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Evaluating the Impact of Perioperative Statin Therapy on Recurrence in Surgical Management of Chronic Subdural Hematoma

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Abstract

Background: Chronic subdural hematoma (cSDH) is a common neurosurgical condition. Despite favorable surgical outcomes, recurrence rates can reach up to 33%. Our objective was to assess whether statin treatment reduces recurrence after surgical management of cSDH.

Methods: This retrospective cohort study included cSDH patients aged ≥18 who underwent surgical treatment in our institution from 2017 to 2019. A comparative analysis was conducted between two groups: perioperative statin (Lipitor group) and surgery only (control group).

Results: A total of 219 patients who underwent surgical treatment for cSDH were identified (2017–2019). Fifty-five cases met the inclusion criteria: Lipitor group (n=25, 45%) and control group (n=30, 55%). Demographics were matched with a minor age difference (67.4 vs. 66.2 years, P=0.78). Anticoagulant use was slightly higher in the Lipitor group (12% vs. 7%), while hypertension was more prevalent in the control group (57% vs. 28%). While the Lipitor group displayed a lower recurrence rate (Lipitor 12%; control 33%), the findings did not attain statistical significance (P = 0.11).

Conclusions: Our study suggests a possible decrease in recurrence rates associated with statin treatment after surgical management of cSDH. Further comprehensive investigations are warranted to confirm and elucidate the clinical implications of these findings.

Keywords: Chronic subdural hematoma; Statins; Burr hole; Recurrence; Surgical evacuation

Abbreviations: cSDH: Chronic Subdural Hematoma; CT: Computed Tomography; DM: Diabetes Mellitus; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Score; HTN: Hypertension; NA: Not Available; VP: Ventriculo Peritoneal

Introduction

Chronic subdural hematomas (cSDHs) are prevalent among neurosurgical patients, characterized by the accumulation of blood and its breakdown products in the subdural space over time [1]. `cSDHs are more common among the elderly, contributing to notable morbidity and mortality with an increased incidence during the last decades, especially considering the aging population and the usage of antithrombotic medications [1-3]. Pathogenesis involves intricate inflammation, leading to the gathering of blood, its breakdown components, exudate, and cerebrospinal fluid within the subdural space [4]. Large cSDHs causing mass effect with neurological deficits and unresolved hematomas with neurological symptoms are usually managed surgically, commonly through burr hole evacuation [1,5-7]. Although most patients show good results from surgical treatment, recurrence is a common problem, with reported rates ranging from approximately 5% to 33% [1,3,7-9]. Recurrence leads to increased morbidity, complications, costs, and reoperation needs, which in turn leads to increased risks of seizure, empyema, infection, and further recurrences [1].

Many factors have been studied as causes of recurrence after initial surgical intervention. Evidence proposes pronounced inflammation in recurrent hematomas, which often results in hematoma architecture that makes evacuation difficult [8,10]. Considering the inflammatory etiology, various pharmacological

interventions hold the inherent plausibility to reduce recurrence rates and have undergone evaluation through randomized trials [1]. One of those is statins (HMG-CoA reductase inhibitors), originally used for high cholesterol management and heart disease, which have established dual regulatory effects on immunoregulation and vascular maturation [5,11]. Subsequently, statins have emerged as surgical adjunctive or standalone treatments in cSDH management [1,2,6,12-20]. Although some conflicting results exist, likely due to underpowered analysis or confounding factors, worldwide studies have shown that perioperative statins are associated with lower cSDH recurrence rates without significant change in mortality levels [16,17,19,21-24].

Despite the absence of consensus regarding the application of statins, our department implemented statin (Lipitor, Atorvastatin) in cSDH treatment starting in November 2018. This decision was made based on evidence from diverse studies and consideration of inflammatory etiology, aiming to mitigate recurrence rates. Given the ongoing uncertainty in literature concerning statins' impact on cSDH recurrence, we analyzed institutionally amassed data since the incorporation of statin-based treatment. In the current study, we compared cSDH patients undergoing Lipitor treatment with those without such intervention within our department from 2017 to 2019. Through this retrospective cohort investigation, we aim to assess the ramifications of statin incorporation within our therapeutic approach. Our objective was to evaluate whether statin therapy resulted in reduced recurrence in patients who underwent surgical management of cSDH.

Methods

Study Design The study utilizes a retrospective cohort comparison design, adhering to the ethical guidelines established in the 1964 Declaration of Helsinki and its subsequent amendments. Approval was obtained from the local ethics committee, with the protocol number RMB-0186-20. Population and Data Collection We conducted a retrospective search of our institution's patient database between January 1, 2017, and December 30, 2019, to identify patients ≥18 years of age who underwent surgical management for cSDH. Data collected included patient age and gender, neuroradiologic test results, surgery count, Ventriculoperitoneal (VP) shunt presence, specific pharmacological treatment (statins, steroids, anticoagulation, and antiaggregating agents), comorbidities (stroke, Diabetes mellitus, dementia, hypertension, coagulation disorder), alcohol consumption history, Glasgow Coma Scale (GCS), Glasgow Outcome Score (GOS), postoperative infection, and mortality.

Further data regarding potential risk factors for Lipitor use were also collected, including sensitivity to statins, pregnancy, and breastfeeding. To minimize confounding, patients with prior steroid or statin use were systematically excluded, as were patients with hematological coagulation disorders, post-surgical infection, shunts, and pregnancy/nursing. Patients who were deceased within six months following surgery, without a direct correlation to the surgical procedure, were also excluded. Treatment Protocol The underlying condition was symptomatic chronic subdural bleeding requiring drainage surgery. Surgeries were performed as inpatient procedures with burr hole trepanation. The treatment protocol involved the administration of perioperative 20 mg Lipitor once daily as an adjunct to the surgery.

The administration of Lipitor was based on established practice in our department and was implemented starting in November 2018. Follow-Up and Recurrence Post-operative follow-up intervals were determined based on the patient's clinical condition. As per departmental protocol, the first follow-up visit typically occurs weeks after drainage, and subsequent visits are scheduled as needed. The assessment of outcomes relied on clinical and imaging follow-up during outpatient visits, emergency room visits, data from the Ofek system (for information outside the hospital), and the PACS system (for imaging features). Routine follow-up for hematoma characteristics utilized brain Computed Tomography (CT). Follow-up was recorded for a maximum of one year.

We defined recurrence of cSDH as imaging evidence of accumulation in the ipsilateral subdural blood collection, presenting with neurological deficits or requiring further surgical intervention. Statistical Analyses Patients were divided into two groups: perioperative treatment with Lipitor (Lipitor group) and those managed surgically only (control group). Clinical indicators were expressed as the mean ± standard deviation ($\bar{X}\pm S$) and as rates. Indicators between groups were compared using the T-test for numeric variables and Fisher's exact test for categorical variables. Factors influencing outcomes (age, gender, diabetes, shunt, comorbidities, anticoagulation, alcohol, infection) were included in the analysis. Statistical significance was set at $P < 0.05$. Analyses were conducted using IBM SPSS Statistics (Version 25).

Results

We identified 219 patients ≥18 years of age who underwent surgical management for cSDH at our institution between 2017 and 2019. Details regarding prehospital medication, comorbidity, and historical data were reviewed, with emphasis on data reported to have an association with cSDH recurrence [8]. Patients not included were those meeting exclusion criteria, lost to follow-up, or lacking data. None of the patients reported having received repeat surgery at another institution. The established criteria were fulfilled by 55 patients included in the final analysis. Of those, 25 were treated with Lipitor (Lipitor group, burr hole plus Lipitor; 45%), while 30 did not receive statins (Control group, burr hole; only 55%). No subjects exhibited diagnosed dementia or alcohol use disorder. Mean age, gender, diabetes, stroke, GOS, and use of antiaggregant therapy were similar between the groups.

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The Lipitor group had a slightly higher rate of anticoagulant therapy use (12% vs. 7%), while the control group had higher rates of hypertension (57% vs. 28%). While hypertension showed a trend towards significance (P=0.06), no statistically significant differences were observed in clinical or demographic data (Table 1). In terms of hematoma resolution and recurrence, the Lipitor group experienced hematoma recurrence in 3 cases (12%), while 22 cases (88%) resolved. Conversely, the control group exhibited higher recurrence rates (10 recurrences, 33%; 20 resolved, 67%), although this difference did not reach statistical significance (P = 0.11). Notably, all 3 patients in the Lipitor group who experienced recurrence underwent one additional surgery, whereas some patients in the control group required multiple surgeries.

Discussion

The present study aimed to investigate the impact of statin treatment on the recurrence rates of cSDH following surgical intervention. Our analysis revealed intriguing insights that contribute to the ongoing discourse within the medical community. The analysis indicated a recurrence rate of 12% in the Lipitor group, with 88% of cases exhibiting successful resolution. Conversely, the control group displayed higher recurrence rates reaching 33%. While the difference appears notable, the lack of statistical significance (P=0.11) warrants cautious interpretation. There was no statistically significant association observed between these two groups. Given the limited sample size, regression analysis was not pursued. The lack of statistical significance may arise from the limited sample size, guided by the objective of mitigating the impact of confounding influences.

Despite these efforts, noteworthy factors surfaced, including a higher incidence of hypertension within the control group. Nevertheless, the estimated GOS exhibited similarity across both groups. Our findings align with current literature largely support the efficacy of statins in cSDH management [1,2,6,12-15,17,18,20], as well as two similar previous studies reporting associations between statins and reduced recurrence rates of cSDH treated surgically [16,19]. Unlike our study, those studies had larger sample sizes, enabling researchers to achieve statistical significance. Our study diverges from two other retrospective inquiries that reported similar recurrence rates between compared groups [22,24]. However, one involved a small sample size (n = 49) and short follow-up [24], while the other considered patients on regular statin regimens rather than those specifically prescribed statins for the condition [22].

Notably, another investigation unveiled negligible differences but examined recurrence following YL-1 puncture needle versus classic burr-hole surgery [23]. Despite apparent conflicting findings, our outcomes align with a recent meta-analysis [21], wherein station-treated individuals exhibited lower recurrence rates (odds ratio 0.80). When examining a subset of studies devoid of intergroup disparities in antithrombotic drug usage, the statin group demonstrated significantly diminished odds of recurrence (odds ratio 0.29). It is pertinent to emphasize that our study also noted a higher proportion of anticoagulation use within the statin group (12% vs. 7%), yet this disparity did not achieve statistical significance (P=0.65). These combined findings suggest a potential synergy between antithrombotic and statin therapies. Despite the absence of statistical significance, our study suggests a trend towards favorable outcomes among patients receiving statin treatment. While our study falls short of establishing a definitive causal link, it provides a foundation for further exploration in larger, prospective studies.

Limitations

Our study's limitations arise from a small, targeted sample size. Due to these constraints, regression analysis was not conducted, leaving certain influences like anticoagulation use uncertain. Additionally, the retrospective nature introduces biases and complicates analysis due to limited collectable data; for example, assessing patient adherence to perioperative statin regimens remains challenging.

Conclusion

Our study provides valuable insights into the relationship between statin treatment and cSDH recurrence after surgical intervention. While statistical significance was not attained, the observed trend suggests a notably lower rate of recurrence among patients treated with statins within the perioperative period. Our findings contribute to understanding statins' potential role in cSDH management.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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