

## RESULTS OF HAEMODILUTION THERAPY IN PATIENTS WITH ACUTE ISCHAEMIC STROKE

Ziya Akar, M.D., Bülent Canbaz, M.D., Cengiz Kудay, M.D., Ertuğrul Sayın, M.D.,

İstanbul University, Cerrahpaşa Medical Faculty Department of Neurosurgery İstanbul - TÜRKİYE

Turkish Neurosurgery 2 : 71 - 74, 1991

### SUMMARY :

In this study, 21 patients between the ages of 40 and 75 (mean age 61) who were within the first 48 hours of acute ischaemic stroke were included. Isovolaemic haemodilution with Dextran 40 (rheomacrodex) was applied, the mean Htc value was  $43 \pm 4.8$  (38-55) before treatment. After five days of haemodilution therapy, the value descended to  $35 \pm 2$  which is a significant change. The ratio of neurological deficits also showed a decrease. Improvement in EEG findings and PO<sub>2</sub> levels observed were not considered significant. No complications were observed during the treatment.

### KEY WORDS :

Brain ischaemia, Cerebral blood flow, Dextran, Haemodilution.

Positive results with haemodilution therapy in patients with acute ischaemic stroke, have recently been reported in the literature (4,5,10,15). Haemodilution, reduces the haematocrit value which is an important risk factor (8) even when it is close to the upper limits of normal and therapy reducing blood viscosity gives rise to an increase in cerebral blood flow (3). Besides, reduction in the viscosity decreases in peripheral resistance, and increases cardiac output (12).

Increase in the cerebral blood flow provides the accumulation and spreading of thrombus and speeds the process of thrombolysis (13). Various authors report the most appropriate haematocrit level for increasing cerebral blood flow to be about 32-33% (10,14). It is also reported that a slight elevation in the oxygen delivery capacity along with increase in cerebral blood flow (6).

It is recommended to start haemodilution within the first 48 hrs. (10). According to the clinical presentation, haemodilution can be isovolaemic, hypovolaemic and hypervolaemic, however the types are not very strictly distinguished (5).

### MATERIAL and METHODS

In this study, 21 patients between the ages of 40-75 (mean age of 61) who are within the first 48 hours of acute ischaemic stroke and cerebral haemorrhage and oedema excluded by CT scan, were included. Recent myocardial infarction angina pectoris, cardiac insufficiency, anticoagulant therapy, serious hypertension (250/130mmHg and above), renal failu-

re, progressive systemic diseases, deep coma, and initial haematocrit values above 55% and below 38% were the criteria for exclusion from the trial. Patients with completely reversible neurological deficits within 24 hours were also excluded.

On the first day, the haematocrit value was tested and 1000 ml dextran 40 (Rheomacrodex) perfusion was given. On the second day according to the haematocrit level, blood was taken from the patient and same volume of dextran 40 transfused within the following 8 hours. With hematocrit levels below 38%, 500 ml dextran 40 was directly perfused without blood removal. The procedure was repeated for 5 days on condition that haematocrit value was maintained above 33%. The patients were discharged with a regimen of dipyridamole (2x75 mg daily) and during follow-up examinations were performed at the end of haemodilution therapy (5th day) and at the end of the first and 3rd months with the modified Scandinavian stroke group scores for evaluation.

### RESULTS

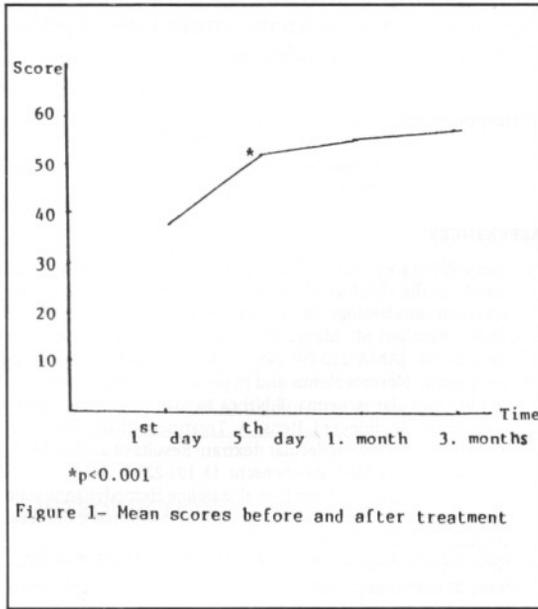
The mean Htc value was  $43 \pm 4.8$  (38-55) before treatment. After five days of haemodilution therapy, the value descended to  $35 \pm 2$  which was a significant change ( $p < 0.001$ ) (Table 2).

The mean score of the patients after haemodilution therapy was 53, while the value was 38 before treatment. This is again a statistically significant change ( $p < 0.001$ ) (Figure 1).

Table : 1 Score Table

Consciousness	Score
Fully conscious	6
Somnolent, can be awakened to full consciousness	4
Reacts to verbal command, but is not fully conscious	2
<b>Eye movements</b>	
No gaze palsy	4
Gaze palsy or nystagmus present	2
Conjugate eye deviation	0
<b>Arm, motor power*</b>	
Raises arm with normal strength	6
Raises arm with reduced strength or mild incoordination	5
Raises arm with flexion in elbow or serious incoordination	4
Can move, but not against gravity	2
Paralysis	0
<b>Hand, motor power*</b>	
Normal strength	6
Reduced strength in full range	4
Some movement, fingertips do not reach palm	2
Paralysis	0
<b>Leg, motor power*</b>	
Normal strength	6
Raises straight leg with reduced strength or mild incoordination	5
Raises leg with flexion of knee or serious incoordination	4
Can move, but not against gravity	2
Paralysis	0
<b>Orientation</b>	
Correct for time, place and person	6
2 of these	4
1 of these	2
Completely disorientated	0
<b>Speech</b>	
No aphasia	10
Limited vocabulary or incoherent speech	6
More than yes/no, but not longer sentences	3
Only yes/no or less	0
<b>Facial palsy</b>	
None/dubious	2
Present	0
<b>Gait</b>	
Walks 5m without aids	12
Walks with aids	9
Walks with help of another person	6
Sits without support	3
Bedridden/wheelchair	0
<b>Sensory deficit</b>	
None	4
Present	0
<b>Maximal score</b>	<b>62</b>

\* Motor power is assessed only on the affected side.



**Table : 2 Haematocrit Levels**

	Before treatment	After treatment
Haematocrit levels*	43+4.8 (38-55)	35+2 (33-40)

The patients were clinically grouped according to their scores: 1. Serious (0-30 points), 2. moderate (31-50), 3. mild (51-62). Before treatment 17 patients (81%) belonged to the 'serious' and 'moderate' groups, at the end of the fifth day 5 patients (24%) were in these groups, while the number was only 2 (9.5%) at the end of the 3rd month (Table 3).

Comparison of the EEG findings before and after treatment yielded the following figures: Ten patients (48%) had mild or serious slowing in background activity before treatment, while 6 (29%) had diffuse or focal slowing in background activity after treatment (Table 4).

No significant changes in serum electrolytes and O<sub>2</sub> and PCO<sub>2</sub> values were noted before and after treatment (Table 5-6).

**Table : 5 Serum Electrolytes**

	Before treatment	After treatment
K	4.2 mEq (3.3 - 5)	4.4 mEq (3.6 - 5)
Na	141.2 mEq (130 - 156)	140.0 mEq (132 - 150)

**Table 6 : Po<sub>2</sub> and PCO<sub>2</sub> Values**

	Before treatment	After treatment
PO <sub>2</sub>	81 MmHg (61 - 108)	85 mmHg (74 - 110)
PCO <sub>2</sub>	38.6 mmHg (32 - 44.5)	38.0 mmHg (34 - 42)

**Table : 3 Clinical Assessment**

Score	Before treatment	After treatment	First control (end of 1st month)	Second control (end of 3rd month)
0-30	5 (24%)	2 ( 9.5%)	2 (9.5%)	1 ( 4.7%)
31-50	12 (57%)	3 (14.5%)	2 (9.5%)	1 ( 4.7%)
51-62	4 (19%)	16 ( 76%)	17 ( 81%)	19 (90.5%)
<b>Total</b>	<b>21 (100%)</b>	<b>21 (100%)</b>	<b>21 (100%)</b>	<b>21 (100%)</b>

**Table : 4 EEG Findings**

EEG	Normal within normal limits	Mild diffuse or focal slowing	Serious diffuse or focal slowing
Prior to treatment	11 (52%)	5 (24%)	5 (24%)
After treatment	15 (71%)	5 (24%)	1 (5%)

## DISCUSSION

In this study, isovolaemic and hypervolaemic haemodilution therapy were applied. However, Dextran 40 used in this study, causes a mild increase in blood volume. Even given in equal volume to volume of removed blood it causes a 40% rise in total plasma volume (14). As a result, the haemodilution applied in this trial was hypervolaemic.

Hypervolaemic haemodilution therapy is especially effective in ischaemic infarction regions in which the collateral circulation may be available (1,11,16). In haemodilution while the first blood sample is being obtained, Dextran 40 perfusion can not be performed simultaneously and this gives rise to a decrease in blood volume which subsequently causes a decrease in blood pressure. As a result, perfusion of the cerebral tissues is injured (5,13).

Considering that patients with ischaemic stroke might not have received enough fluid until they reach hospital, hypervolaemic haemodilution seemed to be more suitable. Because of the platelet activating effect of venesection (13), a method requiring the least blood removal was preferred. The reasons for the exclusion of patients with deep coma, hypertension, cardiac disease and haemorrhagia on CAT scan are the after effects of hypervolaemic haemodilution: This kind of treatment increases the plasma volume to a certain extent and consequently affects cardiac output (11,13). Besides, haemodilution increases cerebral oedema and facilitates cerebral haemorrhagea (17).

Patients whose symptoms completely recovered within the first 24 hours were also excluded from the study with the consideration of a possible ischemic attack. Patients with Htc values below 38% were excluded as the risk of Htc as falling below 33% is high and when Htc value is below 33%, even if the cerebral blood flow increases, the oxygen binding is reduced (7).

A significant improvement in the clinical assessment of the patients was noted. Before treatment 17 patients (81%) were in the serious and moderate groups, at the end of haemodilution therapy 5 patients (24%) were in these groups.

Various authors report positive results with haemodilution therapy (2,3,9). Improvement of EEG findings after haemodilution therapy is again another finding of this study in common with the literature (15).

No adverse effects were observed during treatment.

It is possible to conclude that haemodilution therapy is effective in ischaemic stroke cases if performed under certain conditions.

**Correspondence:** Ziya Akar, M.D.,  
İ.Ü. Cerrahpaşa Tıp Fakültesi  
Nöroşirürji Anabilim Dalı  
Aksaray / İstanbul, TÜRKİYE

## REFERENCES

1. Corry WD, Jackson LJ, Seaman GVF: The effect of hydroxyethyl starch on the rheological properties of human erythrocyte suspension. *Biorheology* 18:517-529, 1981
2. Gilroy J, Barnhart MI, Meyer JS: Treatment of acute stroke with Dextran 40. *JAMA* 210:293-298, 1969
3. Gottstein U: Normovolemic and hypervolemic hemodilution in cerebrovascular ischemia. *Bibliotheca Haematologica* 47:127-138, 1981
4. Gottstein U, Seldmeyer I, Henss A: Treatment of acute cerebral ischaemia with low-molecular dextran: Results of a retrospective study. *Dtsch Med Wochenschr* 13 101:223-7, 1976
5. Grotta C, Pettigrew C, Allen S, et al: Baseline Hemodynamic state and Response to Hemodilution in patients with Acute Cerebral Ischemia. *Stroke* 16:790-795, 1985
6. Henriksen L, Paulson OB, Smith RJ: Cerebral blood flow following normovolemic hemodilution in patients with high hematocrit. *Ann Neurol* 9:454-457, 1981
7. Hint H: The pharmacology of Dextran and the physiological background for the clinical use of Rheomacrodex and Macro-dex. *Acta Anaesthesiol Belg*, 19:119-138, 1968
8. Kannel WB, Gordon T, Wolf PA, et al: Hemoglobin and the risk of cerebral infarction. The Framingham study. *Stroke* 3:409-420, 1972
9. Matthews WB, Oxbury JM, Grainger KMR, et al: A blind controlled trial of Dextran 40 in the treatment of ischemic stroke. *Brain* 99:193-206, 1976
10. Scandinavian Stroke Study Group: Multicenter Trial of Hemodilution in Ischemic Stroke. Back ground and study protocol. *Stroke* 16:885-890, 1985
11. Strand T, Splund K, Erikson S, et al: A randomized controlled trial of hemodilution therapy in acute ischemic stroke. *Stroke* 15:980-989, 1984
12. Sunder - Plasman L, Klovekron WP, Holper K, Hase U, Messmer K: The physiological significance of acutely induced hemodilution. 6th Europ. Conf. Microcirculation, Aalborg 1970. Ditzel J and Lewis DH eds, Karger, Basel pp 23-28, 1971
13. Thomas J: Hemodilution in Acute Stroke: *Stroke* 16:763-764, 1985
14. Wood H, Kee D: Hemorheology of the cerebral circulation in stroke: *Stroke* 16:765-772, 1985
15. Wood JH, Polyjoidia KS, Epstein CM, et al: Quantitative EEG alterations after isovolemic hemodilutional augmentation of cerebral perfusion in stroke patients. *Neurology* 34:764-768, 1984
16. Wood JH, Simeone FA, Fink EA, et al: Hypervolemic hemodilution in experimental focal cerebral ischemia: Elevation of cardiac output regional blood flow and ICP after intravascular volume expansion with low molecular weight dextran. *J Neurosurg*. 59:500-509, 1983
17. Wood JH, Simeone FA, Kron RE, et al: Experimental hypervolemic hemodilution: Physiological correlations of cortical blood flow, cardiac output and intracranial pressure with fresh blood viscosity and plasma volume. *Neurosurgery* 14:709-723, 1984