Effects of Atorvastatin on Conservative and Surgical Treatments of Chronic Subdural Hematoma in Patients

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OBJECTIVE: **To investigate effects of atorvastatin on conservative and surgical treatment of patients with chronic subdural hematoma.**

METHODS: **A retrospective analysis was performed of 109 patients (including 3 outpatients) with chronic subdural hematoma at Northern Jiangsu People's Hospital from April 2014 to October 2015. Patients' gender, age, Glasgow Coma Scale score, symptoms, history of antiplatelet or anticoagulant use, hematoma location, volume of hematoma, operation methods, and application of atorvastatin and its duration were recorded. Prognostic indicators including changes in hematoma volume and neurologic status were extracted. Statistical methods were conducted to evaluate drug efficacy.**

RESULTS: **Seven conservative patients received atorvastatin for 1–6 months (range, 3.57 ± 1.72 months). The volume of hematomas was ± 4.49 mL to 11.40 ± 4.46 mL ($P > 0.05$) after 1 month's atorvastatin treatment. Hematomas disappeared after 6 months in all 7 patients. In surgical patients, gender ($P = 0.797$), age ($P = 0.063$), Glasgow Coma Scale score ($P = 0.216$), history of antiplatelet or anticoagulant ($P = 0.350$), volume of hematoma after admission ($P = 0.896$), location ($P = 0.282$), and operation methods ($P = 0.832$) were nonsignificantly associated with follow-up groups, but atorvastatin was significantly associated with follow-up results ($P = 0.045$).**

CONCLUSIONS: **Atorvastatin has preliminarily been proved to be safe and effective for chronic subdural hematomas in both conservative and surgical patients and can provide a drug treatment strategy for neurosurgeons.**

INTRODUCTION

Chronic subdural hematoma (CSDH) is a common clinical disease, and the overall rate is approximately 14.1 per 100,000 persons per year in the general population.[1,2] In developing countries, the incidence reaches 0.0074% in the elderly.[3] As a result of the increase in life expectancy and the introduction of auxiliary tools, the high incidence and diagnostic innovation have promoted developments in clinical practice. There are multiple treatment techniques, such as conservative treatment, twist-drill craniotomy, minicraniectomy, burr-hole craniotomy, or craniectomy.[4-7] However, the detailed mechanisms and therapeutics of CSDH are controversial.[8] Early intervention and minimally invasive methods are often recommended by neurologists.

A series of studies have suggested that CSDH is caused by impaired angiogenesis in the neomembrane and localized inflammation. Localized inflammation hinders angiogenesis and blood leakage from immature vessels of the neomembrane. Moreover, leaked blood is prevented from being absorbed by local inflammation.[9-12] Statins, which are regarded as the first-line drugs in treating coronary heart disease, have been shown to improve angiogenesis and reduce inflammation.[13] Atorvastatin, a kind of cholesterol-lowering drug, has been shown to promote angiogenesis, inhibit inflammation, and decrease levels of proinflammatory molecules.[14-16]

Key words
- Atorvastatin
- Chronic subdural hematoma
- Conservative
- Surgical
- Prognosis

Abbreviations and Acronyms
CSDH: Chronic subdural hematoma
CT: Computed tomography
GCS: Glasgow Coma Scale
MRI: Magnetic resonance imaging

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Because of the potential mechanisms discussed earlier, intervention with atorvastatin in CSDH is used at some medical centers,[12] but there is still a lack of clinical efficacy and treatment experience. Atorvastatin was introduced in our center in April 2014. In this study, a retrospective analysis was performed to evaluate the efficacy of atorvastatin for conservative and surgical treatments of patients with CSDH.

PATIENTS AND METHODS

Patient Recruitment

In this study, 109 patients with CSDH (including 3 outpatients) at Northern Jiangsu People's Hospital were recruited from April 2014 to October 2015. Our research was approved by the institutional review board of Northern Jiangsu People's Hospital. All the participants were patients with CSDH with proven radiographic evidence, medical history, or symptoms. Patients' gender, age, Glasgow Coma Scale (GCS) score, symptoms, history of antiplatelet or anticoagulant use, hematoma location, volume of hematoma, operation methods, and application of atorvastatin and its duration were recorded.

Evaluation Index

Routine head computed tomography (CT) or magnetic resonance imaging (MRI) was performed before treatment and 1, 2, 3, and 6 months after treatment. The effect of atorvastatin was evaluated by prognostic indicators including changes in hematoma volume and neurologic status. Prognostic levels (3 months) were defined as 1) uncured (volume of hematoma decreased by less than 50%, recrudesced, or even increased with aggravated neurologic symptoms); 2) improved (volume of hematoma decreased by more than 50% but less than 100% with partially or completely resolved neurologic symptoms); or 3) cured (hematomas were not found on CT or MRI scans and neurologic symptoms had completely resolved).

Volume of hematomas were calculated based on the Coniglobus formula: hematoma volume (mL) = 1/2 × the longest diameter of the hematoma layer with the largest area (cm) × the longest diameter perpendicular to the longest diameter (cm) × the thickness of the hematoma (cm). Total volume of multiple hematomas was calculated.

TREATMENT METHODS AND ATORVASTATIN THERAPY

Conservative treatments were chosen based on inclusion criteria: age >16 years, evidence of CSDH on CT or MRI, with or without slight neurologic deficits. A low dose of atorvastatin was applied.[17] After definite diagnosis, an oral dose of 20 mg atorvastatin daily (Pfizer, New York, New York, USA) was taken by patients for 1–6 months. Atorvastatin treatment was terminated when a hematoma had disappeared radiologically with completely resolved neurologic symptoms for more than 2 weeks. During the course of treatment, patients were monitored by CT or MRI, neurologic status, and coagulation, liver, and kidney functions.

Surgical treatments were followed for the diagnosed patients who fulfilled the following inclusion criteria: a need for surgical intervention including undoubted evidence of CSDH by CT or MRI, with symptoms of increased intracranial pressure or brain

Table 1. Clinical Data for Conservative Patients Treated with Atorvastatin

Number	Gender	Age (Years)	Glasgow Coma Scale	Hematoma Location	Symptoms	Antiplatelet or Anticoagulant	Volume of Hematoma (mL)				Atorvastatin Duration (Months)
							Admission	1 Month	3 Months	6 Months	
1	M	58	15	Bil	Headache	N	15(L),8(R)	8(L),<5(R)	<5(R)	0	3.5
2	F	70	13	R	Headache, irritable	Aspirin	25.0	15.0	<5.0	0	4.0
3	M	79	15	L	Headache	N	18.0	13.4	<5.0	0	6.0
4	M	55	15	L	Headache	N	17.3	5.5	0	0	1.5
5	M	67	15	R	Neurologic normal	N	18.0	9.0	0	0	2.0
6	F	48	15	R	Right-sided weakness	N	28.0	17.5	9.6	0	5.5
7	M	63	15	L	Headache	Aspirin	16.5	7.4	0	0	2.5

M, male; Bil, bilateral; N, no; L, left; R, right; F, female.