Trakya Univ Tip Fak Derg 2010;27 Suppl 1:35-38

Review / *Derleme*

Is Thrombolytic Therapy Effective in Elderly Patients? Bleeding?

Trombolitik Tedavi Yaşlı Hastalarda Etkili mi? Kanama?

Elena TANEVA

Department of Cardiology Medical Faculty of Medical University, Sofia, Bulgaria

As the population increases worldwide, the number of elderly patients who present with acute myocardial infarction (AMI) with ST-segment elevation will continue to grow. Thrombolytic therapy (TT) is applied in patients with AMI with ST-segment elevation and aged no more than 75 years. It is recommended percutaneous transluminal coronary angioplasty (PTCA) or by-pass surgery to elderly patients. For PTCA and by-pass surgery there has to be a prepared cardio-surgery medical team, which can be found in big medical hospitals. Patients with AMI with ST-segment elevation over 75 years, which has no TT applied, are with suspicious prognosis for longevity and quality of life. Along with its needed effects TT may cause some unwanted effects such as incidence of major (fatal) or minor bleeding.

Key words: Elderly; acute myocardial infarction; thrombolytic therapy; bleeding.

Dünya çapında nüfus artmakta olduğu için varolan ST segment yükselmeli akut miyokardiyal infarktüsü (AMI) olan yaşlı hasta sayısı da artmaktadır. Trombolitik tedavi (TT) ST segment yükselmeli akut miyokard infarktüsü olan ve 75 yaşından büyük olmayan hastalara uygulanır. Yaşlı hastalara perkutan transluminal koroner anjiyoplasti (PTCA) veya baypas ameliyatı uygulaması önerilir. Perkutan transluminal koroner anjiyoplasti veya baypas ameliyatı için büyük hastanelerde bulunabilen hazırlıklı bir kardiyo-cerrahi ekibi gereklidir. Yetmiş beş yaş üzeri ST segment yükselmeli akut miyokard infarktüsü olan hiç TT uygulanmamış hastaların, yaşam uzunlukları ve kalitelerini tahmin etmek şüphelidir. Trombolitik tedavi istenen etkilerinin yanı sıra büyük (ölümcül) veya küçük kanama gibi istenmeyen etkilere neden olabilir.

Anahtar sözcükler: Yaşlı; akut miyokardiyal infarktüsü; trombolik tedavi; kanama.

As the population increases worldwide, the number of elderly patients who present with acute myocardial infarction (AMI) with ST-segment elevation will continue to grow.

The mission of the European Society of Cardiology (ESC) is to improve the quality of life of European population by reducing the impact of cardiovascular disease. Acute myocardial infarction (AMI) is the principal cardiovascular disease and the principal cause for the mortality of the elderly patients.[1,2] A diagnosis of AMI with ST-segment elevation in elderly dictates a treatment regime, which will rapidly, fully, and durably restore coronary blood flow. The choice is between primary angioplasty and thrombolysis. It is recommended percutaneous transluminal coronary angioplasty (PTCA) or by-pass surgery to elderly patients.[1,3-5] For PTCA and by-pass surgery there has to be a prepared cardio-surgery medical team, which can be found in big medical hospitals. No doubt, the primary angioplasty is the best treatment for all elderly patients but it is so far from being available everywhere and whenever somebody needs that kind of treatment.

Thrombolytic therapy (TT) is applied in patients with AMI with ST-segment elevation to achieve reperfusion

Correspondence (İletişim adresi): Dr. Elena Taneva. Medical University, Medical Faculty, Clinic of cardiology, Intensive care, Sofia, Bulgaria.
Tel: +359 2 952 1046 Fax (Faks): +359 2 952 0337 e-mail (e-posta): etaneva_md@yahoo.com

in a chemical way with the help of a pharmacological medication. But patients not to be over 75 years of age. Many elderly patients who are eligible for an effective therapy to treat heart attacks with thrombolytic agent do not receive that treatment.[5-8] The main reason why application of thrombolytic agents is not used in elderly patients is because of the danger of intracranial hemorrhage and bleeding from the gastro-intestinal tract.[2,9] While elderly patients have a higher risk of bleeding from thrombolytic therapy, they also have higher risk of dying from the acute myocardial infarction.

The aim of this study is to propose recommendations and behavior for reperfusion of coronary arteries with TT of elderly patients and reduce the significance of this problem.

MATERIAL AND METHODS

The investigation was retrospective and was made for a period of seven years (2000-2006)and 3320 patients were hospitalized. From them 585 patients had AMI, and from them 132 (70 men and 62 women) were over 75 years. The study was found in 15 elderly patients (9 men and 6 women). Men's mean age was 82 years and one months (from 76 to 93) and women's mean age was 79 (from 76 to 89) (Table 1). Patients were incoming on the 6th and 11th hour from onset of chest pain. Acute myocardial infarction with ST-segment elevation was diagnosed because of continuous chest pain (over 30 minutes), without reducing it after using Nitrates, ECG and increased enzymes.

All patients received Aspirin (160 mg) and Heparin (5000 IE). Second generation Plasminogen thrombolytic agent tissue plasminogen activator Reteplase (Rapilysin-Hoffmann La Roche) were applied to 15 elderly patients. H2 blocker Famotidine (Quamatel - Gedeon-Richter) were used to prevent bleeding from gastro-intestinal tract.

General, physical and mental state, previous diseases, co-morbidity and haemodynamic indices (arterial pressure no higher than 160/100 and no lower 100/60, pulse rate 60-120) were assessed.

Haemodinamical characteristics (ECG, non-invasive arterial pressure, pulse rate and pulse oxymethria) were traced with monitor Argus–1 (Schiller-Suisse). The investigation included three stages:

a. Complications during TT

b. One month after the hospitalization was over

c. At the begging of January 2007.

The last two stages included investigation of chest pain (character, presence or absence of depression and mortality).

RESULTS

Only 132 patients (3.98%) were over 75 years from all hospitalized during this period. Sixty-three (47.73%) of them had AMI with ST-segment elevation. Forty-eight patients (76.19%) were ineligible because of other disease – type 2 diabetes, Parkinson, previous melaena or insultus cerebri and etc. Intravenous thrombolytic therapy with Reteplase applied to 15 patients (23.81%). Only one flacon bolus dose 0.56 Reteplase 10U for 2 minutes was used to six patients. The second bolus dose was interrupted to four patients and applied after 30 minutes to five others patients. According to ECG-data during TT nine patients had complete thrombolysis (full clot lysis) and other six patients had partial thrombolysis. There was little bleeding from the nose, gums, blood in urine and coughing up blood in seven patients (46.67%). This leaded to stopping the application of thrombolytic agent. There was no intracranial hemorrhage and bleeding from gastrointestinal tract (Table 2).

Four patients had reoccurring chest pain, light form of depression (n=1) and with arrhythmias at the second and third stage (n=3), but all of them were alive. There were no significant differences between male and female, applied with TT.

DISCUSSION

Reteplase (tissue plasminogen activator - pTA) has been used to treat coronary thrombosis from 1996 and its use in the treatment in elderly has recently been investigat-

Table 1. Distribution of patients according to years and age

Years/age	Total patients	AMI	Men>75 years	Women>75 years	AMI with ST-elev.	TT
2000	428	138	8	7	5	1
2001	445	142	16	15	16	1
2002	437	115	11	13	13	2
2003	592	57	8	5	11	3
2004	560	50	11	9	7	3
2005	505	46	10	8	8	3
2006	363	37	6	5	3	2
Total	3320	575	70	62	63	15

AMI: Acute myocardial infarction; TT: Thrombolytic therapy.

Table 2. Distribution according to complication

Complication/stage	During TT	After one month	31.01.2007
Intracranial haemorrhage	-	-	-
Bleeding from GI tract	-	-	-
Blood in urine	2	-	-
Coughing up blood	1	-	-
Bleeding from nose	2	-	-
Bleeding from gums	2	-	-
Chest pain	10	5	4
Depression	10	3	2
Arrithmias	4	3	3
Survival	15	15	15

ed.[1,4] The application of TT there were reduction in reinfarction and refractory ischemia. Using Anticoagulants is the classical treatment. Non-fractioned Heparin is used for reduction in the size of a thrombus and prevents its recurrence.

Many studies[9] showed that the combination of a thrombolytic agent and anticoagulant was of more benefit reperfusion and reduction in the rate of recurring infarction, but combined treatment more frequently lead to acute hemorrhage complication, particular in elderly persons.[10]

Some authors noted that 76% of patients were not eligible for TT. Only 44% were treated.[6] 23.81% had TT in our study.

Thrombolytic therapy may be more likely to cause serious bleeding in people who have certain medical conditions or have recently had certain procedures. Thrombolytic therapy is contraindicated in following conditions:

Blood disease or current or past bleeding problems in any part of the body

- Heart or blood vessel disease
- Stroke (recent or in the past)
- Blood pressure (>160/100 or <100/60)
- Brain tumor or other brain disease, trauma in last two months
- Stomach ulcer or colitis
- Severe liver disease
- Active tuberculosis
- Recent injections into a blood vessel
- Recent surgery, including dental surgery.

People who are given thrombolytic therapy should also be alert to the signs of bleeding inside the body and should check with a physician immediately if any of the following symptoms occur:

- Blood in the urine
- Coughing up blood
- Vomiting blood or material that looks like coffee grounds
- Nosebleeds
- Unexpected or unusually heavy vaginal bleeding
- Dizziness
- Sudden, severe, or constant headaches
- Pain or swelling in the abdomen or stomach
- Back pain or backache
- Severe or constant muscle pain.

The main reason why application of thrombolytic agents is not used in elderly patients is because of the danger of intracranial hemorrhage and bleeding from the gastro-intestinal tract.[2,9] Bleeding in the brain is rare but potentially fatal complication of TT for heart attack. The rate of intracranial hemorrhage was at the average of 1.43%. According to GUSTO-1 (Global Use of Strategies to Open Occluded Coronary Arteries) the risk of stroke increased with age, approaching 3-4% in patients aged over 75 years. In GUSTO-5 there was a strong trend toward increased intracranial haemorrhage, but no more than 1-1.76%.[7,9] In the ASSENT 2 study the incidence of major bleeding (defined as bleeding requiring blood transfusion or leading to haemodynamic compromise) was 5% in patients receiving Tenecteplase and 6% in those receiving Alteplase. The incidence of minor bleeding was 22% with Tenecteplase and 23% with Alteplase (cit. ASSENT 2 study). In our investigation there was no brain or gastro-intestinal bleeding. At the first symptoms of bleeding from the nose, gums, blood in urine and coughing up blood TT was interrupted. Application of non-fractioned Heparin was also stopped. Combined TT is famous for causing bleedings. The bleeding of our patients was transitional and had not appeared after beginning anticoagulative therapy after 12 hours.

Small bleeding (from nose, gums, etc.) is allowed to 25% and is not a contraindication for using TT. Despite all this, there is a reason for saying that this investigation is complete harmless and lead to increasing patients' life duration. Elderly patients treated with TT for AMI with ST-elevation recover mentally and physically as well as younger patients.[11-13]

Patients who are taking thrombolytic medications should not take vitamin E supplements or certain herbal preparations. High doses of vitamin E can increase the risk of hemorrhagic stroke. Ginger, borage, angelica, dong quai, and other herbs can intensify the anticlot-

ting effect of thrombolytic medications and increase the risk of bleeding.[14] The excellent results from the second and third stage of the investigation prove its efficacy. Patients' mental and physical well-being is preserved, as well as their intellectual state.

Mortality six months after TT or PTCA is almost one and the same (from 16% to 26%).[13,15] There is no death case in our study, but this is may be because of the small number of patients.

CONCLUSION

Ageing, related to serious health problems, can be improved with application of TT to eligible elderly patients with AMI with ST-segment elevation as an excellent reperfusion therapy, although big risk of bleeding. Recommendations for treatment of elderly patients are:

- Dose reduction of the Thrombolytic agent
- Arterial pressure no higher 160/100 Hg and no lower 100/60 Hg
- Pulse rate from 60 to 120.

To each patient should be assessed an individual risk for intracranial hemorrhage and prevention of bleeding from gastro-intestinal tract. Thrombolytic therapy can be made with only 1 or 2 flacons thrombolytic agent, applied intravenous in peripherical vein and when chemical reperfusion is carried out, the procedure lasts only 30 minutes. So, TT recanalizations are fast, non-traumatic and preserve physical and mental health in patients. Elderly patients treated with TT recover their physical and mental state and conserve appropriate quality of life.

While the elderly have a high absolute risk of dying when developing AMI they also have an opportunity for better prognosis for longevity if is applied TT.

REFERENCES

1. Moriel M, Behar S, Tzivoni D, Hod H, Boyko V, Gottlieb S. Management and outcomes of elderly women and men with acute coronary syndromes in 2000 and 2002. Arch Intern Med 2005;165:1521-6.
2. A comparison of reteplase with alteplase for acute myocardial infarction. The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) Investigators. N Engl J Med 1997;337:1118-23.
3. Buiatti E, Barchielli A, Marchionni N, Balzi D, Carrabba N, Valente S, et al. Determinants of treatment strategies and survival in acute myocardial infarction: a population-based study in the Florence district, Italy: results of the acute myocardial infarction Florence registry (AMI-Florence). Eur Heart J 2003;24:1195-203.
4. Selker HP, Beshansky JR, Griffith JL; TPI Trial Investigators. Use of the electrocardiograph-based thrombolytic predictive instrument to assist thrombolytic and reperfusion therapy for acute myocardial infarction. A multicenter, randomized, controlled, clinical effectiveness trial. Ann Intern Med 2002;137:87-95.
5. White HD. Debate: Should the elderly receive thrombolytic therapy or primary angioplasty? Curr Control Trials Cardiovasc Med 2000;1:150-4.
6. Krumholz HM, Murillo JE, Chen J, Vaccarino V, Radford MJ, Ellerbeck EF, et al. Thrombolytic therapy for eligible elderly patients with acute myocardial infarction. JAMA 1997;277:1683-8.
7. Topol EJ; GUSTO V Investigators. Reperfusion therapy for acute myocardial infarction with fibrinolytic therapy or combination reduced fibrinolytic therapy and platelet glycoprotein IIb/IIIa inhibition: the GUSTO V randomised trial. Lancet 2001;357:1905-14.
8. White HD. Thrombolytic therapy in the elderly. Lancet 2000;356:2028-30.
9. Brass LM, Lichtman JH, Wang Y, Gurwitz JH, Radford MJ, Krumholz HM. Intracranial hemorrhage associated with thrombolytic therapy for elderly patients with acute myocardial infarction: results from the Cooperative Cardiovascular Project. Stroke 2000;31:1802-11.
10. Lichtman JH, Krumholz HM, Wang Y, Radford MJ, Brass LM. Risk and predictors of stroke after myocardial infarction among the elderly: results from the Cooperative Cardiovascular Project. Circulation 2002;105:1082-7.
11. Väisänen O, Mäkijärvi M, Silfvast T. Quality of life of elderly patients after prehospital thrombolytic therapy. Resuscitation 2005;66:183-8.
12. Taneva E. Is thrombolytic therapy effective in elderly patients? Rejuvenation Res 2006;9:358-61.
13. Rich MW. Thrombolytic therapy is indicated for patients over 75 years of age with st-elevation acute myocardial infarction: protagonist viewpoint. Am J Geriatr Cardiol 2003;12:344-7.
14. Weil A. Western herbal medicine: nature's green pharmacy. In: Pelletier KR, editor. The best alternative medicine. 1st ed. New York: Simon and Schuster; 2002. p. 152-77.
15. Martínez-Sellés M, López-Palop R, Pérez-David E, Bueno H. Influence of age on gender differences in the management of acute inferior or posterior myocardial infarction. Chest 2005;128:792-7.