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Effect of drugs used in different type of myocardial infarction (STEMI or NSTEMI) on mortality

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We examined 416 patients with acute myocardial infarction. 249 patients had STEMI and 167 NSTEMI. 227 were men and 189 women. 142 men had STEMI and 85 men had NSTEMI. 107 women were diagnosed with STEMI and 82 with NSTEMI. 22.5% of patient with STEMI and 20.2% of patients with NSTEMI died ($p = 0.58$). We compared the effect of anticoagulant treatment, clopidogrel, salicylate, nitrate, beta-blocker, angiotensin-converting enzyme inhibitor, statin and trimetazidine therapy on mortality in function of the type of myocardial infarction. There were no differences between mortality of patients with STEMI and NSTEMI with respect of use of heparine, salicylate, nitrate, beta-blocker, ACE inhibitor, statin and trimetazidine. While examining the effect of clopidogrel, we observed a significantly lower mortality rate in patients with NSTEMI compared to the STEMI group ($p = 0.005$). These differences are due to the known variability in clopidogrel absorption and metabolism, which could be influenced by the type of myocardial infarction.

1. Introduction

Coronary heart disease (CHD) is a leading cause of premature death worldwide, 1 of every 5 death in the US in 2004 was due to acute myocardial infarction (AMI) (Mensah and Brown 2007). The in-hospital mortality of AMI declined from 1990 to 1999 from 11.2% to 9.4% (Mensah and Brown 2007). A recent study revealed that in Spain and most developed countries mortality of AMI is responsible for 22% of overall death (Bertomeu et al. 2013). Although considerable improvement occurred in diagnosis and management of AMI, it still continues to be a major public health problem in the industrialized world and is becoming an important problem in developing countries (Rogers et al. 2000).

Acute coronary syndrome includes unstable angina, myocardial infarction with ST-segment elevation (STEMI) and myocardial infarction without ST-segment elevation (NSTEMI) (Hasdai et al. 2002).

The most common known risk factors of AMI are hypertension, diabetes mellitus, hyperlipidaemia (Dawber and Kannel 1966), but beside these factors several other factors have been demonstrated to be associated with the risk of heart attack as age, socioeconomic status, diet, alcohol intake, smoking, hyperuricaemia (Braunwald et al. 2008, Skak-Nielsen 2013).

Reperfusion therapy is recommended for patients with STEMI (primary percutaneous coronary intervention or thrombolysis). Patients with NSTEMI should be treated as patients with unstable angina. Independently of primary treatment both groups should be given a combination of anti-ischaemic and antithrombotic drugs.

The goal of the present study was to find out the correlation between the type of myocardial infarction (STEMI or NSTEMI), in-hospital drug therapy (heparin, salicylate, nitrate, statin, ACE inhibitor, beta-blocker, trimetazidine, clopidogrel) and mortality of patients with acute myocardial infarction.

Table 1: Patients baseline data

Factor	Male	Female	p value
Patients n=	227 (54,6)	189 (45,4)	
Age (year)	64.8 ± 12.5	71.6 ± 11.9	0.001
Admission time (hours)	19.81 ± 27.8	17.3 ± 25.1	0.36
In-hospital days	7.7 ± 5.8	8.7 ± 6.8	0.11
Mortality (%)	17.6	26.5	0.029
Smoking (%)	27	13.8	0.001
Hypertension (%)	51.5	65	0.005
Diabetes mellitus (%)	17.6	22.8	0.19
Previous AMI (%)	21.1	17.5	0.34
STEMI (%)	62.5	43.3	0.21
NSTEMI (%)	37.4	43.3	0.31

2. Investigations and results

416 patients were admitted in the studied period to the hospital, demographic data of patients are listed in Table 1. Females were older than male patients. In-hospital mortality of patients was 21.63%, the mortality of women was significantly higher ($p = 0.029$). Cardiac failure and cardiogenic shock were more frequent in women, occurrence of hypertension and diabetes mellitus was also higher among female, while smoking habit was more common in male patients. Previous AMI and frequency of STEMI was more frequent among men.

Table 2: Use of drugs and effect on mortality in patients with STEMI and NSTEMI

	STEMI	NSTEMI	p=	Mortality STEMI	Mortality NSTEMI	p=
Use of heparin (%)	96.7	92.2	0.36	22.2	18.4	0.36
Salicylate (%)	57	54.4	0.91	23.5	18.2	0.33
Clopidogrel (%)	17.6	28.7	0.005	15.9	4.1	0.05
Nitrate (%)	90.3	90.4	0.34	18.4	14.9	0.34
Beta-blocker (%)	56.2	56.8	0.58	23	18.7	0.43
ACE-inhibitor (%)	60	55.6	0.56	23.4	20	0.52
Statin (%)	26.9	22.1	0.37	16.4	10.8	0.43
Trimetazidin (%)	18.4	23.3	0.16	24.4	25	0.95

96.7% of patients with STEMI and 92.2% of patients with NSTEMI received heparin (Table 2). Significantly more patients not treated with heparin died (20.7% *vs*. 40%, p = 0.042). 22.2 % of patients with STEMI and 18.4% of patients with NSTEMI receiving heparin died (p = 0.36).
57% of patients with STEMI and 54.4% with NSTEMI received salicylate (p = 0.91). There was no difference in the mortality of patients who received salicylate as compared to those who did not (p = 0.89) (Fig.). 23.5% of patients with STEMI and 18.2% of patients with NSTEMI receiving salicylate died (p = 0.33).
17.6% of patients with STEMI and 38.7% of NSTEMI patients received clopidogrel (p = 0.005). Significantly more patients died who were not treated with clopidogrel (p = 0.05). 15.9% of patients with STEMI and 4.1% of patients with NSTEMI receiving clopidogrel died (p = 0.05).
Most of patients both with STEMI and NSTEMI were receiving nitrate therapy (90.3 vs 90.4%). 17% of patients receiving nitrate (64 out of 376) and 65% of patients who did not (26 out of 40) died (p < 0.001), but there was no difference between mortality of patients in function of type of AMI (p = 0.34). 18.4% of patients with STEMI and 14.9% of patients with NSTEMI receiving nitrate died (p = 0.37).
56.2% of STEMI and 56.8% of NSTEMI patients received beta-blocker (BB) therapy (p = 0.58). 23% of patients with STEMI and 18.7% of NSTEMI patients receiving BB died (p = 0.43).
60% of STEMI and 55.6% of NSTEMI patients received angiotensin-converting enzyme inhibitor (ACEI), the difference between mortality of patients receiving or not ACEI therapy was not significant (p = 0.52). 23.4% of patients with STEMI and 20% of patients with NSTEMI receiving ACEI died (p = 0.52).
26.9% of STEMI and 22.1% of NSTEMI patients received statin therapy. Significantly more patients not receiving statin therapy died (p = 0.038). The difference between mortality of patients with STEMI or NSTEMI receiving statin therapy was not significant (p = 0.43) (Table II.)

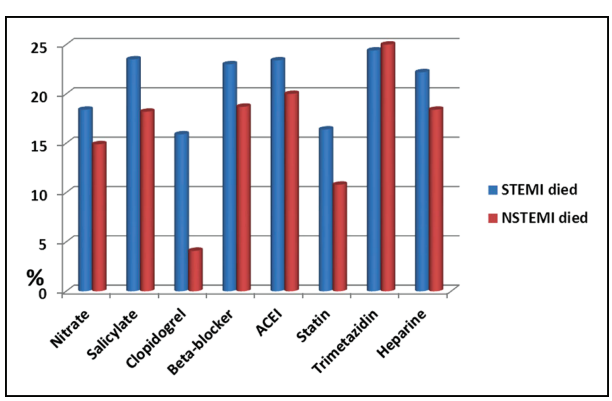

Fig.: Mortality of patients with AMI in function of drugs used.

18.4% of STEMI and 23.3% of patients with NSTEMI were administered trimetazidin (p = 0.16), 24.4% of patients with STEMI and 25% of patients with NSTEMI receiving trimetazidin died (p = 0.95). (Table 2, Fig.).

3. Discussion

Treatment of acute coronary syndrome includes a combination of anti-ischaemic and antithrombotic agents, with coronary reperfusion achieved using fibrinolysis and/or revascularization (PCI or coronary artery bypass graft surgery).
94.9% of patients received heparin. The difference observed between STEMI and NSTEMI groups was not significant. Significantly more patients receiving heparin survived, thus heparin decreased the mortality of our patients. In Montalescot *et al*.'s (2007) study the use of heparins was comparable (95.6%).
Only 56% of patients were treated with salicylate, the difference observed between STEMI and NSTEMI groups was not significant. We have found that salicylate therapy did not influence mortality. The use of aspirin in others studies was 86.8% (Montalescot et al. 2007), in STEMI patients 85.1% (Stenestrand et al. 2007).
22.1% of patients received clopidogrel. Men were more likely to receive clopidogrel than women (25.6% *vs*. 18%), the difference was almost significant. Moreover significantly more patients with NSTEMI were treated with clopidogrel and significantly less patients died who received this drug. We concluded that clopidogrel significantly decreased mortality. It was shown before that addition of clopidogrel to standard fibrinolytic therapy and aspirin in patients with STEMI improves patency rate of the infarct-related artery and reduces ischemic complications (Sabatine et al. 2005) and these drugs are evidence based treatment strategies based on guideline for treating NSTEMI.
Nitrates were administered to most of our patients (90.3%) although regarding anti-ischemic therapy nitrates remain critical in the early management of AMI (Ramanath and Eagle 2007). In the study of Montalescot et al. (2007) the use of nitrate was lower (59.4%). Swedish authors reported only a 23.4% use of nitrate in STEMI patients (Stenestrand et al. 2007). In our study the use of nitrate significantly decreased mortality of both sexes, as Japanese authors found that the use of nitrates does not increase mortality and cardiac events in AMI patients, so they could be beneficial in secondary prevention (Yamauchi et al. 2008).
56.4% of patients received beta-blockers; men were more likely to receive BB. We have not found a correlation between use of BB and in-hospital mortality. Use of BB in our STEMI patients was 56.2%, similar to Montalescot *et al.*' s study (62.4%) (Montalescot et al. 2007), in Stenestrand *et al*.' study it was 84.7% in STEMI patients (Stenestrand et al. 2007).
58.6% of patients received ACE-inhibitors; men were more likely to receive it. More women died in the ACEI treated group, than men, otherwise the use of ACEI had no significant

influence on mortality. Use of ACEI in Montalescot *et al.*'s study was lower (28.7% (Montalescot et al. 2007), in Stenestrand *et al.*'s study it was 27.8% in STEMI patients (in our STEMI patients it was higher, 60%) (Stenestrand et al. 2007). 25% of patients were treated with statins. Use of statins in Montalescot *et al*.'s study was almost double (46.5%) (Montalescot et al. 2007), in Stenestrand *et al*.' study it was 56.2% in STEMI patients (in our STEMI patients it was lower, 26.9%) (Stenestrand et al. 2007). Significantly less death occurred in patients treated with statins, so use of statins in acute phase decreased mortality (Vincze and Brugos 2008, 2011).

Studies conducted by others concluded that statin treatment before AMI could decrease the necrotic area in mice (Jones et al. 2001), moreover the use of statin before coronarography decreases the ST segment elevation and helps in reperfusion and decreases the size of the necrotic area (Ishii et al. 2006). In our patients statin treatment before admission to hospital was as low as 8.4%, other lipid level lowering drugs were not used. We did not find a significant correlation between mortality and statin use before AMI (Vincze and Brugos 2008, 2011). We found that significantly more patients died in the group of patients who were not treated with statins after AMI in hospital (Vincze and Brugos 2008, 2011). These results suggest that hyperlipemic patients had a worse outcome after AMI and underline the necessity of statin use in every AMI patient within the first 24 hours (Fonarow et al. 2005), which could prevent early complications and mortality.

In conclusion administration of salicylates, beta-blockers, ACEI, trimetazidin did not decrease significantly the in-hospital mortality of patients with AMI, while administration of heparin, clopidogrel, nitrates and statins significantly decreased the in-hospital mortality of patients with AMI. Only use of clopidogrel decreased significantly the in-hospital mortality of patients with NSTEMI as compared to patients with STEMI.

4. Experimental

416 patients treated with acute myocardial infarction in the Department of Internal Medicine, Medical Health Science Center, University of Debrecen, Hungary. Both STEMI (ST-elevation MI) and NSTEMI (non-ST elevation MI) patients were included. Clinical data, risk factors, previous diseases, family history, co-morbidities of patients were analyzed based on medical charts and history taking. Correlation of medical treatment and effect on mortality was analyzed. Mortality in function of the type of AMI and drug therapy used for the treatment were analyzed. Statistical analysis was made using SPSS and Microsoft Excel programs, p values less than 0.05 were considered statistically significant.

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