. Pharmacogenomics, pharmacokinetics and pharmacodynamics: interaction with biological differences between men and women. Br J ClinPharmacol 2014;171:580-94.