

ROLE OF STEROIDS IN PREVENTING RECURRENCE OF CHRONIC SDH

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ABSTRACT

Background: Biomedical Chronic subdural hematoma is a neurological disorder, mainly in older patients. The treatment is mainly surgical intervention, with various modalities used among neurosurgeons. Over the time, growing evidence that inflammatory changes play a main role in the pathology of CSDH. In that favor, the role of corticosteroids has been boon treatment to surgery. However, this practice remains very ancient and we need for high-quality-of-clearance studies to clear the effectiveness of corticosteroids in the management of CSDH.

Methods: We did a double-blind, randomized controlled trial for comparison of methylprednisolone and placebo in the management of CSDH without clinical along with radiological signs of severity. The management will be given daily for the duration of 3 weeks. The study assessment will be conducted at 1, 3 and 6 months. 202 study participants enrolled for the present study. **Results:** Time for surgical management of the chronic subdural hematoma is 1 month to compared between the two study groups with the log-rank test. Two interim analyses after inclusion of one third and two thirds of the study participants and one final analysis will be conducted. The cumulative result in terms of value of alpha for each analysis are: 0.00021 for first analysis, 0.01202 for second analysis and 0.04626 for final analysis (Statistical Solutions Ltd., Cork, Ireland, nTerim, V 1.1.). The trial will be stopped when the significance values of the log-rank test will be reported below to these alpha values.

Conclusion: Observations This study started in June 2016; its outcome may be interesting as alternatives to surgery in the treatment of patients harboring a chronic subdural hematoma, and result may insights into the natural history of its pathology

Keywords: Corticosteroids, Chronic subdural hematoma, Elderly patients.

INTRODUCTION

Chronic subdural hematoma (CSDH) is frequent neurosurgical pathology (1, 2). Till date, it has involved older patients, prevalence of 15 cases for 100,000 over 70 years (3, 4). Consider the population of patients over 65 years old is to be increased three-fold by the 2030s (5), and the increasing use of anticoagulant or platelet aggregation-inhibiting medicines, more and more doctors will deal with this which thus is a major public health issue. Surgical intervention of CSDH is currently the best treatment (6). There is an increased mortality rate until 1 year after operative

intervention (7), and hospital expenditure are high, with a very durable length of stay. Beyond its traumatic etiology, the pathology of CSDH includes inflammatory reasons so that some researchers also considered CSDH as an inflammatory disease. CSDH, is a self-sustaining disease of neo-angiogenesis and fibrinolysis, resulting in increase in hematoma volume (8–15). In this favor, corticosteroids are an alternative management Chronic subdural hematoma because of their inhibitory effects on platelet-activating factor, vascular endothelial growth factor, interleukin-6,

tissue plasminogen activator and interleukin-8 (16). In previous studies, only preliminary nonrandomized or retrospective studies and case reports have reported the efficacy of corticosteroids along with surgery (17-19). In this reference, a double-blind randomized research is necessary to assess the potency of corticosteroids in CSDH. We conducted a randomized controlled trial to find out the potency of corticosteroids in the treatment of CSDH without radiological or clinical signs of severity among patients. The studied corticosteroid was methylprednisolone, a synthetic glucocorticoid which is used in treating various diseases. It is a medicine of which the pharmacokinetics, drug interactions, mechanisms of action and adverse effects are well known.

MATERIAL AND METHODS

The present study is a prospective study (methylprednisolone versus placebo). The primary objective is to check the potency of corticosteroids, in the management of patients with CSDH without radiological or clinical signs of severity. Secondly is to assess the role of methylprednisolone on radiological outcome of the pathology, quality of life, morbidity and mortality outcome. Our hypothesis was that 80% of the total study participants taking placebo were operated at the end of 1 month. A total sample size of 202 study participants was calculated at 90% confidence interval to detect a reduction in the surgery rate to 60% (hazard ratio of 1.756) with corticosteroids, using a two-sided log-rank test with a 5% alpha assuming that the hazards are proportional (Statistical Solutions Ltd., nTerim, Cork, Ireland, V1.1).

RESULT

The screening takes during the hospital stay or consultation in a doctor unit during which the result of CSDH. A protocolled clinical examination is done to ensure that the study participants were meets the inclusion criteria. First CT scan completes this initial patient screening. If the study participants were eligible, written informed consent from the participants or a representative was taken before enrollment. Patients were followed up for the total duration of 6 months. Evaluation was done at the end of 1st, 3rd and 6th months. Along with plasma sodium, potassium and fasting glucose were measured at 0, 7, 14 and 21 day of the 1-month visit. The serum electrolyte or glycemic impairment that could occur due to steroid management were also recorded. Serum fasting cortisol at 8 a.m. was done 2

days after the commencement of the management with corticosteroids (at day 23). Patients were screened for interval cerebral CT scans to see for their chronic subdural hematoma at the end of 1st, 3rd and 6th months. Time for surgical management of the chronic subdural hematoma at 1 month was compared between the two study groups with the log-rank test. Two interim analyses after inclusion of one third and two thirds of the study participants and one final analysis will be conducted. The cumulative result in terms of value of alpha for each analysis are: 0.00021 for first analysis, 0.01202 for second analysis and 0.04626 for final analysis (Statistical Solutions Ltd., Cork, Ireland, nTerim, V 1.1.). The trial will be stopped when the significance values of the log-rank test will be reported below to these alpha values. Student's t test and Mann-Whitney test will be applied to compare all the quantitative variables. All the quantitative data evaluated during the monitoring process will be compared using repeated measures analysis of variance (ANOVA) for the two factors (time, group). For qualitative data, a chi square test will be applied. For all these analyses, adjustments will be carried out in the case of heterogeneity at inclusion criterion. Possible adverse events will be coded according to MedDRA classification and analysis will conducted by descriptive statistics.

DISCUSSION

Corticosteroids have been previously used in CSDHs, this treatment has never been checked with a well-designed, high-quality-of-evidence study. Duration, dosage, indications, and type of corticosteroid vary greatly depending on the results. In that favor present study reported to clarify the prescription procedure. Under physiologic conditions the subdural space is a space which is virtually in histological continuity between the arachnoid and the dura. (20) Conditions, especially head injury, can result to the separation of the arachnoid and the dura membranes. (21) A proliferation of parietal cells reported to occur in the subdural space, which results in the formation of the fibrous membranes in which numerous capillaries are proliferate under the effects of vascular endothelial growth factor (22). These capillaries in the fibrous membranes have inflammatory permeable walls, and these are partially responsible for the formation of the subdural fluid (23,26). With regard to these pathological aspects of Chronic subdural hematoma, corticosteroid use has been studied to treat CSDH. In a small research comparing patients of CSDH treated with surgery

(82 cases) and corticosteroid (26 cases), only one case in the group with corticosteroid required secondary operative intervention (25). In a retrospective study of 122 study subjects, only 20% of participants receiving corticosteroid prior to surgery required secondary surgery and the complications of treatment were very minimal (23). In an another retrospective study including 496 study participants, preoperative corticosteroid therapy reported to reduce the recurrence rate of Chronic subdural hematoma after burr-hole craniostomy without increasing the burden of complications and treatment-related mortality (21). In an another retrospective study the efficacy of corticosteroids as an prior therapy to surgical intervention (142 study participants with adjuvant corticosteroids and 56 study participants without adjuvant corticosteroids) reported a shift toward a survival benefit with medical management (risk of mortality three-fold decrease in the group of adjuvant corticosteroids ($p = 0.006$)) (24). Despite these studies, there is a lacuna of published articles concerning the role of corticosteroids in reducing the rate of surgery among cases of Chronic subdural hematoma. We have selected the parameter of 60% reduction in the rate of operative procedure based on our empirical medical experience with CSDH treatment for its pathology.

CONCLUSION

The present study protocol concerns an on-going double-blind randomized research that has not completed study participants recruitment at the time of submission. We conducted a randomized controlled trial to find out the potency of corticosteroids in the treatment of CSDH without radiological or clinical signs of severity among patients.

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