

## Impact of Anticoagulant Medication on Chronic Subdural Hematoma Incidence

Rahul Ranjan<sup>1</sup>, Rajendra Kumar<sup>2</sup>, Priyanka Kumari<sup>3</sup>

<sup>1</sup>Senior Resident, Department of General Surgery, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India,

<sup>2</sup>Assistant Professor, Department of Surgery, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India,

<sup>3</sup>Senior Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar, India,

Received: 19-09-2023 / Revised: 17-10-2023 / Accepted: 13-11-2023

Corresponding Author: Priyanka Kumari

Conflict of interest: Nil

### Abstract

**Introduction:** Chronic subdural hematomas (CSH) often manifest as a consequence of mild trauma in the elderly population. Nevertheless, it has been observed that there has been a rise in the population of individuals diagnosed with chronic subdural hematoma who were undergoing consistent anticoagulant treatment. The present study aims to demonstrate the correlation between the use of earlier generation anticoagulant medications and the increased incidence of hemorrhagic subdural cranial hematoma (HSCH). This association is mostly attributed to challenges in effectively managing the international normalised ratio (INR) and the potential risk of drug overdose.

**Method:** The study was done in the Jawaharlal Nehru Medical College and Hospital, Bhagalpur, in India over the period spanning from September 2021 to September 2022.

**Results:** The findings indicate that the highest proportion of patients, accounting for 24.71%, were on anticoagulant treatment and fell within the age range of 51 to 60 years. In 37.07% of instances, individuals who had anticoagulant medication exhibited INR values within the normal range, while 35.95% of these patients displayed INR levels beyond the threshold. Nineteen individuals in our study had deaths, all of whom were on anticoagulant treatment with earlier generation medications.

**Conclusion:** The broad use of anticoagulant medication, both for preventive and therapeutic objectives, is a significant strategy in addressing the high incidence of hemorrhagic stroke and cerebral haemorrhage. The improper and excessive use of anticoagulant medication, along with the excessive reliance on complex terminology and the development of newer generations of anticoagulant pharmaceuticals, contributes to a heightened occurrence of hemorrhagic subarachnoid cerebral haemorrhage (HSCH). The use of novel anticoagulant medication is favoured due to its reduced reliance on regular laboratory testing. The monitoring of International Normalised Ratio (INR) is a crucial aspect in clinical practise.

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

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

### Introduction

The aetiology of chronic subdural hematoma (CSDH) remains uncertain despite its prevalence as a frequent form of intracranial haemorrhage. There has been a rise in the prevalence of chronic subdural hematoma (CSDH) is on the rise among the older population, with reported worldwide occurrences ranging from 1 to 13.5 cases per 100,000 individuals [1-4]. A notable prevalence of chronic subdural hematoma (CSDH) is reported in individuals who are 65 years of age and older, with an incidence rate ranging from 60 to 80 cases per 100,000 individuals within this cohort [5].

The management of chronic subdural hematoma (CSDH) is rather straightforward, largely involving the implementation of a simple surgical procedure

known as burr-hole trephination and drainage. The prognosis is favourable, however, studies have indicated a rather high recurrence rate ranging from 2% to 38% [6-9]. Despite the extensive study that has been undertaken on the relatively high rates of recurrence, the findings of the studies on the mechanism and the risk factors remain controversial [10, 11]. The purpose of the present study was to analyze the association between the use of antiplatelet or anticoagulant medication and CSDH recurrence in patients at a single institution.

### Methods

The study was conducted at the Jawaharlal Nehru Medical College and Hospital, Bhagalpur, in India

between September 2021 to September 2022, including a total of 349 patients with HSCH who underwent surgical intervention from 2016 to 2021. During the conducted examinations, the primary objective was to investigate the factors contributing to the rising prevalence of HSCH individuals, with particular emphasis on both the senior demographic and, notably, the younger cohort.

The patients were categorised into three groups based on the kind of anticoagulant medication administered. The infrequent laboratory monitoring of anticoagulants such as Aspirin, Cardiopirin, and

Plavix is chosen for their protective effects. The use of traditional anticoagulants such as Farin, vitamin K, and Sintrom necessitates obligatory laboratory monitoring. New anticoagulants, which exhibit selective activity towards either thrombin or coagulation factor Xa, have been developed to eliminate the need for laboratory monitoring.

### Results

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

**Table 1: Total number of operated patients from HSCH**

Years	Number of operations	Without AkTh	With AkTh
2016	34	28	6
2017	47	33	14
2018	62	45	17
2019	68	50	18
2020	72	53	19
2021	66	51	15
All	349	260	89

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
	19	68	2
All	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 of INR	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**

Outcomes	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 patient's 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

There has been a notable rise in the prevalence of people diagnosed with HSCH, both inside our nation and globally. The rise in life expectancy is a contributing cause to the prevalence of this condition, with advancements in diagnostic and therapeutic capabilities in metropolitan areas, which have also resulted in a higher number of affected individuals. One concerning observation pertains to the rising prevalence of HSCH patients in younger age groups, with an increasing trend in the proportion of HSCH patients who have had surgical interventions and are receiving anticoagulant

medication. Regrettably, there has been a growing prevalence of individuals afflicted with cardiovascular ailments, necessitating the use of anticoagulant medication [8]. In our examination of patients treated by HSCH, it was shown that 25.50% of them were on anticoagulant therapy. This finding aligns with previous research indicating a substantial proportion of patients receiving such treatment [9, 10]. The research findings indicate a higher prevalence of the use of older generation anticoagulation medication. Specifically, our analysis reveals that 76.40% of patients received treatment with anticoagulants from the older generation. Continuous laboratory monitoring (INR) and appropriate dose are necessary for the administration of these medications [11]. Frequently, patients inadvertently exceed the

recommended dosage of medications, either owing to lack of attention or the inherent challenges associated with maintaining strict control. Our study findings indicate that a notable proportion of patients, namely 35.95% of those receiving treatment with older generation anticoagulants, had an International Normalised Ratio (INR) over 3. The INR number serves as a critical determinant in the decision-making process regarding the need of immediate surgical intervention. This becomes particularly problematic in cases when a hematoma exerts significant pressure on the brain, potentially resulting in imprisonment and fatal consequences.

In the conducted research, it was observed that the surgical procedures were delayed for a majority of patients, namely 56.17% of them. In the majority of instances (71.91%), patients who had surgery for HSCH experienced full recovery. The occurrence of death in patients receiving older generation anticoagulant therapy was observed in 19 individuals, representing a statistically significant higher incidence compared to the group receiving protective therapy and new generation anticoagulant therapy. In the latter group, none of the 18 cases resulted in death (Fisher's exact test:  $p=0.009$ ). The novel oral anticoagulants have selective action on thrombin (ximelagatran, dabigatranetexilate) or coagulation factor Xa (rivaroxaban, apixaban, edoxaban). In contrast to traditional anticoagulants such as vitamin K antagonists, the aforementioned agents exhibit a fast beginning of action and possess a broader therapeutic range. Moreover, they do not need the monitoring of prothrombin time (PT) by laboratory analysis and seldom interact with dietary and pharmaceutical substances. The anticoagulant action of new parenteral anticoagulants is achieved by either indirect means, such as with semuloparin and idrabiotaparinux, or through direct inhibition of the Xa factor, as shown with Otamixaban. Additionally, these anticoagulants may also block coagulation factor IXa, as seen with RB006. The primary characteristics of these medications are a prompt beginning of action and a consistent anticoagulant effect. However, the majority of these substances may be rapidly neutralised with the use of an appropriate antidote [12].

The surgical procedure was repeated in 19 patients as a result of hematoma recurrence. It is worth noting that these patients were undergoing medication with anticoagulants from the previous generation. Thrombin and FXa have efficacy throughout a broad spectrum of plasma concentrations, therefore enhancing safety in the context of their inhibition and reducing the likelihood of overdose. Consequently, it is advisable to consider the use of next generation anticoagulants [13].

## Conclusion

The extensive use of anticoagulant medication, for both prophylactic and therapeutic intentions, results in a high incidence of hemorrhagic subdural and subarachnoid haemorrhages (HSCH). The excessive or irregular administration of anticoagulant medication, namely the overuse of older generation anticoagulants, results in a high incidence of uncontrolled haemorrhaging. The inadequate management of international normalised ratio (INR) levels, particularly when using older generation anticoagulants, might contribute to a higher incidence of hemorrhagic subdural cranial hematoma (HSCH), either owing to patient ignorance or incapacity.

The use of novel anticoagulant medication is favoured due to its reduced reliance on regular laboratory investigations, specifically the need for International Normalised Ratio (INR) monitoring. Regrettably, the financial circumstances of our patients preclude the adoption of the novel anticoagulant medication of the latest generation.

## Acknowledgement

We are thankful to the patients and their caring relatives without them the study could not have been done. We are thankful to the supporting staff of our hospital who were involved in the patient care of the study group.

**Source of funding:** None

## References

1. Nagulic I (1975) Subduralni Hronichni Hematom. Neurohirurgija. ed Medicinski fakultet Beograd 76-79.
2. Adhiyaman V, Ashar M, Geneshram KN (2002) Chronic Subdural Haematoma in the Eldely . Postgrad Med Jurnal 78: 71-75.
3. Haruhide I, Shinjoro Y, Toshio K, Hidetaka M (1976) Role of Local Fibrinolysis in the Ethiology of Chronic Subdural Haematoma. Journal of Neurosurgery 45: 26-31.
4. Sambasivan M (1997) An Overview of Chronic Subdural Haematoma: Expiriance with 2300 cases. Surgical Neurologu 47: 418-422.
5. Joao-Luiz VA, Vinicisu RF, Luciano H, Jose-Carlos EV, Jamil FN (2015) Chronic Subdural Haematoma: Epidemiological and Prognosis Analysis of 176 Cases. Rev.Col.Bras 42-45.
6. Liliang PS, Tsai YD, Liang CL, Chen HJ (2002) Chronic Subdural Haematoma in Young and Extremely aged Adults: Comperative Study of two Age Groups. Injury 4: 345-348.
7. Jenkins PV, Rawley O, Smith O (2013) Elevated factor viii levels and risk of venous thrombosis. British Journal of Haematologu 6: 653-656.
8. Gallagher AM, Setakis E, Plumb JM (2011)

- Risks of Stroke and Mortality Associated with Suboptimal Anticoagulation in Atrialfibrillation Patients. *Thromb Haemost* 106: 968-977.
9. Hart RG, Pearce LA, Aguilar MI (2007) Meta-Analysis: Antithrombotic Therapy to Prevent Stroke in Patients who have Non Valvularatrial Fibrillation. *Ann Intern Med.* 146: 857-867.
  10. Wan Y, Heneghan C, Perera R (2008) Anticoagulation Control and Prediction of Adverse Events in Patients with Atrial Fibrillation. A systematic review *Circ Cardiovasc Qual Outcomes* 1: 84-91.
  11. Higashi MK, Veenstra DL, L. Kondo M, Ann K (2002) Association between Cyp2c9 Geneticvariants and Anticoagulation-Related Outcomes during Warfarin Therapy. *JAMA* 3: 1690-1698.
  12. Turpie A (2007) Oral, Direct Factor X A Inhibitors in the Development for the Prevention and Treatment of Thromboembolic Diseases. *Arterioscler Thromb Vasc Biol.* 27: 1238-1247.
  13. Obrenovic-Kiricanski B, Subotic S (2006). Surgery for Patients with Mechanical Heart Valves: Adjustment and Tailoring of Anticoagulant Therapy, *Acta Chirurgica Iugoslavica.* 3: 23-27.