Predictors And Outcomes Of Status Epilptecus In Patients With Cerebral Venous Thrombosis

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ABSTRACT

Background: status epilepticus (SE) is a serious complications of cerebral venous thrombosis (CVT). the risk factors associated with SE occurrence and the out come is a debate issue.
Aim of study: To estimate predictives of development of SE in CVT patient, and compare the relative risk of SE in determining death and disability compared with those patients without SE.
Methods: this is a Comparative case sires study of 29 CVT patient were admitted to Al-Yarmook teaching hospital from January , 2019 to march , 2021. Patients were followed up and re-assed at 3 months and 6 months after discharge and outcomes were classified on the basis of modified rankin scale .
Results: of 29 patient with CVT admitted to Al-yarmook teaching hospital 11 Patients (37.9%) had SE . presence of decrease conscious level (GCS ≤8) (p=0.0001) , motor weakness (p= 0.003) and supra tentorial brain lesion on MRI (p= 0.0001) specially Hemorrhagic type (p=0.003) all were risk factors to development of status epilepticus and disability were higher in status epilepticus group 3 months after discharge (p=0.006) but after 6 months both status epilepticus and without SE group all had good recovery (p=0.345) .
Conclusion: predictive of SE development were decreased level of consciousness , motor weakness and supratentorial lesion on brain mri specially hemorrhagic type . The presence of SE were associated with higher rate of disability 3 months after discharge but after 6 months all patients achieved good recovery .

Keywords: cerebral venous thrombosis · status epilepticus · Outcome

Introduction

Thrombosis of the Dural sinus and/or cerebral veins (CVT) is relatively rare. and primarily affects individuals younger than the age of 50. Women make up about 75% of those with CVT.[1] Seizures occur in one-third of adults and nearly one-half of children with CVT factors associated with the development of seizures include the presence of a venous infarction, hemorrhagic transformation and intracranial hypertension.[2] Diagnosis made by high clinical suspicion and imaging of the brain MRI/magnetic resonance venography is the recommended imaging for the diagnosis of cerebral venous thrombosis. [3] Contrast-enhanced MRV is more sensitive in demonstrating the thrombus within small veins.[4] Conventional angiography is reserved for selected situations when the diagnosis is uncertain.[5] Risk factors are Female sex, OCP, pregnancy, puerperium, and hormone therapy.[6] Transient triggers are, CNS or ear/sinus/mouth/ face infections, exposure to drugs head trauma, or procedures like lumbar puncture, jugular catheter placement.(6) Chronic triggers include hereditary or acquired thrombophilias.[6]

Anticoagulation is the standard treatment for patients with CVT.[7] For those with provoked CVT, warfarin (target INR of 2.0 to 3.0) for 3 to 6 months is recommended. Patients with unprovoked CVT may be treated with warfarin for to 12 months.

In patients with recurrent CVT, venous thromboembolism after CVT, or first CVT with severe thrombophilia, indefinive anticoagulation may be considered, [3] outcomes are generally favorable. [8]

Materials And Methods

Study Design

This is Comparative case series study . all patient with CVT were admitted to Al-Yarmook teaching hospital neurology department from January , 2019 to march , 2021 and they were divided into 3 groups based on their presentation with status epilepticus, epileptic seizure or without seizure is observed.

Patient And Methods

Patients interview or medical records were used to retrieve the following data:

The CVT presentation was considered acute if the patient was hospitalized within 2 days of symptoms, subacute if within 3–30 days, and chronic if after 30 days. [9]

Status epilepticus was defined as continuous seizure activity or two or more seizures without recovery of consciousness lasting longer than 30minutes. while epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. [10]

Seizure or status epilepticus were categorized as acute symptomatic if occurred within the first 7 days of initial symptoms of CVT; while seizure or status epilepticus were defined as remote if seizure or status epilepticus occurred after 7 days after the initial symptom. [11]

Demographic information, duration of illness from the onset of first symptom, and presence of headache, seizure, focal neurological deficit were noted.

GCS on admission were noted. Presence and type of risk factor Brain MRI /MRV finding were noted.

All patient were investigated for Blood counts, hemoglobin level, coagulation profile, erythrocyte sedimentation rate, serum chemistry, HIV serology, chest radiograph, and electrocardiogram were carried out.

The patients were investigated for prothrombotic conditions such as proteins C, protein S, and antithrombin III deficiency, factor V Leiden , antinuclear antibody, anti dsDNA, antiphospholipid antibody, and lupus anticoagulant. after conformation of the diagnosis of CVT, all patients had received low-molecular-weight heparin (enoxaparin, 100 unit/kg s.c twice daily), warfarin was prescribed after 5-15 days of heparin with target INR (2-3) in addition to the AED (for the patients who develop seizure or SE and no prophylactic AED is given to without seizure group). Acetazolamide and/or mannitol were prescribed to those with raised intracranial pressure and after clinical improvement they were discharged with regular monitoring of INR every 21 days and follow up at 3 and 6 months .

Death during hospital stay and its causes were noted. Patients were followed up and re-assed at 3 and 6 months from discharge , and outcomes were classified on the basis of MRS as poor (MRS > 2) or good recovery (MRS < 2). [12]

Statistical Analysis

Analysis of data was carried out using the available statistical package of SPSS-27 (Statistical Packages for Social Sciences- version 27). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test (χ^2-test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05.

The Results

General condition of participants

Total number of study patients were 29 case, 27 of them were females while only 2 were males . Patients ages ranging from 16 - 61 years , With mean and SD 31.3 ± 10.4 Mean and SD duration of illness until hospitalization were 10.3 ± 6.7 . Eleven Patients (37.9%) had SE, ten Patients (34.4 %) had epileptic seizure and eight Patients (27.5%) without seizure. Number of Seizures were ranging between (1-5) seizures.

Risk factors for developing status epilepticus

Comparison between status epilepticus (SE) group and without SE group shows no significant difference between two groups in demographic and risk factors but GCS were much lower in SE group and motor weakness were much commoner in SE group and p value were 0.0001 and 0.002 respectively and supratentorial parenchymal lesion were in dependent factor for development of SE with (p value 0.018).

SE were more common in hemorrhagic infarction and p value was 0.003. death were not significantly different between two groups and disability using MRS at 3 months were higher in SE group p value 0.003. While disability at 6 month were not significantly between two groups p value = 0.236 .

Table (1) comparison between status epilepticus group and without status epilepticus group

		Status epilepticus		Without SE		P value
		No	%	No	%	
Age (years)	<20years	1	9.1	1	5.6	0.923
	20---29	5	45.5	9	50.0	
	30---39	3	27.3	6	33.3	
	=>40years	2	18.2	2	11.1	
	Mean±SD (Range)	31.9±11.6 (17-61)		30.9±9.9 (16-61)		
Gender	Male	-	-	2	11.1	0.252
	Female	11	100	16	88.9	
Headache	Present	11	100	18	100	-
	Absent	-	-	-	-	
Duration of illness (days)	Acute (<3)	2	18.2	1	5.6	0.427
	Subacute (3-30)	9	81.8	16	88.8	
	Chronic (>30)	-	-	1	5.6	
	Mean±SD (Range)	7.4±4.1 (2-14)		12.2±7.6 (2-35)		

Type of lesion	Hemorrhagic infarction	7	63.6	2	11.1	0.003*
	Infarction	4	36.4	7	38.9	
	No parenchymal lesion	-	-	9	50.0	
Risk factor	OCP	8	72.7	12	66.7	0.821
	Puerperium	2	18.2	2	11.1	
	Dehydration	1	9.1	2	11.1	
	Anemia	-	-	1	5.6	
	SLE	-	-	1	5.6	
Death at hospital	Dead	1	9.1	-	-	0.193
	Alive	10	90.9	18	100	
MRS at 3 months	0	-	-	12	66.7	0.003*
	1	4	40.0	4	22.2	
	2	4	40.0	-	-	
	3	2	20.0	1	5.6	
	4	-	-	1	5.6	
MRS at 6 months	0	8	80.0	17	94.4	0.236
	1	2	20.0	1	5.6	
Papilledema	Present	8	72.7	12	66.7	0.732
	Absent	3	27.3	6	33.3	
The 6th Cranial nerve palsy	Bilateral	8	72.7	7	38.9	0.121
	Unilateral	3	27.3	7	38.9	
	No palsy	-	-	4	22.2	
Motor deficit	Yes	11	100	8	44.4	0.002*
	No	-	-	10	55.6	
Glasgow Coma Scale	≤8	11	100	3	16.7	0.0001*
	>8	-	-	15	83.3	
	5	5	45.5	-	-	
	6	3	27.3	-	-	
Glasgow Coma Scale	7	3	27.3	1	5.6	
	8	-	-	2	11.1	
	10	-	-	1	5.6	
	11	-	-	1	5.6	
	13	-	-	2	11.1	
	14	-	-	2	11.1	
	15	-	-	9	50.0	
MRI Supratentorial Parenchymal Lesion	Yes	11	100	11	61.1	0.018*
	No	-	-	7	38.9	
Number of sinus involved	Single	8	72.7	17	94.4	0.100
	Multiple	3	27.3	1	5.6	
Superior Sagittal Sinus	Yes	7	63.6	9	50.0	0.474
	No	4	36.4	9	50.0	
Transverse sinus	Bilateral	-	-	1	5.6	0.418
	Right	6	54.5	5	27.8	
	Left	1	9.1	1	5.6	
	No	4	36.4	11	61.1	
Others	Yes	-	-	4	22.2	
	No	11	100	14	77.8	
Others	Cortical vein	-		1		
	Deep venous	-		1		
	Right sigmoid	-		2		

Discussion:

In this study Eleven Patients (37.9%) had SE, ten Patients (34.4 %) had epileptic seizure and eight Patients (27.5%) without seizure .and this disagree with the study of Kalita et al on 90 patients with CVT, 42 had seizures; of them, 10 (11%) had SE. [13]

While Anadure et al reported the incidence of generalized, focal and focal with secondary generalized seizure in patients with CVT 65% , 25% and 10 % respectively. [14]

In the present study, 55% patients had acute symptomatic seizure and 45% late seizure, which is quite higher than the reported by Mahale et al studied seizures in CVT and found that 46% of patients with CVT had acute seizures. [15]

In this study male cases represent 6.9 % And female represent 93.1% of patients and this disagree with , Sha et al found that female patients represented 55 % of patients. [16]

Patil et al performed a retrospective study on 50 patients and found that 42% of whom were males and 58% were females. [17]

In current study patients ages ranging from 16 - 61 years, with mean 31.3 with SD 10.4 which is comparable with most previous studies. In an International multicenter study of 11400 CVT hospitalized patients, Nasr et al reported an average age of 38.1 years. [18]

While Haghighi et al retrospectively investigated 465 Iranian patients with confirmed CVT and showed that their mean age was 29.52±34.8 years. [19]

Most common symptom was headache which was present in all Patients which agrees with Headache is the most common manifestation of CVT and is observed, to varying degrees, in 80–90% of patients reported by Agostoni,et al. [20] And Gunes et al. [21]

In this study papilledema present in most cases of all three groups and this agrees with Wasay et al who reprted Papilledema is a common manifestation of CVT that is observed in 28–67.5% of CVT patients. [22]

Ferro et al found that papilledema is more frequent In patients with chronic onset or a late visit than in patients with acute onset. [23]

Coutinho et al found that papilledema was more common in patients with cortical hemorrhage (44 vs. 9%) than in those without, [24] in this study motor weakness encountered in 19 patient (65.5 %) and were more common in SE group and seizure group carry risk for SE, [25] also agrees with Ferro et al in his studies of 91 registered patients, reported that 34% of them had early symptomatic seizures. Especially, patients with motor deficits. [26]

Supratentorial brain parenchymal lesion (specially hemorrhagic infarction) was a predictor of occurrence of SE or seizure and this agrees with masuhr et al that reported Early intracranial hemorrhage and infarction were independent predictors of early epileptic seizures and Patients with focal motor deficits, cortical venous thrombosis and intracranial hemorrhage carried the highest risk for SE, [25] also agrees with Ferro et al in a study of 91 registered patients, reported that 34% of them had early symptomatic seizures. Especially, patients with motor and with focal edema, ischemic infarcts or hemorrhages had early symptomatic seizures. [26]

SSS was found to be the most affected sinus in the present study (63.6% 0f patients in SE and in 50% of seizure patients group), and this agrees with Davoudi et al showed that the this region (supratentorial parenchyma) as the only location in the CNS that independently correlated with development of epileptic seizures. This explains the significant association of SSS occlusion with the development of seizure in CVT patients. [27]

Ocp were the most common risk for development of cvt in all groups and this agrees with Amoozegar et al which confirmed that OCP can significantly increase the incidence of CVT in women at reproductive age. [28]

another study done by Beier et al showed no evidence that the use of exogenous sex hormones (i.e., oral contraceptives) increases the risk of seizures in young adults without epilepsy. [29]

In this study death encounterd in 3.4% , recorded in SE group the patient who had refractory SE and was admitted to RCU.

Ferro et al find that risk factors associated with death in CVT were age >37 years old, male sex, coma, mental status disorder, hemorrhage on admission CT scan, deep brain veins thrombosis, infection of the central nervous system, and cancer. (26)

In this study the disability of at 3 month in the SE group were much higher than other group but after 6 months from discharge all patient in this study achieved good recovery after 6 months and their MRS were < 2 and this agree with Mehvari et al in his studies did not find association of seizure with disability . (30)

THE CONCLUSION:

- Status epilepticus occurs in more than one third of patients with CVT.
- Risk factors for occurrence of Status epilepticus were decreased level of consciousness , motor weakness and supratentorial brain mri lesion specially if hemorrhagic infarction lesion type .
- The presence of SE, however, does not determine the occurrence of death and disability in treated patients.

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