

Residual Thrombolytic Agents Left in Intravenous Lines After Infusion

İNFÜZYONDAN SONRA İNTRAVENÖZ SETLERDE KALAN TROMBOLİTİK AJAN MİKTARLARI

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Summary

It's clear that early intravenous (IV) thrombolysis is very important in the management of acute myocardial infarction (AMI). The most widely used thrombolytic agents are streptokinase and tissue plasminogen activator (t-PA). In our daily practice we observed that some amount of thrombolytic drugs were left in IV lines after the infusion. Therefore the patient receives lower drug doses than intended which may affect the therapeutic efficiency and increase the economic costs. We designed this study to find out the amount of residual drug and its economic cost. On 48 patients with AMI, we measured the residual amounts of streptokinase and t-PA left in 3 different kinds of infusion sets. Residual streptokinase amount in the IV lines was 12.3 ± 1.9 ml for IV pump sets, 20.8 ± 3.3 ml for infusomat sets, and 9.3 ± 2.4 ml for simple serum lines; for t-PA these amounts were 12.8 ± 2.1 ml, 21.4 ± 3.9 ml, and 9.1 ± 2.7 ml, respectively. A statistically significant higher amount and ratio of loss of thrombolytic agents were found in infusomat sets ($p < 0.05$). These results suggest that to prevent the loss of thrombolytic drugs, it would be better to use simple IV lines or if the other lines are to be preferred, a 100 ml isotonic saline solution should follow the original drug through the same line to wash out the residual drug left in these lines.

Key Words: Cost-effectiveness, Thrombolytic drugs, Infusion line

T Klin J Med Res 1999, 17:19-22

Many years elapsed between the first report of intracoronary clot lysis in an experimental animal and the wide spread use of thrombolytic therapy in acute myocardial infarction (AMI) was established. It's now clear that thrombolysis recanalizes thrombotic occlusion associated with AMI, and restores

Received: Jan. 11, 1999

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T Klin J Med Res 1999, 17

Özet

Akut miyokard infarktüsünün (AMI) tedavisinde erken intravenöz (IV) trombolitik tedavi çok önemlidir. En fazla kullanılan trombolitik ajanlar streptokinaz (SK) ve doku plazminojen aktivatörüdür (t-PA). Pratik uygulamada infüzyon sonrası bir miktar trombolitik ajanın IV setlerde kaldığını gözlemledik. Bu çalışmanın amacı; infüzyon sonrası serum setlerinde ne kadar miktarda ilaç kaldığının ve bunun ekonomik maliyetinin hesaplanmasıdır. Kırk sekiz AMI' lü hastada 3 değişik infüzyon seti kullanılarak verilen SK ve t-PA' nın setlerde kalan miktarını ölçtük. IV pompa setleri kullanıldığında 12.3 ± 1.9 ml, infuzomat setleri kullanıldığında 20.8 ± 3.3 ml ve basit serum setleri kullanıldığında 9.3 ± 2.4 ml rezidü SK kaldığını ölçtük. Bu oranlar t-PA için sırası ile 12.8 ± 2.1 ml, 21.4 ± 3.9 ml ve 9.1 ± 2.7 ml idi. infuzomat setlerinde kalan trombolitik ajan miktarı istatistiksel olarak daha fazla bulundu ($p < 0.05$). Bu çalışmada gördük ki; trombolitik tedavi verirken basit serum setlerinin kullanılması daha ekonomiktir ve eğer diğer setler kullanılıyor ise sette trombolitik ilaç kalmaması için infüzyon bittikten sonra aynı setten 100 ml izotonik sodyum klorür verilerek setteki arta kalan ilaç temizlenmelidir.

Anahtar Kelimeler: Ekonomik maliyet, Trombolitik ajanlar, İnfüzyon seti

T Klin Araştırma 1999, 17:19-22

coronary flow, reduces infarct size and improves myocardial function^{1,2}. Thrombolytic agents are expected to lyse the **thrombus** and cause reperfusion of the ischemic myocardium which may result in dramatic recovery. Bioavailability of the drug to the ischemic zone is of prime importance; and thrombolysis should be done as soon as possible within the first 6 hours of chest pain. In order to get the maximum therapeutic efficacy, all of the thrombolytic drug, up to the last drop should be infused to the patient.

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Intravenous thrombolysis has several important advantages over intracoronary use. Drug administration is very easy, because only the placement of a peripheral intravenous (IV) line is required, therapy may be initiated early in a variety of locations (home, ambulance, helicopter, emergency department...) by paramedical persons³. There is no doubt that early IV thrombolytic therapy improves survival in patients with AMI^{1,4}. In AMI, streptokinase (SK) and tissue plasminogen activator (t-PA) are the most frequently used thrombolytic agents for recanalisation of the occluded coronary arteries. In our daily practice we observed that some amount of thrombolytic drugs are left in IV lines following infusion. There are not enough data in the literature regarding IV infusion lines and residual drug amounts left in these lines. We designed this study to find out the amount of residual drug left and its economic cost.

Methods

The study group consisted of 48 patients who were hospitalised for AMI in Ege University, School of Medicine, Coronary Care Unit. Thrombolytic therapy was considered for patients diagnosed as AMI by typical chest pain, ECG findings, and creatinin kinase-MB enzyme elevations within the first six hours of chest pain, without any contraindication for thrombolytic agents. Right ventricular infarctions were excluded because they could affect central venous pressure (CVP). Central venous pressure was measured by using a venous catheter from the right internal jugular vein. All the study group had normal CVP values. Twenty-five of the patients received streptokinase and the rest t-PA in the first 6 hours of their infarction. Standard streptokinase (1.5 million units in 200 ml of 0.9 % solution of sodium chloride in one hour infusion) and accelerated t-PA (100 mg in 100 ml of special solution of t-PA in 90 minutes infusion) regimens were preferred. Thrombolytic therapies were applied through three different infusion sets: Lifecare 5000 IV pump set (Abbott), Original-Infusomat-Lcitung (Braun) and Mediset (Eczacibasi-Baxter) by a 20 G branule via the antecubital veins by the coronary care unit nurses who were unaware of the study. These IV lines' lengths were 264 cm, 250 cm and 155 cm, respectively. In order to prevent drug interaction, thrombolytic

agents were given via separate lines as recommended. We used 9 IV pump sets for streptokinase and 8 for t-PA infusion, 8 infusomat sets for each of the thrombolytic drug infusion, 8 simple serum lines for streptokinase, and 7 for t-PA infusion. The height of all the fluid bottles was 100 cm above from the right atrial level of the patients. At the end of the thrombolytic therapy we collected the residual drug in the IV lines in a volume calibrated sterile bottle for measuring. If the amount was large, we signed the fluid level in the IV line, then washed out the thrombolytics with a saline solution. The same amount of fluid was measured by filling the IV line with saline solution to the signed level. Patients were grouped in respect to the 3 different forms of IV infusion lines. All group results are expressed as mean \pm standard deviation. Comparisons between streptokinase and t-PA data were obtained with student's t test. Statistical comparison of the groups of different IV lines was performed by using the variance analysis. Differences were considered to be significant for p values <0.05 .

Results

Clinical characteristics of the patients enrolled in the study are displayed in Table 1. There were 12 female and 36 male patients with a mean age of 57 ± 8 years. Twenty-six of them had anterior myocardial wall infarcts, 15 patients had inferior wall infarcts, and 7 patients had inferolateral wall infarcts. Mean CVP value was 7.6 ± 2.5 mmHg. We

Table 1. Patient characteristics (mean \pm SEM)

Variables	
Number of patients	48
Sex	
* Female	12 (25%)
* Male	36 (75%)
Age (mean)	57 ± 8
AMI location	
* Anterior	26 (54%)
* Inferior	15 (31%)
* Inferolateral	7 (15%)
CVP mmHg	7.6 ± 2.5

Abbreviations: AMI = Acute myocardial infarction, CVP = Central venous pressure, SEM = Standard error of mean)

Table 2. Loss volume and loss ratio of thrombolytic agents regarding different types of intravenous lines (mean±SEM)

	IV pump set	Infusomat set	Simple serum line	p value	
Volume loss (ml)					
* SK	12.8±2.1 (n=9)	21.4±3.9 (n=8)	9.1±2.7 (n=8)	* 1-2, * 2-3	<i>i</i>
* t-PA	12.3±1.9 (n=8)	20.8±3.3 (n=8)	9.3±2.4 (n=7)	* 1-2, * 2-3	
Ratio loss (%)					
* SK (n=25)	6.4%	10.5%	4.5%		
* t-PA (n=23)	12.8%	21.0%	9.1%		

Abbreviations: SK = Streptokinase, t-PA = Tissue plasminogen activator, SEM = Standard error of mean, * p<0.05

found that the residual amount of streptokinase in the IV lines was 12.3±1.9 ml for IV pump sets, 20.8±3.3 ml for infusomat sets, and 9.3±2.4 ml for simple serum lines; for t-PA these amounts were 12.8±2.1 ml, 21.4±3.9 ml, and 9.1±2.7 ml, respectively. A statistically significant higher amount and ratio of loss of thrombolytic agents were found in infusomat sets (p<0.05). Although the residual amount of fluids left in the IV pump sets were higher than simple serum line sets, the difference between these two lines were not significant (p>0.05) (Table 2). Considering that the optimum total volume of streptokinase was 200 ml, and the total volume of t-PA was 100 ml; 4.5-10.5% of streptokinase and 9.1-21% of t-PA was left in the different IV lines.

Discussion

Reperfusion therapy with thrombolytic agents is most successful when it is given as soon as possible following the onset of symptoms in patients with AMI (5). Tissue plasminogen activator appears to be somewhat more efficacious than streptokinase for opening occluded artery at 90 minutes, and hence has been associated with a lower mortality rate than streptokinase. Although the methods have varied among different cost effectiveness analysis for acute thrombolytic therapy, all have shown intravenous thrombolysis with streptokinase to be well worth the cost under a variety of assumptions in patients of all age ranges and even in high risk patients (6-8).

Thrombolytic agents, especially t-PA, are expensive drugs. One therapeutic dose of t-PA costs about \$ 2000 and streptokinase \$ 150 per patient. These agents are given to the AMI patients within small amounts of fluids. In our daily practice we noticed that a significant amount of thrombolytic drug solution was left in IV lines. To the best of our knowledge there is no data in the literature up to now regarding IV lines and residual drug amounts left in these lines after infusion.

We found that there was significantly less residual amount of drug left in simple IV lines, however with these lines infusion time can not be properly adjusted. On the other hand infusomat and IV pump lines can sensitively adjust infusion rates but the problem is that there were significant amount of drug left in these lines. Therefore the patient receives lower doses of drug than intended which may affect the therapeutic efficiency and increase the economic costs.

In our study we showed that there is a loss of \$ 182-410 per patient during t-PA therapy, while this loss is between \$ 4-8 for streptokinase. This economic loss is very important, especially during t-PA therapy.

We recommend that to prevent the waste of thrombolytic drugs and to obtain maximum therapeutic effect, these drugs should be infused through simple IV lines or if the other lines are to be preferred, a 100 ml of isotonic saline solution should follow the original drug through the same line to wash out.

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