Original Research

The impact of oral anticoagulants on the characteristics of subdural hematomas and other brain lesions in patients with traumatic brain injury

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Abstract

Background and aim. The aim of the study was to determine the impact of prior anticoagulant treatment on the characteristics of intracranial hematomas.

Methods. We included in this retrospective study 135 patients who were diagnosed with subdural hematoma in the context of traumatic brain injury. We recorded the demographic and clinical data, the paraclinical examinations and the characteristics of subdural hematoma evidenced by preoperative computed tomography (CT). We also reported the other brain injuries, entailed by primary and secondary lesions, as described by CT.

Results. The anticoagulation therapy was recorded in 35 patients, at the moment of diagnosis. Acute subdural hematoma was recorded in 89 (65.9%) patients, 21 (60%) of these had anticoagulation therapy on admission. There were 46 (34.1%) patients with chronic subdural hematoma, 14 (40%) of these were on anticoagulant therapy. The midline shift was significantly moved in patients with anticoagulation therapy. The thickness of the subdural hematoma was significantly higher in patients with anticoagulation. We did not find any significant association of the other brain lesions (cranial fracture, extradural hematoma, intraparenchymal hematoma, nor intracranial hypertension, brain herniation, brain swelling), and the presence of anticoagulation therapy.

Conclusion. The study showed that anticoagulants significantly influence some neuroimaging aspects of the SDH in head trauma.

Keywords: anticoagulants, coagulation status, subdural hematoma, brain trauma, preoperative computed tomography.

Background and aims

Traumatic brain injury (TBI) is an important medical, economic and social problem, which has a high rate of mortality and morbidity. Considering the public health policy, the implementation of prevention, education and rehabilitation strategies in TBI, the international incidence of TBI varies between countries [1-3].

The anticoagulant drugs are an indispensable therapy in the prevention and treatment of thromboembolic venous disease or prevention of ischemic stroke in patients with atrial fibrillation. The success of the therapy is associated with the risk of bleeding in some particular cases, such as in minor head trauma, emergency surgery and also, spontaneous hemorrhage cannot be excluded [4]. Currently there are two types of oral anticoagulants used for long term primary or secondary prevention: vitamin K antagonists and direct oral anticoagulants. In low-income countries, vitamin K antagonist are mostly used in patients with atrial fibrillation and only used in patients with mechanical heart valves [5]. The large majority are elderly patients with a high risk of TBI, due to a higher rate of falling. Thus, they are at risk

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of brain hemorrhage, which can be life-threatening.

Subdural hematoma (SDH) is a frequent neurosurgical pathology, with a good presumed prognosis for the operated patients. In addition, a high recurrence of SDH is an important factor against the long-term outcome of surgery for these patients. SDH is the most frequent brain injury after TBI [6]. Some researchers theorized that an acute SDH after minor head trauma, especially in elderly patients, could be related to the antithrombotic drugs [7,8]. Also, the most likely mechanism of TBI in these patients is falling on the same level [8].

The imaging data showed an important impact of these drugs on the growth and progression of SDH [9]. Several studies examine the influence of prior oral anticoagulation on the characteristics of SDH after TBI, but their results are contradictory. Some found that patients under anticoagulation treatment had a statistically significant thicker SDH or larger midline shift, while others did not [10-12]. The size of the SDH and midline shift are important factors that determine if a surgical evacuation is needed and they are also predictors of the patient's outcome [13,14].

The aim of this study was to determine the impact of prior anticoagulant treatment on the characteristics of SDH.

Methods

The study was retrospective, transversal, analytical, and observational. It included 137 consecutive patients admitted to the Department of Neurosurgery of the Emergency County Hospital of Cluj-Napoca, between January 2012 and December 2019. This study was approved by the Clinical Ethics Committee of the Iuliu Haţieganu University of Medicine and Pharmacy in Cluj-Napoca.

The inclusion criteria in the study were: patients that suffered a TBI and were diagnosed with an acute SDH described on the computed tomography (CT) scan on admission. Also, patients with a history of a SDH from a TBI, who presented with a rebleed, were included.

The exclusion criteria were: patients with traumatic brain injury without hematoma on the CT scan, patients with cancers, epilepsy, liver failure, chronic alcoholism, blood disorders (hereditary, autoimmune) associated with a bleeding risk or antiplatelet/systemic non-steroidal anti-inflammatory treatment. Patients that followed treatment with drugs that could increase the therapeutic effect of oral anticoagulants (antibiotics, antifungals, amiodarone), were not included.

The following parameters were noted: demographical characteristics, the mechanism of the head injury (collapse, fall from a high level, traffic accidents, hitting, spontaneous condition), the clinical status on admission evaluated by Glasgow Coma Scale (GCS), the presence of anticoagulation therapy and the anticoagulation status evaluated by activated partial thromboplastin time (APTT and INR).

The following imaging features of the hematoma from the CT scan of the head were recorded: acute or rebleed of a chronic hematoma, localization, the maximal thickness of hematoma (measured in mm) and the midline shift (measured in mm). Other imaging data included: presence of secondary brain lesions (intracranial hypertension, brain swelling, brain herniation) and the other traumatic brain lesions (cranial fracture, extradural hematoma, intraparenchymal hematoma, contusion and laceration). The type of neurosurgical intervention was noted.

Statistical analysis was performed using the MedCalc® Statistical Software version 20.014 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021). Quantitative variables were analyzed for normality of distribution with Shapiro-Wilk test and expressed as median and 25-75 percentiles, or mean ± standard deviation. Qualitative variables were expressed as frequency and percent. Comparisons between groups were performed using the Man-Whitney test or chi-square test. A p value <0.05 was considered statistically significant.

Results

Demographic and clinical data are presented in table I. Anticoagulation therapy was taken by 37 patients (35 with acenocoumarol, 1 with dabigatran, 1 with rivaroxaban). The two patients treated with direct oral anticoagulants were not included, in order to achieve a more homogenous group. The patients who received anticoagulant drugs as chronic therapy were significantly older (76.7±8.3 years) than patients without therapy (65±15.1 years) (p<0.001). Considering the group of patients taking anticoagulation drugs, there was a more significant proportion of male subjects undergoing this therapy 19 (54.3%) (p=0.01). The clinical status on

Table I. Demographic, clinical and paraclinical data.

Variable		Without anticoagulation therapy (n=100)	Anticoagulation therapy (n=35)	p
Age (years)		65.02 (15.168)	76.71 (8.369)	<0.001
Sex, n (%)	F	22 (22%)	16 (45.7%)	0.01
	M	78 (78%)	19 (54.3%)	
GCS		10.5 (4 ; 15)	8 (3 ; 14)	0.3
APTT (seconds)		25.2 (23.5; 29.725)	32.5 (27.6; 38.1)	<0.001
INR		1.12 (0.98; 1.19)	1.7 (1.43; 2.86)	<0.001
Days of hospitalization		7(4; 10)	6 (4; 14)	0.6

Sex: F-female; M-male.

admission evaluated by GCS did not report any relation with the anticoagulation therapy in patients with acute or chronic SDH. Only 13 (37.1%) patients from the anticoagulation group had and INR>2, and, of those, only 6 (17.7%) had an INR>3.

Data related to the SDH can be found in table II. Acute SDH was recorded in 89 (65.9%) patients, 21 (60%) out of these were on anticoagulation therapy on admission. Fourteen (40%) patients with chronic SDH and rebleeding also had anticoagulation therapy on admission. The midline shift was significantly higher for patients with anticoagulation therapy (p=0.02). The thickness of SDH was significantly associated with the anticoagulant therapy (p=0.006).

In table III we present the primary lesions (cranial fracture, extradural hematoma, intraparenchymal hematoma) and the secondary lesions (intracranial hypertension, brain herniation, brain swelling) that were associated with SDH. Their imaging characteristics are also described. We did not find any important significance regarding their association with the anticoagulation therapy.

Table II. Characteristics of subdural hematoma.

Variable		Without anticoagulation therapy (n=100)	Anticoagulation therapy (n=35)	p
Midline shift, mm		4 (0 ; 7)	6 (2;11)	0.02
Thickness of hematoma, mm		18.5±8.5	23.2±8	0.006
SDH, n (%)	acute	68 (68%)	21 (60%)	0.5
	chronic (rebleed)	32 (32%)	14 (40%)	
Surgery, n (%)	conservative	8 (8%)	3 (8.6%)	0.09
	craniotomy	43 (43%)	8 (22.9%)	
	craniectomy	49 (49%)	24 (68.6%)	
Localization of hematoma, n (%)	right convexity	44 (44%)	16 (45.7%)	0.1
	left convexity	29 (29%)	15 (42.9%)	
	bilateral convexity	27 (27%)	4 (11.4%)	
Mechanism of injury, n (%)	fall on the same level	60 (60%)	24 (68.6%)	0.7
	fall from a high level	23 (23%)	2 (5.7%)	
	traffic accidents	6 (6%)	1 (2.9%)	
	hitting	5 (5%)	2 (5.7%)	
	spontaneous condition	6 (6%)	6 (17.1%)	

Table III. Primary and secondary brain lesions.

Variable		Without anticoagulation therapy (n=100)	Anticoagulation therapy (n=35)	p
Cranial fracture, n (%)	skull dome	67 (67%)	30 (85.7%)	0.2
	skull base	17 (17%)	3 (8.6%)	
	skull dome and base	9 (9%)	1 (2.9%)	
Extradural hematoma, n (%)	absent	84 (84%)	34 (97.1%)	0.07
	present	16 (16%)	1 (2.9%)	
Intraparenchymal hematoma, n (%)	absent	74 (74%)	32 (91.4%)	0.06
	present	26 (26%)	3 (8.6%)	
Localization of Intraparenchymal hematoma, n (%)	right convexity	(11 39.3%)	3 (75 %)	0.3
	left convexity	12 (42.9%)	1 (25%0	
	bilateral convexity	5 (17.9 %)	0 (0%)	
Contusion and laceration, n (%)	absent	68 (68%)	29 (82.9%)	0.2
	contusion	8 (8%)	1 (2.9%)	
	contusion and laceration	24 (24%)	5 (14.3%)	
Localization of contusion and laceration, n (%)	right convexity	12 (37.5%)	2 (33.3%)	0.5
	left convexity	9 (28.1%)	2 (33.3%)	
	bilateral convexity	10 (31.3%)	1 (16.7%)	
	in the brainstem	1 (3.1%)	1 (16.7%)	
Intracranial hypertension, n (%)	absent	40 (40%)	10 (28.6%)	0.3
	present	60 (60%)	25 (71.4%)	
Brain herniation, n (%)	absent	84 (84%)	24 (68.6%)	0.08
	present	16 (16%)	11 (31.4%)	
Signs of meningitis, n (%)	absent	88 (88%)	31 (88.6%)	1
	present	12 (12%)	4 (11.4%)	
Brain swelling, n (%)	absent	39 (39%)	10 (28.6%)	0.3
	brain swelling	55 (55%)	21 (60%)	
	malignant cerebral edema	6 (6%)	4 (11.4%)	

Discussion

The present study investigated the effects of anticoagulation therapy on the characteristics of SDH in patients that suffered a TBI. Our results showed that patients that were on anticoagulant treatment were older, females, their SDH was thicker and had a bigger midline shift. These patients tended to undergo a craniectomy. They also were less likely to display an extradural or intraparenchymal hematoma.

There are 1.7 million people estimated in United States who suffer a TBI every year and in the European Union the annual incidence rate of TBI is 262:100,000. The proportion of the patients with TBI that are on anticoagulants is constantly increasing (up to 38% in 2014) [15]. In our study the incidence of anticoagulant use in patients with TBI was 25.9%. Taken into consideration the exclusion criteria the results are in accordance with the literature.

Patients with TBI in our study tended to be elderly, especially taking into consideration that the most frequent mechanism of action was collapsing/ falling to the ground. Peck et al. reported a retrospective review of patients aged 55 years and older, admitted to a Level I trauma center with blunt force TBI. The hypothesis of their study was to find out if patients treated with anticoagulants or antiplatelet medication, before the injury, would have a worse outcome compared with patients not using these drugs. The results showed that older TBI patients had a higher rate of mortality and other adverse results caused by therapy. They also had a higher risk of developing a new intracranial hemorrhage [16]. Dziedzic et al. mentioned that patients on drugs affecting hemostasis were older [12]. The results of our study were in accordance with literature data. Patients who received anticoagulation therapy were significantly older than patients without therapy, as it is prescribed for long term in the elderly with cardiovascular diseases [5].

The highest rates of falling on the same level are recorded in children and also for adults aged 75 years and older. One in four adults over 65 and older report at least one falling incident each year [17]. Looking at the causes of TBI, in our study the fallings were the most frequent ones, especially in the anticoagulants group, as they were older with a higher tendency of tripping and falling. Even if the significance threshold was slightly exceeded, the trend is obvious. Oral anticoagulants constitute an independent and well-known risk factor for immediate and delayed brain hemorrhage in patients with TBI after falling [18].

The neurological assessment was related to a large range of GCS scores, from GCS 15 up to comatose status. In this study the GSC score had not a significant correlation with the anticoagulation therapy, even though patients with anticoagulant had lower GSC score, probably due to the larger size of the hematoma and advanced age. This large distribution of GCS score was also reported in a previous study published by Gonugunta [19]. Moreover, the initial GCS score seems to be an important predictive factor of the outcome [11,20,21].

The hematoma thickness is a discussed parameter in terms of anticoagulation disorders, neurological status and prognosis. In the study by Dziedzic et al. there was a statistically significant difference of the mean hematoma thickness, when comparing the oral anticoagulants subgroup with the control group. Their results showed a 19.8±6.8 mm mean thickness of the SDH in the oral anticoagulation drugs subgroup and the heparin subgroup respectively [12]. Analyzing the effect of warfarin, Pieracci et al. observed an increased probability of intracranial hemorrhage in patients who took warfarin, with an admission INR >2. Besides, they reported the increased severity of the traumatic brain injury and the increased overall mortality after intracranial hemorrhage for these patients [18]. On the other hand, other studies reported no correlation between the anticoagulation therapy and the size of hematoma. Following the recurrence of chronic SDH, Torihashi et al. concluded that antiplatelet or anticoagulant drugs might facilitate the growth of chronic SDH, but they did not report a significant effect of antiplatelet and anticoagulant therapy on the hematoma recurrence [22]. Our results showed a significant statistical difference between patients with anticoagulants and those without regarding the hematoma thickness and the midline shift. Even though the difference is statistically significant, it could have been clinically more relevant, if more patients would have had the INR in the therapeutic range (only 37.1% with an INR>2].

Conclusion

The study showed that anticoagulants significantly influence neuroimaging aspects of the SDH in head trauma. The thickness of the SDH and the midline shift were correlated with the presence of anticoagulation therapy. The neurological status was not affected by anticoagulants. Neither secondary brain effects, nor traumatic lesions were in a correlation with anticoagulation therapy.

Limits of the study

The number of patients with anticoagulant therapy and head trauma was small due to the exclusion criteria. Most likely a higher number would give us important information regarding the influence of anticoagulants on the characteristics of SDH.

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