

Influence of Anticoagulant Drugs on the Occurrence of Chronic Subdural Hematoma

Vesna Nikolov^{1,2*}, Aleksandar Kostic^{1,2}, Misa Radisavljevic¹, Boban Jelenkovic¹ and Predrag Milosevic¹

¹Clinics of Neurosurgery, CC Nis, Serbia

²Faculty of Medicine, University of Nis, Serbia

*Corresponding author: Vesna Nikolov, Clinics of Neurosurgery, CC Nis, Serbia, Tel: +381653094135; E-mail: v.novak@yahoo.com

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Abstract

Introduction: The chronic subdural hematomas (HSCH) usually occur as a result of minor trauma with older people. However, it has been noted that there is an increase in the number of patients with chronic subdural hematoma who were on a regular anticoagulant therapy. To show that a use of anticoagulant drugs of the older generation in a much higher percentage leads to the appearance of HSCH due to the difficulty of controlling the INR and drug overdose.

Methods: The research has been conducted on the Department of Neurosurgery, in Clinical Center Nis in the period from January 2010 until December 2015.

Results: The largest number of these patients was 24.71% at anticoagulant therapy and belonged to the age group of 51 to 60 years. In 37.07% of cases, patients who were treated with anticoagulant therapy had INR values in the normal range, while 35.95% of them had INR over third. In 19 patients we have the fatalities occurred and all of them were on anticoagulant therapy for older generation.

Conclusion: Wide application anticoagulant therapy, as in protective and therapeutic purposes tip to the frequent occurrence of HSCH. Irregular appropriate use of anticoagulant therapy, overuse of long words, anticoagulant iholder generation of drugs leads to an increased incidence of HSCH. The use of anticoagulant therapy of new generation is preferred because it does not require frequent laboratory analyses. Monitoring INR- a.

Keywords: Chronic subdural hematoma; Anticoagulants; Prothrombin time; INR

Introduction

Treatment of patients with a chronic subdural hematoma (HSCH) has lately been increasingly common. Due to the mechanism of formation, it is usually found in the elderly population. Patients aged over 70 years are usually subjected to the treatment. HSCH is usually caused by mild or repeated head injuries. They are more common among elderly people who constantly fall and hit their head. According to their morphological characteristics, HSCH falls into secondary incurred injuries of focal character, and with other intracranial hematoma belong to injuries that generally require surgery treatment [1]. The higher rate of occurrence of this condition in the elderly may be because the brain becomes smaller as people age. This causes an extra space in the skull, allowing the veins to be more easily damaged during head injury [2].

HSCH belongs to the group of extra-axial craniocerebral injuries that represents an organized collection between the dura and arachnoidea and is a result of breaking the bridge veins under the effect of the force on the skull, which is over time subject to liquefaction and increases its volume [3]. It encapsulates and grows further due to the transfer of cerebrospinal fluid through the capsule into the hematoma. It grows for weeks and months acting as a tumor. It puts pressure on the brain tissue and gives corresponding symptoms and signs. In the clinical picture, a patient faces a headache, somnolence, confusion, incoherent thinking, bradypsychia, apathy, epileptic seizures, hemiparesis on the opposite side of the formation of the hematoma, or in the later stage deep consciousness disturbance and the occurrence of Hutchinson's papillary on the side of the hematoma.

The highest frequency of the appearance of the hematoma by Sambasivan [4] is between V and VII decade of life, while Joao Louis claims that these are persons aged 70 to 79 [5]. However, in recent years, an increase in the number of people with HSCH of younger age group has been recorded [6]. By the analysis of patients treated at the NHK in Nis in the period from January 2010 to December 2015, we have found that a

good number of patients, of both younger and older age, was on the anticoagulant therapy applied either for prophylactic or therapeutic purposes.

Increased unwanted blood clotting is a characteristic of thromboses and embolism [7]. In a word, such conditions are called thromboembolic conditions. Emboli are in 80-90% of cardiac origin. Most often these are heart failures, myocardial infarction, primary cardiomyopathy, built-in artificial valve replacement, heart and arterial aneurysm. Embolisms are common in heart arrhythm disorders, especially in atrial fibrillation. Thromboses occur due to the increase of the atheromatous plaque and related thrombus and are more common in dehydration, hypotension, infectious diseases, cancer, dysproteinemia, disseminated intravascular coagulation and other pathological conditions. As we ourselves are witnesses that lately the rate of cardiovascular diseases has increased, it is also the cause of a more frequent application of anticoagulants, both for prevention and therapy.

Materials and Methods

The test was performed at the Department of Neurosurgery in Nis in the period from January 2010 to December 2015, where 349 HSCH patients were operated on. During the tests, the focus was on searching the causes of the increasing number of HSCH patients in both elderly and much more significantly in the younger population.

Depending on the applied anticoagulation therapy, the patients were classified into three groups:

1. The application of anticoagulants as protectors (Aspirin, Cardipirin, Plavix), preferred sporadic laboratory control.
2. The application of old anticoagulants (Farin, vitamin K, Sintrom), mandatory laboratory control.
3. New anticoagulants (act selectively either on thrombin or coagulation factor Xa), do not require laboratory control.

Test Results

From a total of 349 operated patients, 89 of them (25.50%) were the on anticoagulant therapy, applied both for therapeutic and preventive purposes (Table 1).

Table 1: Total number of operated patients from HSCH.

Years	Number operations	of	Without AkTh	With AkTh
2010	34		28	6
2011	47		33	14
2012	62		45	17
2013	68		50	18
2014	72		53	19
2015	66		51	15
All	349		260	89

	100%	74.49%	25.50%
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Patients aged 71-80 years were most often treated and accounted for 27.79% (Table 2).

Table 2: Age of patients operated on HSCH.

Age	Without AkTh	With AkTh
41-50	24	17
51-60	55	22
61-70	75	18
71-80	77	20
<80	29	12
All	260	89

The lowest percentage of patients, 2.24% of them, used anticoagulant medicines of the new generation, while as many as 76.40% of patients were on anticoagulants of the old generation 21.34% used anticoagulants as a prophylactic measure (Table 3).

Table 3: Type applied AkTh.

Age	Protective Th	Old AkTh	New AkTh
41-50	5	11	1
51-60	4	17	1
61-70	4	14	0
71-80	5	15	0
Over 80	1	11	0
All	19	68	2
	21.34%	76.40%	2.24%

In 64.04% of the cases, the patients who were on the anticoagulant therapy had INR values within normal limits, while 35.95% of them had the value of INR of over 3 (Table 4).

Table 4: Values of INR at the reception.

Value INR	of	Protective Th	Old Ak	New Ak	All
0.8-2.9		19	36	2	57
					64.04%
Over 3		0	32	0	32
					35.95%
All		19	68	2	89

In 43.82% of cases, surgery was performed within 24 hours. The same percentage of patients was treated with between 24 and 48 hours of the receipt, while 12.35% of the patients were delayed for even more than 48 h for receiving the correction

treatment, plasma and washed platelets, and the normalization of the INR values (**Table 5**).

Table 5: Possible surgery.

Time	Protective Ak	Old Ak	New Ak	All
Within 24 h	19	18	2	39
				43.82%
24-48 h	0	39	0	39
				43.82%
Over 48 h	0	11	0	11
				12.35%
All	19	68	2	89
				100%

Complete recovery occurred at 71.91% of the patients, while at 21.34% death occurred, in the patients who were on the older generation anticoagulant therapy (**Table 6**).

Table 6: The outcome of patients.

Thurnout	Protective Th	Old Ak	New Ak	All
Recovery	18	44	2	64
				71.91%
Neurological deficit	0	6	0	6
				6.74%
Death	0	19	0	19
				21.34%
All	18	69	2	89
				100%

In the group with the protecting therapy, all 18 patients (100%) had a complete recovery and the frequency of this outcome was in this group statistically significantly higher than in the group with the anticoagulant therapy of the old generation where at 44 (64%) of the patients full recovery was recorded (Fisher's exact test: $p=0.001$).

Death outcome in the group with the old generation anticoagulant therapy occurred at 19 (21.34%) patients, which is a statistically significantly higher incidence than in the group with the protective therapy, wherein death has not occurred in any of 18 cases (Fisher's exact test: $p=0.009$).

Table 7: Reoperations.

Reoperated	Protective Th	Old Ak	New Ak
Number of patients	0	19	0

In 21.34% we were forced to repeat the surgery (**Table 7**), and these were also patients who were treated with the old generation anticoagulants.

Discussion

An increase in the number patients with HSCH is observed both in our country and the world. The extension of life age is one of the factors for the increase of this disease, as well as the application and the possibility of the adequate diagnosis and treatment of people in urban areas, which also led to an increase in the number of these patients. The worrying fact is the increase in the number of HSCH patients of younger age, as well as the increasing number of HSCH patients who underwent surgery and who are on the anticoagulation therapy. Unfortunately, there is an increasing number of patients with cardiovascular diseases in which the application of the anticoagulant therapy is inevitable [8]. In our analysis of the HSCH-operated patients, we have found that 25.50% were on the anticoagulation therapy, whereby other studies have also shown a significant number of patients who are on the anticoagulation therapy [9,10]. It is observed that the application of the older generation anticoagulation therapy is much more frequent in our study whereby we concluded that as much as 76.40% of patients were treated with the old generation anticoagulants. These medicines require continuous laboratory monitoring (INR) and the adequate dosage [11]. Often due to negligence, but also because of the impossibility of control, patients overdose themselves with these medicines as shown in our research, whereby it was observed that in 35.95% of the patients treated with the old generation anticoagulants INR was over 3. This INR value prevents urgent surgical intervention which can be a problem if it is a hematoma that by its size greatly compresses the brain mass, leading to incarceration and death outcome.

In our study, the surgery was postponed with 56.17% of patients. With most of the patients operated on for HSCH, i.e. in 71.91% of the cases, there was complete recovery observed. Death outcome in the group with the older generation anticoagulant therapy occurred in 19 (21.34%) patients, which is a statistically significantly higher incidence than in the group with the protective therapy and the new generation anticoagulant therapy, where death outcome has not occurred in any of the 18 cases (Fisher's exact test: $p=0.009$). The new oral anticoagulants act selectively on thrombin (ximelagatran, dabigatraneteksilat) or coagulation factor Xa (rivaroxaban, apixaban, edoxaban). Unlike conventional anticoagulants, vitamin K antagonists, they have a rapid onset of effect and a relatively wide therapeutic spectrum, do not require laboratory control of the prothrombin time (PT), and rarely interact with food and medicines. New parenteral anticoagulants achieve their anticoagulant effect by an indirect (semuloparin, idrabiotaparinux) or direct inhibition of Xa factor (Otamixaban), as well as by the inhibition of coagulation factor IXa (RB006). The main features of these medicines have a rapid onset of effect and a predictable anticoagulation effect, but

with most of them, it is possible to achieve a rapid neutralization by an adequate antidote [12].

With 19 patients the surgery was repeated due to recurrence of hematoma and these were also patients on the old generation anticoagulants therapy. Thrombin and FXa are effective in a wide range of concentration in the plasma, which enables a higher degree of safety during the inhibition thereof and a lower the risk of overdose, and is therefore recommended to use the new generation anticoagulants [13].

Conclusion

A wide application of anticoagulant therapy, both in protective as well as therapeutic purposes, leads to a frequent occurrence of HSCH.

The inordinate or irregular taking of anticoagulant therapy, in other words, the overdose with the old generation anticoagulants, leads to a frequent occurrence of uncontrolled bleeding. Difficult control of INR, when using the older generation anticoagulants, whether due to the negligence or inability of patients, leads to an increase in the occurrence of HSCH.

The application of the new generation anticoagulant therapy is preferred because it does not require frequent laboratory analyses, i.e. INR monitoring.

Unfortunately, the financial situations of our patients do not allow the implementation of the new generation anticoagulation therapy.

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