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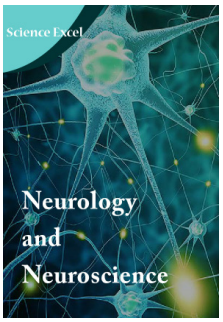
Retrospective study



Best Clinical Approach for Stroke Management

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Introduction

Stroke is the leading cause of severe long-term disability and death among all diseases worldwide [1]. Each year in the United States, more than 690 thousand adults experience an ischemic stroke [2] and additional 240 thousand experience a transient ischemic attack (TIA) [3].

Approximately 25% of stroke cases are recurrent events, often occurring within the first year of a prior stroke or transient ischemic attack (TIA) [4]. On average, the annual risk for future ischemic stroke after an initial ischemic stroke or TIA is ≈3% to 4% [5]. The mortality rate is 41% after a recurrent stroke versus 22% after a primary stroke [6]. In addition, the risk of recurrent stroke is up to 10% in the week after a transient ischemic attack (TIA) or minor stroke [7].

Even though the disability rate has been improved significantly with acute use of TPA (tissue plasminogen activator) and vascular intervention, risk factor control and antithrombotic usage still play a fundamental role with absolute risk reduction of new fatal and nonfatal strokes 30% (95% CI 24%-35%) [8].

This is however complicated by the patient's individual age, sex, existing illness, type and characters of individual strokes etiology et al. Three medications are approved by the U.S. Food and Drug Administration: aspirin, clopidogrel (Plavix), and aspirin/dipyridamole (Aggrenox) plus a recently approved ticardipine [9].

Aspirin is the leading medication which has been thoroughly studied and which has been shown to significantly reduce stroke risk [10]. In this large scale study, aspirin reduced the risk of recurrent ischemic stroke at 6 weeks by about 60% with a similar effect at 12 weeks and disabling or fatal ischemic stroke by about 70%. In 1998, the FDA approved the use of aspirin 50 mg to 325 mg for the prevention of ischemic stroke [11]. The American Stroke Association also recommend aspirin 50 mg to 325 mg for secondary stroke prevention [12].

In a randomized, double-blind CAPRIE trial with ischemic stroke, MI or vascular death as the primary outcome, analysis showed a 5.32% annual risk of the primary outcome in the clopidogrel group versus 5.83% in the aspirin [13].

The ACCP guidelines recommend the combination of aspirin and ER dipyridamole (25 mg/200 mg twice daily) over aspirin alone (Grade 1A) [14]. This recommendation comes as a result of two published trials, ESPS-2 and ESPRIT [15,16]. These trials have also provided evidence that aspirin, dipyridamole and the combination would reduce the risk of stroke from 16-38% (ESPS-2).

The FDA recently approved ticargelor (brilinta) for stroke prevention as well [17].

However, antiplatelet agents such as aspirin also increase bleeding risk. A reasonable estimate of the risk of hemorrhagic stroke associated with the use of aspirin in primary prevention patients is 0.2 events per 1000 patient-years, which is comparable to estimates of the risk associated with the use of aspirin in secondary prevention patients [18].

The recommendation against combination therapy for secondary stroke prevention is based on data from two studies (Match studies [19]). Dual antiplatelet therapy is also associated with high early risks of major bleeding that decline over time [15]. In another recent CHANCE trial which correlated dual antiplatelet with different infarction patterns, the patients who have multiple infarcts, received the most benefit from dual therapy with Plavix and ASA [20].

Among patients with recent cerebral ischemia, intensive triple antiplatelet therapy did not reduce the incidence and severity of recurrent stroke or TIA (the TARDIS study).

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Due to the significantly increased risk of major bleeding triple antiplatelet therapy should not be used in routine clinical practice.

How about anticoagulation medication use? This double-blind trial, which was stopped early because of higher rates of death and major hemorrhage in the warfarin arm, showed that the primary end point (ischemic stroke, brain hemorrhage, and nonstroke vascular death) occurred in 22% of patients in both treatment arms [21].

Method

Our retrospective study took place at a comprehensive stroke center. We reviewed the rate of recurrent stroke in ischemic stroke patients over a four-year period (from 2014-2017).

All of the acute ischemia stroke patients were grouped into TPA group, clot retrieval group and non tpa or clot retrieval stroke group. Ischemic stroke patients were also grouped according to their discharged stroke medication (aspirin, Plavix, aspirin+Plavix, Coumadin, eliquis, aspirin+eliquis and et al). Thirty days recurrent ischemia stroke patients were particularly reviewed and used as an end point of the study. The group with the most recurrent stroke rate is considered less helpful in preventing secondary stroke comparing with less recurrent stroke rate. The difference was measured by X square group and intergroup analysis. P value <0.05 is considered significant and P<0.01 is remarkably significant.

Furthermore, the patients who received TPA as well as clot retrieval will also be for the recurrent stroke rate comparing with patients without TPA treatment under the same secondary prevention stroke medication. Same statistic measures will be implanted in this group of study.

Preliminary data

Out of total 1153 patients with ischemia stroke in the year 2014-2015, we analyzed 63 of them with recurrent stroke. The findings are: Asperin only group the recurrent rate is 21/406, Plavix only group 10/139, ASA+Plavix group 22/412, Coumadin group 8/94, Eliquis group 1/69 and Xarelto 1/33.

On the other hand the study in 2016, there are total 64 recurrent stroke out of 713 stroke patients studied. The ratios are: Asperin only group 6/139, Plavix only group 5/63, ASA+Plavix group 28/316, Coumadin group 2/18, Eliquis group 11/89, ASA+Eliquis group 9/69 and Plavix+Eliquis group 3/9.

Further statistical analysis showed that the Eliquis alone (P=0.049) or in combination with ASA (P=0.031) or Plavix (P= 0.002) is superior to ASA alone in stroke prevention. Although Eliquis is not shown to be superior to warfarin but eliquis+Plavix is significantly better than all the other measurements: Plavix (P=0.014), ASA (P=0.00228), warfarin (P=0.0139) and ASA+Eliquis (P=0.0072).

Conclusion

This study showed that Eliquis is the best choice for secondary stroke prevention and combination of Eliquis with Plavix has the best secondary stroke prevention result. Further randomized controlled studies are warranted and new medication is also expected to be tested as well.

Discussion

Apixaban (Eliquis) is the new oral anticoagulation agent developed along with a few others as daabigatran (Pradaxa), rivaroxaban (Xeralto). It has a lower risk of bleeding than warfarin but slightly higher than aspirin. Comparing with aspirin, the stroke risk is lower in Eliquis in patients with chronic atrial fibrillation who are not suitable to take warfarin [10]. Apixaban is similar in effective to warfarin for stroke prevention [11]. However, our study showed that apixaban may be better than warfarin in stroke prevention.

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