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Effects of preadmission beta-blockers on neurogenic stunned myocardium after aneurysmal subarachnoid hemorrhage: A meta- analysis

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ABSTRACT

Objective: Spontaneous subarachnoid hemorrhage is mostly caused by the rupture of an aneurysm. Neurogenic stunned myocardium (NSM) is one of the most frequent complications caused by aneurysmal subarachnoid hemorrhage (aSAH). The possible pathogenesis of NSM may be that the catecholamine peak resulting from aSAH leads to subendocardial ischemia or coronary artery spasm. We designed this meta-analysis to find out whether beta-blockers (BB) can significantly reduce the incidence of NSM and improve the outcomes of aSAH.

Patients and methods: We systematically searched PubMed, Embase, Cochrane library, Elsevier and Medline from inception to Feb 2016. All studies related to the preadmission beta-blocker with aSAH were included.

Results: Three retrospective studies and 691 patients were included. The incidence of mortality [OR = 0.68, 95%CI (0.08–3.50), P = 0.57], cardiac dysfunction [OR = 0.55, 95% CI (0.05–6.49), P = 0.63], cerebral vasospasm (OR = 0.52 95% CI(0.18–2.56), P = 0.50] had no statistical difference between the preadmission BB group and no BB group.

Conclusion: The preadmission beta-blocker cannot decrease the incidence of mortality, cardiac dysfunction, cerebral vasospasm in patients with aSAH. A further research of the usefulness of preadmission beta-blocker in patients with aSAH will be needed.

1. Introduction

Subarachnoid hemorrhage (SAH) may be induced by two reasons: trauma and spontaneity (aneurysmal, 75%–80%, and nonaneurysmal). The peak age of the aneurysmal subarachnoid hemorrhage was 55–60 years old, Clinical manifestations of SAH included sudden severe headache, vomiting, syncope, and the irritation of the brain. Despite of the advance in medical and surgical management, aneurysmal subarachnoid hemorrhage (aSAH) remains a disease with significant morbidity and mortality. The complications of aSAH included hydrocephalus (obstructive and traffic), neurogenic pulmonary edema, neurogenic stunned myocardium (NSM) [1–4], and cerebral vasospasm (delayed cerebral ischemia). NSM is one of the most serious complications.

NSM has been commonly reported in patient with aSAH [5]. It was defined as abnormal cardiac function without coronary heart disease or myocardial abnormalities. The peak period of the disease was 2 days to 2 weeks after SAH. These patients had an elevation of troponin [6], but such elevation was much less occurred in the myocardial infarction. Most of NSM patients fully recovered in 5 days. Early echocardiogram in the hospitalization demonstrated the function of left ventricle [7–9] decreased. An abnormal early ECG, such as QT interval prolongation, T wave change, heart rate disorder can be observed. The pathogenesis of NSM may be that the catecholamine peak leads to subendocardial ischemia or coronary artery spasm [10–12]. A series of historical studies showed that beta-blockers may decrease the catecholamine peak and improve the outcomes of aSAH [13,14]. We designed this meta-analysis to find out whether beta-blockers can significantly reduce the incidence of NSM and improve the outcomes of aSAH.

2. Patients and methods

2.1. Search strategy

The following search keywords “aneurysmal,” “subarachnoid hemorrhage,” “echocardiogram,” “cardiac,” “beta-blocker,” “myocardium” were used to search in PubMed; the Embase; the Cochrane Library and the Medline database. The last date of retrieval was February 2016. The search was limited to studies in humans. Database searches were restricted to articles published in any language and any year. References of original articles and review articles were also identified.

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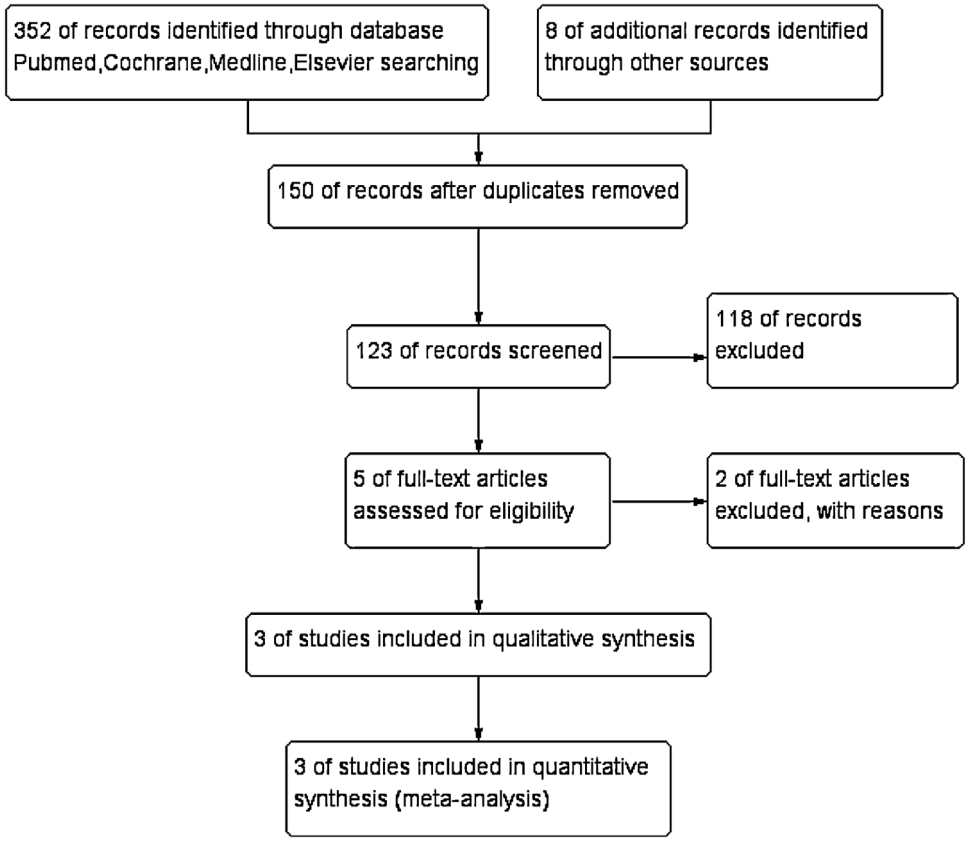

Fig. 1. Study flow diagram.

2.2. Selection criteria

The relevant clinical trials were carefully manually selected based on the following criteria: (1) patients with aSAH, (2) treatment with beta-blockers before admission, and (3) outcomes were reported as neurogenic stunned myocardium, cardiac-related complications, cerebral vasospasm and the adverse events. If there were multiple publications about the same trial, only the most recent publication (and the most informative) was selected for our research.

2.3. Data extraction

Two reviewers, using a standardized form, extracted data independently and disagreements were resolved by discussion or a third reviewer. The following data were selected for extraction from each trial: study details, demographic information, baseline demographic and clinical characteristics, including Hunt-Hess score, Fisher grade, troponin levels, left ventricular ejection fraction , past medical history, and adverse events (hypotension, pulmonary edema, and so on).

Two reviewers assessed the quality of eligible studies independently. If we could not determine from the full-text articles, we contacted the authors. If it remained unclear, we discussed with a third author whether the study should be excluded. If it was not eliminated, we performed a sensitivity analysis.

We assessed the following items using The Cochrane Collaboration's tool for assessing the risk of bias: Were incomplete outcome data adequately addressed (attrition bias)? Were reports of the study free of suggestion of selective outcome reporting (reporting bias)? Did the study conceal other problems that could put it at a risk of bias?

2.4. Statistical analyses

We used the RevMan 5.0 software for statistical analysis. To assess the effect of preadmission beta-blocker on the improvement and prognosis of patients with cardiomyopathy, we extracted the outcome of such patients, including Hunt-Hess score, Fisher grade, past medical history and adverse events. To explore the impact of preadmission beta-blocker (any drug that belongs to beta blockers, dose unlimited), we performed analysis of the incidence of neurogenic stunned cardiomyopathy with beta blocker and without beta blocker before admission. To represent the relationship between preadmission beta-blocker and no beta-blocker, we transformed pooled effect sizes into relative risk (OR) with 95% confidence intervals (CIs). We primarily used fixed effects modeling with the Mantel Haenszel method to conduct outcome meta-analysis from included studies. When a statistically significant heterogeneity evaluated using the I^2 statistic ($> 50\%$) and Q test ($P < 0.10$)

Table 1
Concomitant diseases and drug used before admission.

Sutdy ID	Past medical history(No. of patients)	drug before admission(No. of patients)
Chalouhi 2016	hypertension(120) heart disease (15)	anrihypertensive medication (73)
Crago 2014	hytertension (94) heart disease(22) pulmonary(20) cancer (18) diabetes mellitus (12) drug abuse (13) alcohol abuse(19) gastrointestinal problems (17) other (73)	diuretics(23) vasodilators(5) calcium channel blockers(7) statins(21) other(114)
Liang 2013	diabetes(15) myocardial infarction(8)	aspirin (33) estrogen(13)