Heparin effects on mobility problems of non-hemorrhagic stroke patients

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Abstract: Stroke is the second leading cause of death worldwide. Ischemia is the most common cause of it which is being treated by combined therapy. One important management of acute stroke candidate for recanalization (r-TPA) that can perform for some patient with special condition in 3 to 4/5hours of onset in a few centers in Iran. there are many studies with different results regard to anti-coagulant therapy in acute stroke. The aim of this study was determination of heparin effects on mobility problems among non-hemorrhagic stroke patients. In regard of absence of diagnostic tools & teams of acute ischemic stroke treatments with r-TPA.
In a double-blind randomized controlled clinical trial, 60 non-hemorrhagic stroke patients in Kashani Hospital in Shahrekord were randomly assigned in according to scale definition of NIHSS(part 5 & 6 : motor arms & legs) into two groups with same motor signs(0=no drift – 1=drift – 2 = cant's resist gravity-3 =no efforts against gravity- 4 = no movement UN=untestable): experiment and control groups. While experiment group were subcutaneous received 5000 to 10000 unit BID every day for 3 days +aspirin 100-325 mg, control group were received only 100-325 mg aspirin. Muscular power and dyspnea &pulses of peripheral veins for evaluation of lung emboli & DVT and radiological data in CT(the first and third days) were evaluated after 3 days in two groups.
There was no statistically significant difference between two groups in age, gender, power of all limbs, and duration of hospitalization. There was no significant difference between two groups in muscular power of upper and lower limbs in first day, but it was significant in the third day. In comparison of the muscular power of limbs of patients less than 55 years between two groups, there was no significant difference in the first day; however, it was significant in the third day. For patients more than 55, the significant difference was seen only in the third day in the power of left side limbs.
This study recommends using heparin in non-hemorrhagic stroke patients which is more efficient than using only aspirin.
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1. Introduction

Cerebrovascular accident (CVA) or stroke is a syndrome which is identified by acute onset of neurologic disorders and is prolonged at least 24 hours, and it is a reflection of local involving of central nervous system (Giele et al., 2004; David et al., 2002). Stroke is the third leading cause of death among worldwide and one of the most important neurologic disabling disorders which increases with age, with higher mortality among elderly, and higher prevalence in men than women (Cecil et al., 2000).

Heparin and low molecular weight heparin (LMWH) are using for treatment of acute stroke (Giele et al., 2004). unfractionated heparin (UFH) with molecular weight of 3000-30000 dalton and mean of 15000 dalton used in the treatment of thrombosis with different results , but also has a probability of bleeding risk (Hirsh et al., 2001; White and Ginsberg, 2003).

Due to severe and irreversible complications of stroke, the patients have not only motion-verbal problems, but also various mental complications, as well as economic costs. The aim of this study was to evaluate treatment effects of heparin on muscular power disorders of acute non-ischemic stroke patients.

2. Material and Methods

In a clinical trial, 60 non-hemorrhagic stroke patients, with confirmed nonhemorrhagic stroke diagnosed by computed tomography scan (CT- scan) or magnetic resonance imaging (MRI), in Kashani Hospital in Shahrekord were randomly assigned into two groups: experiment and control groups in 2011. While experiment group were subcutaneus received

5000 -10000 BID units heparin every day for 3 days with aspirin, control group were received only 100-325 mg aspirin. Muscular power, deep veins thrombosis and lung emboli were evaluated after 3 days &CT-scan repeated in two groups. Prothrombin time (PT) and partial thromboplastin time (PTT) and INR of all patients were checked every day. Exclusion criteria were patients with hemorrhagic ischemic stroke, trauma, secondary neurologic complications, metabolic disorders (hypokalemia, hyponatremia …). Both groups have received one gram antacid aluminum hydroxide syrup. Both groups were re-CT scanned after 3 days and were compared on clinical issues. Muscular powers of patients were evaluated. In according to scale definition of NIHSS (part 5 & 6 : motor arms & legs) into two groups with same motor signs(0=no drift – 1=drift – 2 = cant;s resist gravity-3 =no efforts against gravity- 4 = no movement UN=untestable): experiment and control groups. Data were obtained by questionnaire and results of CT-scan. Chi-square and t-students test were used in SPSS (version 17) software.

3. Results

Table 1 compares muscular power of upper and lower limbs in two groups in first day of study. Demographic characteristics of both groups on age, gender and muscular power did not show any significant difference (P>0.05). Muscular power mean of both right and left upper and lower limbs were statistically significant between two groups (P<0.05).

As the results shows, among control group, CT-scan results in the third day were normal in 76.6% of the patients (see Table 2). Chronic small vessel and middle cerebral artery (MCA) have been observed in 16.6% and 6.6% of control group patients respectively. Among experiment group, CT-scan was normal in 40%, 30% had involvement of chronic small vessels, and MCA were observed in 20% of patients. Lacunar infarction and posterior cerebral artery (PCA) were also observed in 6.6% and 3.3% respectively.

Table 1- Comparison of muscular power of upper and lower limbs in the first day

Muscular power	Group	Mean ± S.D.*	P-value
Right upper limbs	Experiment	3.60 ± 1.56	0.16
	Control	3.03 ± 1.56	
Right lower limbs	Experiment	3.60 ± 1.58	0.21
	Control	3.07 ± 1.68	
Left upper limbs	Experiment	2.87 ± 1.69	0.55
	Control	2.60 ± 1.75	
Left lower limbs	Experiment	3.07 ± 1.72	0.67
	Control	2.87 ± 1.90	

*. S.D. = Standard Deviation

Table 2- Comparison of muscular power of upper and lower limbs in the third day between two groups

Muscular power	Group	Mean ± S.D.*	P-value
Right upper limbs	control	3.93 ± 1.28	0.003
	experimental	4.73 ± 0.64	
Right lower limbs	control	3.97 ± 1.29	0.01
	experimental	4.67 ± 0.71	
Left upper limbs	control	3.13 ± 1.61	0.001
	experimental	4.47 ± 1.10	
Left lower limbs	control	3.33 ± 1.66	0.01
	experimental	4.27 ± 1.28	

*. S.D. = Standard Deviation

At the end of third day, mean muscular power was increased compared to the first day in two groups (Tables 3 and 4). The difference among groups was statistically significant (P<0.05). At the end of study, the association between muscular power and age were evaluated in two groups. While patients with age less than 55 in experiment group showed increased muscular power of all limbs in the third day compared to control group (P<0.05), the muscular power in the third day in experiment group was increased only in upper left limb (P>0.05).

Table 3- Comparison of muscular power of limbs in the first and third days in control group

Muscular power	Control Group	Mean ± S.D.*	P-value
Right upper limbs	first day	3.60 ± 1.56	0.005
	Third day	3.93 ± 1.28	
Right lower limbs	first day	3.60 ± 1.58	0.003
	Third day	3.97 ± 1.29	
Left upper limbs	first day	2.87 ± 1.69	0.003
	Third day	3.13 ± 1.61	
Left lower limbs	first day	3.07 ± 1.72	0.003
	Third day	3.33 ± 1.66	

*. S.D. = Standard Deviation

Table 4- Comparison of muscular power of limbs in first and third days in experiment group

Muscular power	Group	Mean ± S.D.*	P-value
Right upper limbs	first day	3.03 ± 1.56	0.001
	Third day	4.73 ± 0.64	
Right lower limbs	first day	3.07 ± 1.68	0.001
	Third day	4.67 ± 0.71	
Left upper limbs	first day	2.60 ± 1.75	0.001
	Third day	4.47 ± 1.10	
Left lower limbs	first day	2.87 ± 1.90	0.001
	Third day	4.27 ± 1.28	

*. S.D. = Standard Deviation

4. Discussions

There was a statistically significant variation in muscular power of limbs in experiment and control groups in our study. We found that simultaneously consumption of heparin with other antithrombotic drugs such as aspirin is more efficient in improvement of motion complications of patients with non hemorrhagic ischemic stroke.

Lip et al reported the decreasing rates of mortality, recurrence, complications, and motion disability in patients with consumption of 5000 unit heparin twice a day (Lip et al., 2002). If heparin and aspirin prescribe at the same time, this effect will increase. Our study confirmed this finding; i.e., simultaneous consumption of aspirin and heparin compounds (LMWH) is more efficient than consumption aspirin alone on the motion complications of non hemorrhagic ischemic stroke. Berge et al in a clinical trial showed that there is no evidence for preferring LMWH than aspirin in the treatment of atrial fibrillation (AF) patients (Berge et al., 2000). Our results are not consistent with their results due to potential consumption of aspirin and heparin in experiment group and their related mechanism of revascularization. Coull et al reported that aspirin can improve disability and motion problems of ischemic stroke patients (Coull et al., 2002).

Our study showed that age is an important factor in the recovery after stroke, especially in patients less than 55. This finding is consistent with the findings of Moonis et al that confirmed the positive effect of younger age on better prognosis (Moonis and Fisher, 2002). The comparison of LMWH and unfractionated heparin in acute thromboembolism carried out by Chen et al in 2005 showed no difference between the effect of these two heparins (Chen et al., 2005).

No one in our study showed hemorrhagic complications or mortality which is consistent with the results of Schmulling study (Schmulling et al., 2003). Strand found that the dilution of blood can have positive effect on the decreasing of complications (Strand et al., 1984). The study of Haley showed that the effect of heparin in the treatment of stroke still needs more attention (Haley et al., 1988). In another study, it has been confirmed that heparin can decline the risk of thromboembolism in acute ischemic patients, but not in intracranial bleeding and declining of disability (Williamson and Street, 2003).

Conclusion:

It can be resulted from our findings that despite the effectiveness of aspirin in the improvement of muscular power among ischemic stroke patients, the effect of heparin is more than aspirin. The effect is more efficient in younger patients than the others. Further large studies are necessary to confirm the effects of heparin and bleeding complications.

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