

LOW DOSE HEPARIN; THERAPEUTIC BENEFIT IN POSTPARTUM CEREBRAL VENOUS THROMBOSIS

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ABSTRACT...Objective: To evaluate the therapeutic benefit of low dose heparin in cerebral venous thrombosis, occurring during period of puerperium. **Study design:** Descriptive study. **Setting:** Department of Medicine DHQ Hospital Mirpur (Department of Obs/Gynae DHQ Hospital Mirpur(AK)). **Period:** January 2010 to November 2011. **Method:** This study was carried on 100 patients with history of postpartum cerebral venous thrombosis. Out of which 48 on heparin and 52 formed the control group. The ages of all patients were between 20 to 30 years. Parameter recorded included history. Blood pressure, the diagnosis was supported by cranial computed tomography. The secondary causes were ruled out on the basis of history and physical examination. The data and results were analyzed in SPSS. **Results:** Out of 48 patients in heparin group 30 with non-haemorrhagic lesion and 18 with haemorrhagic infarction). 52 in control group. 34 non-haemorrhagic lesion and 18 with haemorrhagic infarct. In non-haemorrhagic CVT, there is no death in heparin group as compared to 5 deaths in control group. In patients with haemorrhagic lesions, there were 5 deaths in heparin group as compared to 7 deaths in the control group. Heparin fared better than the control group, both in patients with haemorrhagic as well as non-haemorrhagic lesions. **Conclusions:** Low molecular weight (LMWH) at low doses is safe and effective for both non-haemorrhage and haemorrhagic infarct of postpartum cvt with regard to recovery and outcome as compared to control group.

Key words: Postpartum ,cerebral venous thrombosis, low molecular weight heparin (LMWH)

INTRODUCTION

Cerebral venous thrombosis (CVT), is an important cause of stroke in puerperium, which is frequently observed in Pakistan. Treatment of cvt has been controversial and methods include steroids, systemic or local thrombolytic agents and anticoagulant.

Case control study by authors, suggested beneficial effect of heparin in the treatment of CVT¹. They also reported absence of serious side effect even in patients with haemorrhagic in fraction. Having observed favourable response to heparin, in an earlier control trial in patients with non-haemorrhagic puerperal CVT, the authors planned to assess the use of low dose heparin in patients with haemorrhagic cvt as well. This communication describes our experience in treating 48 patients of cvt with low dose of heparin as compared to 52 patients treated without heparin during the same period. Imageology like CT and MRI Scan have improved the diagnostic yield of cerebral venous thrombosis CVT². However, its management remains a challenge³⁻⁵ the present study was carried out to study the role of heparin in CVT. Therapeutic outcome of 100 patients of postpartum cvt manifesting within 01 month of delivery,

was analyzed 3the diagnosis was supported by MRI scan. 48 patients, 30 with non-haemorrhagic in fraction and 18 with haemorrhage infarction, received 2500 units of subcutaneous heparin, 03 times a day within 24 hours of hospitalization till 30th postpartum day. 52 patients during the same period, 34 with non-haemorrhagic infarction and 18 with haemorrhagic infarction, who did not receive heparin, formed the control group 4 among the heparin group, 22 patients made full recovery. There were 5 death, all among 5 the patients with haemorrhage lesion. In control group, only 9 patients recovered completely ($p < 0.001$) and 5 died ($p < 0.001$) there were no adverse effects of heparin. Low dose heparin is safe and efficacious in post-CVT, even in patients with haemorrhage infarction.

PATIENTS AND METHODS

48 patients of CVT, presenting within 01 month of delivery or abortion, confirmed by MRI scan and admitted under care of the authors, were started on low dose heparin (2500 units subcutaneously 03 times a day) within 24 hours of admission to the hospital⁶⁻¹⁰. The treatment was continued till 30th postpartum day or symptomatic relief. Heparin was then tapered and

stopped over one week. 52 other patients of CVT, admitted during the same period to another clinical unit but who did not receive heparin, formed the control group.

11 the clinical data was collected on structured data sheet. Mannitol was used in all patients. Anemia was corrected with oral iron or blood transfusion whenever indicated. The diagnostic criteria for cvt were:1) acute onset of headache, convulsion / or neurological deficit within 01 month of delivery or abortion,2) absence of past history of cerebrovascular disease or cardiac disease,3) MRI scan showing direct signs of CVT excluding evidence of cerebral arterial infarction /or oedema. And4)confirmation of diagonosis by trans-femoral angoigram in doubtful lesion.

Ecg was done routinely¹²⁻¹⁵ echo cardiogram(echo) was carried out whenever indicated. All patients were evaluated on Glasgow com a scale at admission to assess the severity. They were assessed for activities of daily living at the time of discharge and were categorized into five groups¹⁶⁻¹⁸. The heparin and the control groups were compared with regard to the clinical features and the outcome.

RESULTS

There were 48 patients in heparin group(30 with non-haemorrhagic lesion and 18 with haemorrhagic infarction) and 52 in the control group (34with non-haemorrhagic lesion and 18 with haemorrhagic infarction). In non-haemorrhagic CVT there were no deaths in the heparin group as compared to 5 deaths in the control group. In patients with haemorrhagic lesion, there 5 deaths in the heparin group as compared to 7 in control group. Heparin therapy was well tolerated and there were no complications. At discharge, the heparin group fared better than the control group, both in patients with haemorrhagic as well as non-haemorrhagic lesions.

DISCUSSION

Heparin has been in use since 1942 but reports indicating the beneficial as well harmful effects have been published. Kratenbulh, in a study of 17 patients of CVT, noted that heparin was safe and effective. Fairburn

Table-I.			
Heparin Group	Non-haemorrhagic infarct	Haemorrhagic infarct	Outcome
No. 48	No. 30	No. 18	22 Fully recovered
	Non death	05 death	

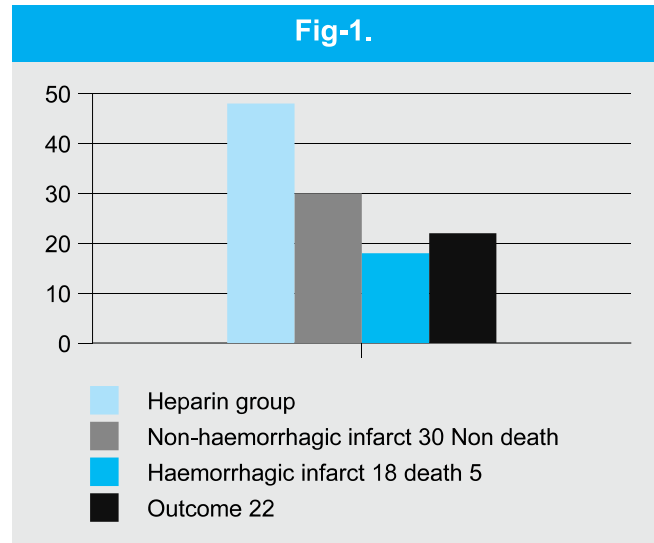
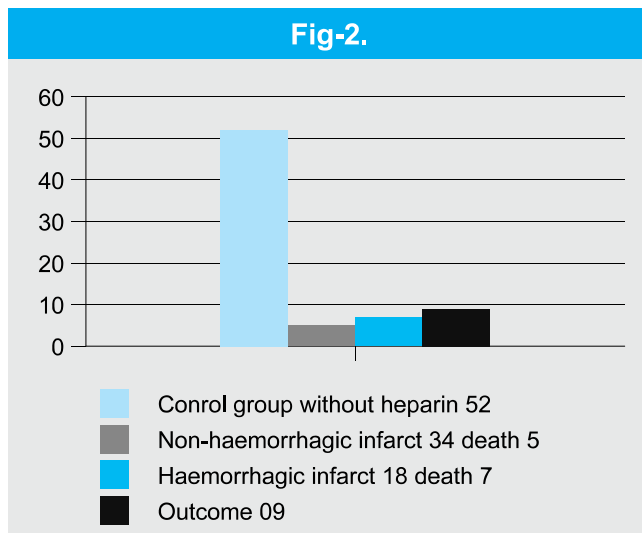


Table-II.			
Control group without heparin	Non-haemorrhagic infarct 34	Haemorrhagic infarct 18	Outcome
No. 52	5 Death	7 Death	9 Fully recovered
Total: No. 100			

reported total recovery in CVT with heparin patients due to oral contraceptive use and good result in 01 patient during pueperium. In an uncontrolled trial of heparin in pueperium. Srivasan observed 05 deaths in heparin group (n=42) as compared to 21 deaths (n=47) in the group who did not receive heparin. However, apprehensions have been expressed regarding bleeding into the infarcted brain and elsewhere due to heparin. Gettlefiner and Kokman observed development of CVT in 02of the 03 patients receiving ant-coagulants. In first ever reported control trial involving 20 patients of CVT,

Einhaulpl documented significant reduction in mortality and better rate of recovery in patients in patients receiving heparin. Nagaraja in control trial of 57 patients with non-haemorrhagic puerperal CVT observed beneficial effect of low dose heparin without any haemorrhagic complications. Haemorrhagic as non-haemorrhagic, while one of the clinical unit in the same hospital treated these patients¹⁹⁻²⁵ without heparin.



The two groups were more or less matched for clinical and CT-parameters. There were no haemorrhagic complications in heparin group. Repeat MRI scan, did not reveal any increase in bleeding and the oedema was same as before. The results indicate favourable outcome with low dose heparin in non-haemorrhage CVT, even in haemorrhagic there was a reduction in mortality in heparin group. At discharge 84.8% cases with non-haemorrhagic infarct in the heparin group were independent as compared to 40% of controls. In patients with haemorrhagic lesions 48.2% were independent in heparin treated group as compared to 7.5% of control. While this study was not a randomized trial, it certainly establishes the safety and efficacy of low dose heparin in all forms of CVT. It is noteworthy that during low dose heparin therapy. Monitoring of clotting parameters is not required. Low dose heparin does not alter the clotting parameters as most of it gets bound to endothelium and hence circulating free heparin is negligible. Thus the clotting parameters remain normal but progression of thrombosis is prevented. This makes the regimen suitable even for peripheral centers with limited facilities.

However, it is still necessary to establish the safety of conventional dose of heparin in puerperal haemorrhagic CVT²⁶⁻³⁰. It has been suggested that low molecular weight heparin (LMWH) may be more effective and safe in prevention of thromboembolism after spinal injury related deep venous thrombosis as compared to standard heparin³¹⁻³⁸.

LMWH has also been used in acute ischaemic strokes with favorable results. convenient dosage schedule, more predicable anticoagulant response, efficacy and safety warrants trial of LMWH in puerperal, cerebral venous thrombosis.

CONCLUSIONS

Low molecular weight heparin(LMWH) at low doses is safe and effective for both non-haemorrhagic and haemorrhagic infarct of postpartum cvt with regard to full recovery and outcome as compared to control group.

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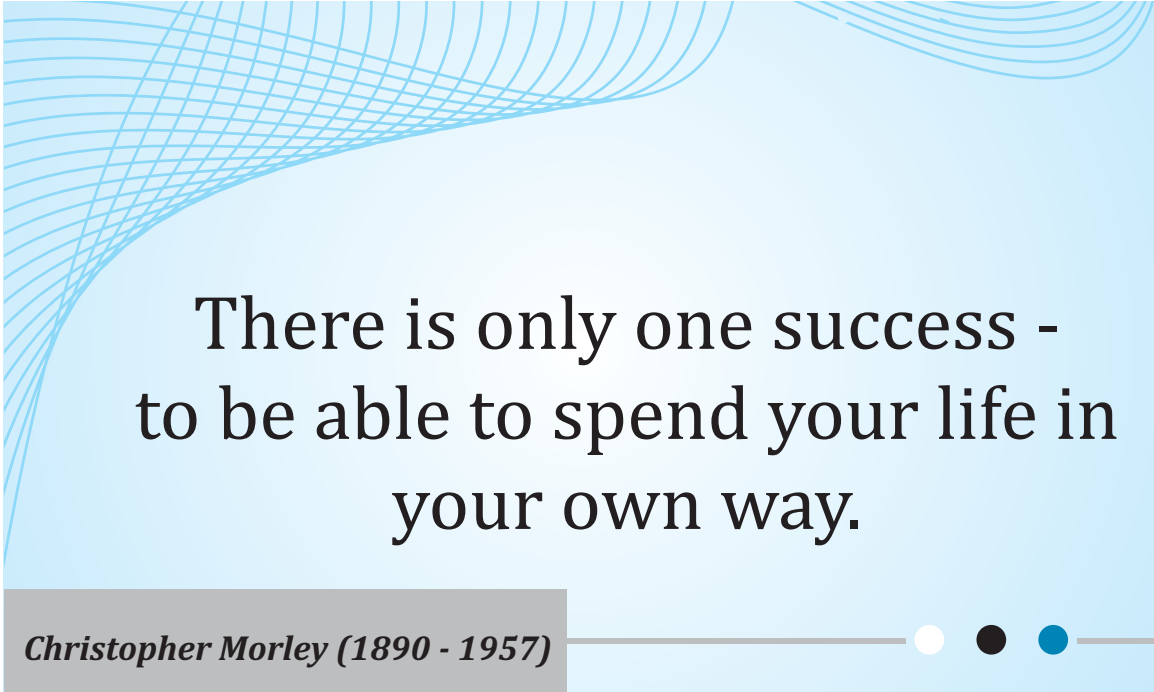
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