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REVIEW ARTICLE

Prediction of post hemorrhagic stroke seizures

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ABSTRACT

Background and Purpose: Seizures are a serious complication of spontaneous intracerebral hemorrhage (sICH) which increases morbidity of the patients.**Patients and Methods;** cross sectional analysis of patients admitted to Zagazig Neurology Department and Intensive Care Unit(ICU) (n=125and follow-up to 6 months) for detection of early and late onset seizures. within 7 days of ICH and among 7-day survivors for detection of early seizures (ES) and late seizures (LSs) occurring >7 days from ICH. Using CT brain and CT angiography for diagnosis and to measure the volume of hemorrhage, also using CAVE score for evaluation or ES and LSS.**Results:** Of our study on 125 patients with sICH 58 were males and 67 were females , there were cortical hge 36% , BG(Basal Ganglia) 23.2%, Thalamic he 25.6%,cerebellar he 10.4% and brain stem was 4.8%, while intraventricular extenstion was 9.6% and with SAH 7.2 % , also 18 patients (14.4%) had ES within 7 days of sICH. Among the 7-day survivors, 10 patients (8%) developed LSs.

There were a statistically significant association between early ES and LSs with the volume of intracerebral hemorrhage and CAVE scale.

Conclusions: about 14 % of patients with sICH will develop seizures with in the first 7 days . while 8% will develop LSs after one week of sICH The

risk of this adverse outcome can be estimated by CAVE scale which is a simple score based on baseline variables.

Keywords: spontaneous IntracerebralHemorrhage (sICH)- Early seizures(ES), Late onset seizure(LSS) and subarachnoid hemorrhage(SAH).

INTRODUCTION

Cerebro-vascular Stroke is one of the most common causes of death worldwide, (1).The incidence of stroke is more common in middle and low income countries ,due to increased life expectancy(2).Among different stroke types , ICH is the second common subtype of stroke and ranged from 10 % to 20 % of all strokes subtypes(3).Spontinious intracerebral hemorrhage may be of unknown etiology and is the most frequent subtype of intracerebral hemorrhage(4).Acute sICH represents a common cause for symptomatic epilepsy (5).The symptomatic or secondary seizures among patients with SICH ranged between 5% - 14% within the first days of stroke (6).

Post hemorrhagic stroke seizures can be classified into early seizure (ES) which occurs within the first 7 days after stroke and late seizures(LSS) developing after 1 week from stroke onset , seizures may be focal or generalized.(7).Early seizures may occur due to pathological changes producing acute disturbance of brain integrity, metabolic homeostasis, and depolarization of the nerve cells , whereas late seizures may be due to neuronal reorganization and formation of epileptogenic foci (8).CAVE score(C cortical, A age of patient, V volume of hemorrhage and E early onset seizure) is a recent score developed by Haapaniemi E,and colleagues in 2014 to evaluate the risk of developing post heamorrhagic stroke epilepsy (9).

PATIENTS AND METHODS

This Cross sectional study was executed in Neurology ICU and stroke unit in Department of Neurology in Zagazig University Hospital, during the period from September 2018 to October 2019. In current study 125 patients with sICH were admitted stroke unit and ICU.

Inclusion criteria:

Patients with Primary spontaneous intracerebral hemorrhage, proved by brain Ct and or CT angiography.

Exclusion criteria; Known epileptic patients , Patients with receiving oral anticoagulation, Patients with brain tumors or other space occupying lesions , Patients with abnormal vascular lesion AVM and Patients with hypoglycemia and renal failure or electrolyte disturbance.

Ethical Concerns

The study committed to the ethical guidelines of declaration of Helsinki. Written informed consents were obtained from all participants and or their relatives.

Score assessments

The score is calculated as the following, cortical involvement (0 or 1) , younger age <65 years(0 or1) , larger ICH volume at baseline >10 mL(0 or 1) ,and ES within 7 days of ICH were associated with development of LSs (0 or 1) , The CAVE score (0–4 points) consists of cortical involvement of ICH (1 point), age <65 years (1 point), volume >10 ml (1 point), and ES within 7 days of ICH(1 point). (9).

All patients were subjected to general and neurological examination, random blood sugar, liver and kidney function tests, and electrolyte assay to exclude possible metabolic causes of epilepsy.

Statistical analysis;

Table(1) Patients demographic data, risk factors, radiological findings and seizures

Variables		frequency	Percentage %
sex	M	58	46.4%
	F	67	53.6%
Site of hge	cortical	45	36%
	Basal ganglia	29	23.2%
	Thalamus	32	25.6%
	Cerebellum	13	10.4%
	Brain stem	6	4.8%
	With intraventricular	12	9.6%
	With SAH	9	7.2%
Perifocal edema	yes	60	48%
	no	65	52%
smoking	yes	38	30.4%
	no	87	69.6%
DM	yes	30	24%
	no	95	76%

Data collected throughout history, basic clinical examination, investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp) (10).

RESULTS

The demographic data of our patients according to results in table (1) showed that, we have 58 males with percentage 46.4% and 67 females with percentage 53.6% .the mean age was 61.2 years with SD ± 9.4.

According to hematoma site the percentage of cortical hematoma site was 44% (55 case) ,while the least percentage was infratentorial site was 16% (16 case).the risk factors for intracerebral hematoma in the participants, hypertension was the highest percentage 56 % , and lowest percentage was previous stroke 7.2%.

Regarding seizure onset we have 18 case that have seizure in first week (14.4%), and , 10 cases only (8%) have late seizure onset after one week.

Table (2) shows significant difference between intracerebral hemorrhage volume at time f admission and early onset seizures (p value <0.05). As well as there was a significant difference between intracerebral hemorrhage and late onset seizures as showed in table (3)

Tables (4&5) shows that the CAVA scale was applied for all participants, the scores ranged from 0 to 4 , the mean value was 1.08 ±1.096 with significant difference between CAVA scale and early onset seizures,(p value <0.05).Also the mean value was 1.144 ±1.175 for late onset seizures and also there is significant difference between CAVA scale and late seizures after intracerebral hemorrhage (p value <0.05)

Variables		frequency	Percentage %
HTN	yes	70	56%
	no	55	44%
Hepatic	yes	31	24.8%
	no	94	75.2%
Dyslipedemia	yes	47	37.6%
	no	78	62.4%
Previous stroke	yes	9	7.2%
	no	116	92.8%
Early Seizure	yes	18	14.4%
	no	107	85.6%
Late seizure	yes	10	92%
	no	115	8%
Death after 2 weeks	yes	14	11.2%
	no	111	88.8%

Table(2) Relationship between intracerebral hemorrhage (at admission) volume and early onset seizure

ICH volume 1 and early onset seizure	Paired Differences				95% Confidence Interval of the Difference	T test	P value
	Mean	Std. Deviation	Std. Error Mean				
				Lower	Upper		
	2.485	12.11595	1.46927	21.92084	27.78621	16.916	.001

t; paired t test, $p < 0.05$ is significant.

Table(3) Relationship between intracerebral hemorrhage (after 1 week) volume and late onset seizure

ICH volume 2 and late onset seizure	Paired Differences				95% Confidence Interval of the Difference	t	P value
	Mean	Std. Deviation	Std. Error Mean				
				Lower	Upper		
	2.399	11.64109	1.38154	21.23671	26.74751	17.366	.001

t ; paired t test, $p < 0.05$ is significant

Table (4) Relationship between CAVE score and early onset seizure

CAVE scale and EARLY onset seizure	Paired Differences				95% Confidence Interval of the Difference	T test	P value
	Mean	Std. Deviation	Std. Error Mean				
				Lower	Upper		
	1.08000	1.09692	.09811	.88581	1.27419	11.008	.000

t ; paired t test, $p < 0.05$ is significant.

Table (5) Relationship between CAVE score and late onset seizure.

CAVE scale and late onset seizure	Paired Differences				95% Confidence Interval of the Difference	T test	P value
	Mean	Std. Deviation	Std. Error Mean				
				Lower	Upper		
	1.14400	1.17572	.10516	.93586	1.35214	10.879	.000

t ; paired t test, $p < 0.05$ is significant

DISCUSSION

Spontaneous non-traumatic intracerebral hemorrhage (ICH) is the second mainly common

subtype of stroke and is associated with high mortality and morbidity throughout the world (3) CAVA scale was developed by Department of Neurology, Helsinki ,University Central Hospital,

neurology emergency team through retrospective analysis to all successive primary ICH patients treated from January 2005 to March 2010.(9)

Early seizures was found to be more in higher CAVA scale ,cortical hematoma or large sized hemorrhage ,this was also proved by Bianca ,and his team (11) , The pathogenesis of early seizures post intracerebral hemorrhage is attributed to cellular biochemical dysfunction, e.g., due to increased extracellular glutamate after hypoxia and the direct toxic effect of blood degradation products (12 &13), Data from another study suggested, that disruption blood–brain barrier , or dysfunction and accumulation of albumin within astrocytes as a pathological mechanism , potentially connected with, the epileptogenic mechanism of vascular lesions.(14).

The incidence of ES in our study was 14.4%, which is relatively higher than the incidence determined by Jerzy,(15), in his publication he found the incidence is 8.1% but he studied 714 patients, which may explain this difference.

In another study done by De Herdt, he had incidence of ES 14%, which was at the same range of our results, and his patient number was 522 patients(16).

The possibility of late seizure LS ranged from 7.1% at 1 year after ICH to 11.8% at 5 years. This is was reported in (16,17,18,19) .

Previous studies have showed the relationship between younger age and seizures.(20,21) ,Despite of different design of these studies(mixed population of hemorrhagic and ischemic stroke), age below 65 years was revealed as a factor associated with seizures after ICH. Several previous studies(16,22,23,24,25), stated that cortical and lobar ICH are highly epileptogenic lesions, due to

Hemosiderin deposits and its potential epileptogenic triggering effect.

CAVE score is simple to be remembered and calculated, and constructed on 4 variables freely available soon after the ICH, and has been validated in an independent prospective ICH cohort.(9)

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