

Postoperative seizures after treatment of spontaneous supratentorial intracerebral hematoma at Sawanpracharak Hospital

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- Objective** : *To study the relationship of factors associated with seizures in surgical groups of supratentorial intracerebral hematoma patients.*
- Design** : *Retrospective analysis*
- Setting** : *Department of Surgery, Sawanpracharak Hospital.*
- Materials and Methods** : *Retrospective study of registration records of patients with supratentorial intracerebral hematoma were reviewed regarding their age, sex, history of hypertension, diabetes mellitus, smoking, alcoholism, Glasgow Coma Scale, midline shift, size of hematoma, early hydrocephalus and prophylactic antiepileptic drug. Analysis of the relationship of each factor in seizure and non-seizure groups were done by Chi-Square test, Fisher's exact test and Odd ratio at 95 % confidence level.*

- Result** : *Throughout the study period at the hospital, 214 patients with supratentorial intracerebral hematoma underwent surgical evacuation. Factors that were statistically significantly related to seizure and non-seizure were: age ($P=0.004$), sex [OR 3.62 (1.01-12.98); $P=0.037$], smoking habit [OR 3.44(1.17-10.13); $P=0.02$] and early hydrocephalus [5.45 (1.68 -17.66); $P=0.01$]; and, the factors that were unrelated to seizure and non-seizure included hypertension, diabetes mellitus, alcoholism and use of prophylactic antiepileptic drug.*
- Conclusion** : *Seizures that follow surgical treatments of spontaneous supratentorial intracerebral hematoma in this study were related to age, sex, smoking, and early post operative hydrocephalus.*
- Keywords** : *Seizure, Supratentorial intracerebral hematoma.*

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ฐิตพล โล้วพฤษภมณี. อาการชักหลังการรักษาด้วยวิธีผ่าตัดผู้ป่วยเลือดคั่งในสมองส่วนบนของ
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วัตถุประสงค์ : เพื่อศึกษาความสัมพันธ์ของปัจจัยที่มีผลต่อการเกิดอาการชักในผู้ป่วย
เลือดในคั่งสมองส่วนบนที่ได้รับการผ่าตัดรักษา

รูปแบบการวิจัย : Retrospective analysis

สถานที่ทำการศึกษา : หอผู้ป่วยศัลยกรรม โรงพยาบาลสวรรค์ประชารักษ์

ตัวอย่างและวิธีการศึกษา : รวบรวมข้อมูลจากเวชระเบียนผู้ป่วยในของผู้ป่วยเลือดคั่งในสมอง
ส่วนบน ข้อมูลประกอบด้วย อายุ เพศ ประวัติความดันโลหิตสูง
เบาหวาน สูบบุหรี่ ดื่มสุรา ระดับความรู้สึกตัว [Glasgow Coma
Scale (GCS)] ระยะการเคลื่อนที่ของสมองผ่านแนวกลาง (midline shift)
ขนาดของก้อนเลือด (size of hematoma) การเกิดภาวะช่องน้ำใน
โพรงสมองโต (early hydrocephalus) และการใช้ยากันชักใน
การป้องกันโรคลมชัก ศึกษาและวิเคราะห์ความสัมพันธ์แต่ละปัจจัย
เบื้องต้นกับการเกิดภาวะชักและไม่ชักในกลุ่มผู้ป่วยโดยใช้สถิติ
Chi-Square test, Fisher's exact test และ Odd ratio ที่ระดับความ
เชื่อมั่นไม่น้อยกว่าร้อยละ 95.

ผลการศึกษา : ผู้ป่วยจำนวน 214 รายที่มีเลือดคั่งในสมองส่วนบน และได้รับการ
ผ่าตัดรักษา จากการศึกษาพบว่าปัจจัยที่มีความสัมพันธ์กับการเกิด
โรคลมชักประกอบด้วยอายุ ($P = 0.004$) เพศ [OR 3.62 (1.01-12.98;
 $P = 0.037$)] การสูบบุหรี่ [OR 3.44 (1.17 - 10.13); $P = 0.02$] และการเกิด
ภาวะช่องน้ำในโพรงสมองโต [5.45 (1.68-17.66); $P = 0.01$], ส่วนปัจจัย
ที่ไม่มีความสัมพันธ์กับการเกิดอาการชัก ประกอบด้วย ภาวะความดัน
โลหิตสูง เบาหวาน การดื่มสุรา และการใช้ยากันชัก ในการป้องกัน
โรคลมชัก

สรุป : โรคลมชักหลังการรักษาด้วยวิธีการผ่าตัดผู้ป่วยเลือดคั่งในสมอง
ส่วนบน จากการศึกษาพบว่ามีความสัมพันธ์กับอายุ เพศ ประวัติ
การสูบบุหรี่ และภาวะช่องน้ำในโพรงสมองโตหลังผ่าตัดของผู้ป่วย.

คำสำคัญ : โรคลมชัก, เลือดคั่งในสมองส่วนบน

Seizure is phage the first manifestation of an intracerebral hemorrhage (ICH). There is insufficient information that relates seizures to clinical presentation, the course and outcome of ICH. Previous studies on patients with ICH indicated that seizures occurred in only a small percentage of patients. However, there is increasing number of case reports of the phenomenon from recent papers.⁽¹⁾ Cerebrovascular disease is a common and well-known etiology of seizures in the elderly.⁽²⁻⁴⁾ Seizures are common during the early phase after a stroke and has been recorded with a frequency of 2.5 % to 5.7 % within the first 14 days after a stroke.^(5,6) According to the criteria adapted for the post-traumatic seizure, an early seizure is defined when it occurs within two weeks after ICH and late seizure when it occurs after two weeks.⁽⁴⁾ Seizures regularly occur at the onset of ICH and serve as a clinical marker.^(2,7,8)

Previous studies found factors that were associated with seizure following post operative supratentorial ICH which were only the patients age, but no others associated factors were identified.

In clinical practices, however we found that there were small groups of patients who had seizure following a surgical operation on supratentorial ICH, but seizures were a major cause of morbidity and mortality of patients. This study was aimed to identify factors that are associated with seizure following a supratentorial ICH operation.

Materials and Methods

The study design was a retrospective analysis with the samples consisting of 214 consecutively patients who were admitted to the

Department of Surgery of Sawanpracharak Hospital, Nakornsawan province, from 2002 to 2005. They were diagnosed with supratentorial ICH. These ICH cases were identified mainly on the diagnosis on their admission. All patients who were suspected of stroke and underwent neurologic evaluation by computerized tomography (CT) scan of the brain were done on arrival at the hospital. All CT-scan findings were evaluated by a neurosurgeon and a radiologist.

In this study revealed that only deep seated ICH (putamen, caudate nucleus, internal capsule and thalamus). Patients who had seizures that were associated with the following conditions: primary intraventricular hemorrhage, infratentorial ICH, ICH due to brain tumor, vascular malformations, aneurysm, infection, bleeding diathesis (thrombocytopenia, anticoagulation therapy) and hemorrhagic infarction (non-homogeneous high-density areas confined to a vascular territory) were excluded from the study. Every recruited subject had a single large hematoma. According to the criteria adapted for the post-traumatic seizure, an early seizure is defined when it occurs within two weeks after ICH and late seizure when it occurs after two weeks.⁽⁴⁾ However, due to limitations of long-term follow up, only cases of early onset of seizure in surgical groups of supratentorial ICH were studied.

All patients who had seizures postoperative were generalize tonic-clonic convulsion. Diagnosis of seizure was based on direct observation of seizures either by medical staff at the time of hospitalization, history taking by a clinician in charge of the patients, or determined by a reliable description such as that given by the patient himself/herself, their family members, or even eye witness when seizure occurred.

However, transient amnesia and isolated changes in the level of consciousness were not classified as seizures.

Personal data including sex, age, underlying diseases (e.g., diabetes mellitus (previous diagnosis of diabetes and / or past or present use of antidiabetic agents), history of hypertension), personal history (e.g., alcoholism, smoking), Glasgow Coma Scale (GCS) on admission, volume of ICH, midline shift (MS), prophylactic AED therapy and early episode of hydrocephalus were collected.

Severity of neurological status was classified by Glasgow Coma Scale (GCS) into 3 groups (mild $GCS \leq 8$, moderate 9 – 12, and severe $GCS 13 - 15$). The volume of ICH was classified into 3 groups ($< 30 \text{ cm}^3$, 31 to 60 cm^3 and $> 60 \text{ cm}^3$) by Kothari calculation and Broderick classification^(9, 10) and MS was also classified into 3 groups (MS 1 - 5 mm, MS 6 – 10 mm. and MS > 10 mm).

Early onset of seizure that occurred soon after clinical events were classified as associated with this events. Administration of antiepileptic drug (AED) for prophylaxis of seizure was based on the judgment of the responsible clinician. All patients used Phenytoin for prophylaxis of seizure in both intravenous and oral form. Some cases of post operative ICH had early hydrocephalus that needed a ventriculostomy or ventriculo-peritoneal shunt (VP shunt).

Statistical Analyses

Statistical analyses were performed using the SPSS software package for Windows (SPSS 11). The characteristics of the subjects were described in terms of frequency and percentage. Student's t - test was used for continuous data, and Chi-Square test and

Fisher's exact test were used for discreet data. The level of statistical significance was set at $P < 0.05$. Odd ratio (OR) and 95 % confidence interval (95%CI) were also considered.

Results

There were 214 consecutive patients admitted to the Department of Surgery of Sawanpracharak Hospital from 2002 to 2005 with the diagnosis of supratentorial ICH. Seventeen patients (7.9 %) had episode of post-operative seizure. The age of the patients ranged from 33 to 90 years old (male 40 to 68 and female 33 to 90). One hundred and twenty-five patients were male (58.41 %). One hundred and seventy patients had history of hypertension 170 (79.44 %); 36 (16.82 %) of the the patients had history of diabetes mellitus (DM); 93 (43.46 %) who were smokers; 68 (31.78 %) had alcohol consumption. CT characteristics of the patients, hemorrhagic size < 30 ml were 13 (6.08 %), 31 - 60 ml were 135 (63.08 %) and > 60 ml were 66 (30.84 %). MS of 0 - 5 mm were 91 (42.52 %), MS 6 - 10 mm were 102 (47.67 %) and MS > 10 mm were 21 (9.81 %). Regarding the GCS of the patients, GCS 3 - 8 were 51 (23.83 %), GCS 9 - 12 were 91 (42.52 %) and GCS 13 -15 were 72 (33.65 %). Patients who had early hydrocephalus were 19 (8.88 %). Those who had prophylactic AED therapy were 116 (54.21 %).

Comparing the factors between seizure group and non seizure, we found that the mean age was (SD) 51.2 ± 8.5 years in the seizure group, and 59.7 ± 11.9 years in the non-seizure group. There was statistical significant association between seizures and age groups ($P = 0.004$). 14 males (11.2 %) and 3 females (3.4 %) were seizure with

statistic significance (OR, 3.62; 95% CI, 1.01 - 12.98; P = 0.037) (Table 1). The underlying risk factors hypertension and diabetes mellitus had no association with seizure. 12.9 % of smokers and 4.1% of non-smokers had seizure with statistic significance (OR, 3.44; 95%CI, 1.17-10.13; P = 0.02) (Table 2). 13.2 % of alcoholism and 5.5 % of non-alcoholism had seizure but with no statistical significance (OR, 2.63; 95 % CI, 0.97 – 7.15; P = 0.51)(Table 2).

Based on the analyses of CT characteristics,

hemorrhagic size and midline shift were not associated with seizure, and GCS had no association with seizure (Table 3).

Prophylactic AED therapy had no association with seizure but in the cases of early post-operative hydrocephalus, there was statistical significance of 26.3 % of early post operative hydrocephalus and 6.2 % of them who had no early post operative hydrocephalus were seizure with statistical significance (OR,5.45; 95%CI, 1.68-17.66; P = 0.01) (Table 4).

Table 1. Demographic features of the patients with and without seizures in relation to an intracerebral hematoma.

Data	Seizure (n = 17)	Non-seizure (n=197)	OR (95% CI)	P value
Age (years)				
Mean (S.D.)	51.2 (8.5)	59.7(11.9)	-	0.004
Range	40 - 68	33 - 90	-	
Sex No (%)				
Male	14 (11.2)	111 (88.8)	3.62 (1.01 – 12.98)	0.037
Female	3 (3.4)	86 (96.6)		

Table 2. Risk factors of the patients with and without seizures in relation to an intracerebral hematoma.

Data	Seizure No (%)	Non-seizure No (%)	OR (95% CI)	P value
Hypertension - Yes	13 (7.6)	157 (92.4)	0.83 (0.26 – 2.68)	0.76
- No	4 (9.1)	40 (90.9)		
Diabetes - Yes	1 (2.8)	35 (97.2)	0.29 (0.04 – 2.25)	0.32
- No	16 (9.0)	162 (91.0)		
Smoking - Yes	12 (12.9)	81 (87.1)	3.44 (1.17 – 10.13)	0.02
- No	5 (4.1)	116 (95.9)		
Alcoholism - Yes	9 (13.2)	59 (86.8)	2.63 (0.97 – 7.15)	0.51
- No	8 (5.5)	138 (94.5)		

Table 3. CT characteristics and Glasgow Coma Scale (GCS) of the patients with and without seizures in relation to an intracerebral hematoma.

Data	Seizure	Non-seizure	P value
	No (%)	No (%)	
Hemorrhagic size (CC)			
< 30	0 (0)	13 (100)	0.54
31 – 60	11 (8.1)	124 (91.9)	
> 60	6 (9.1)	60 (90.9)	
Midline shift (mm)			
0 -5	7 (7.7)	84 (92.3)	0.52
6 -10	7 (6.9)	95 (93.1)	
> 10	3 (14.3)	18 (85.7)	
Glasgow Coma Scale (GCS)			
3 – 8	3 (5.9)	48 (94.1)	0.82
9 – 12	8 (8.8)	83 (91.2)	
13 – 15	6 (8.3)	66 (91.7)	

Table 4. Characteristics of the patients with and without seizures in relation to an intracerebral hematoma.

Data	Seizure	Non-seizure	OR (95%CI)	P value
	No (%)	No (%)		
Early hydrocephalus	- Yes	5 (26.3)	5.45 (1.68 -17.66)	0.01
	- No	12 (6.2)		
Prophylactic	- Yes	8 (6.9)	0.73 (0.27 – 1.98)	0.54
	- No	9 (9.2)		

Discussion

The incidence of seizures that followed ICH was low in the pre-CT era. Small ICH was now readily seen on CT scan, and the diagnosis incidence of ICH has actually arisen since 1975. The occurrence of seizures following ICH varies considerably from series to series ranging 0 % to 23 %.^(1-4, 6, 7, 11) In this study the incidence of seizures is 7.94 %.

The incidence of seizures is more common in lobar ICH than deep-seated ICH (lobar ICH incidence 32 % to 54 %.^(1, 4, 12, 13) and deep-seated ICH incidence 0 % - 19 %).^(1, 2, 4)

There was statistical significant association between seizures and sex (OR, 3.62; 95%CI, 1.01-12.98; P = 0.037), the incidence of seizure in males was high than females. However, this is different from

the studies of Passero S, et al⁽⁵⁾, Labovitz DL, et al⁽²⁾ and Berger AR, et al⁽⁷⁾ who found that sex was not a predictor of seizure.

There was statistical significant association between seizures and age ($p = 0.004$). The present study shows seizure that followed ICH had a potentiality to occur in younger patients, which was the same as in the study of Arboix A, et al⁽¹⁴⁾ but it is different from that of De Reuck J, et al⁽¹⁵⁾ and Passero S, et al⁽⁵⁾ who found that age was not a predictor of seizure.

Furthermore, from our study, personal and underlying risk factors including history of hypertension, diabetes mellitus were not predictors of seizure as the other studies described.^(2, 15) The findings from CT characteristics and Glasgow Come Scale (GCS) showed that they were not predictors of seizure as reported by other studies.^(5, 7)

This study found that alcoholism was not a predicting factor of seizure, but the study of Marchal C⁽¹⁶⁾ found that seizures occurred in 5 – 15 % of individuals with alcohol drinking; they were more than 20 % of newly diagnosed epilepsies in adults who were alcoholic seizure. Chan AW,⁽¹⁷⁾ Hillbom M, et al⁽¹⁸⁾ and Gordon E, et al⁽¹⁹⁾ studies found that prevalence of epilepsy in alcohol-dependent patients might be at least triple that of the general population, whereas the prevalence of alcoholism was only slightly higher than in the general population. Alcohol affects the brain through several mechanisms that influence seizure threshold; these include the effects on calcium and chloride flux through the ion-gated glutamate NMDA and GABA receptors.

There was statistical significant association between seizures and smoking (OR, 3.44; 95%CI, 1.17-10.13; $P = 0.02$). The coincidence of seizure

patients with smoking behavior groups was much higher than those in the non-smoking groups, which was the same as the studies of Kobau R, et al⁽²⁰⁾ Elliott JO, et al,⁽²¹⁾ and Ferguson PL, et al⁽²²⁾ who found that patients who were smokers had higher incidence of epilepsy than non-smoking groups. This finding is, however, different from the studies of De Reuck J, et al⁽¹⁵⁾ and Labovitz DL, et al⁽²⁾ who found that smoking was not a predictor of seizure.

The findings from CT characteristic and Glasgow Come Scale (GCS) are not predictors of seizure as reported in other studies.^(5, 7)

Most neurosurgeons who practiced in each group of the patients still have their own ideas regarding the treatment and use prophylactic antiepileptic drug (AED). Currently, we learn that use of prophylactic AED therapy in the prevention seizures for patients with ICH who have not had seizure from study of Berger AR⁽⁷⁾ remains controversial and the study of Passero S, et al⁽⁵⁾ was non-statistical significant.

There was a statistical significant association between seizures and early hydrocephalus (OR, 5.45; 95%CI, 1.68 - 17.66; $P=0.01$), the incidence of seizure in patients who had early post operative hydrocephalus developed more seizure than those who did not have hydrocephalus. However, this is different from the study of Passero S, et al⁽⁵⁾ and Berger AR, et al⁽⁷⁾ who found that hydrocephalus was not a predictor of seizure.

This study revealed that only deep seated ICH (putamen, caudate nucleus, internal capsule and thalamus). However, due to limitations of long-term follow up, only cases of early onset of seizure in surgical groups of supratentorial ICH were studied.

Conclusion

The incidence of seizures following surgical treatment of spontaneous supratentorial ICH patients was high in younger patients, male gender, people with smoking behavior and those who had early post operative hydrocephalous.

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