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A REVIEW OF STROKE AND ROLE OF ANTIPLATELET THERAPY IN TUBERCULAR MENINGITIS

Neurology

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ABSTRACT

A recent Vietnamese trial has suggested that the addition of aspirin to the anti-tuberculosis drug regimen improves the outcome of patients with tuberculous meningitis. In TBM, stroke has been reported in up to 60% of the patients and is associated with a poor outcome. Addition of aspirin leads to a significant reduction in the risk of new infarctions among patients with tuberculous meningitis.

KEYWORDS

TBM, Aspirin, Antiplatelet, Stroke.

Introduction

Aspirin is an anti-inflammatory drug that inhibits the activity of cyclooxygenases [1]. It is the cornerstone of antiplatelet therapy for the secondary prevention of ischemic stroke [2]. However, its role in the prevention or management of stroke in tuberculous meningitis is unclear. A recent Vietnamese trial has suggested that the addition of aspirin to the anti-tuberculosis drug regimen improves the outcome of patients with tuberculous meningitis. However, the addition of aspirin showed no significant benefits in terms of reduction in mortality or prevention of new infarctions [3].

Tubercular Meningitis (TBM)

The worldwide prevalence of tuberculosis is 159 per 100,000 population, and 35% of these patients reside in China and India. The prevalence of tuberculosis in India is 211/100,000 population, which amounts to approximately 2,532,000 patients in India [4]. Ten percent of extra pulmonary tuberculosis involves the central nervous system (CNS), which has a higher mortality and morbidity. The clinical manifestations of tuberculous meningitis (TBM) are attributable to diverse pathological changes such as meningitis, encephalitis, hydrocephalus, tuberculoma, infarction, and arachnoiditis occurring at different time points in isolation or in various combinations. The treatment of central nervous system (CNS) tuberculosis is challenging and is compounded by limited CNS penetration of antituberculous drugs, paradoxical worsening, infarction, hydrocephalus, and above all, emerging drug resistance [5-8].

Tuberculous meningitis (TBM) is the most severe manifestation of tuberculosis and is associated with exudates, tuberculoma, hydrocephalus and stroke. Small and medium size intracranial vessels are usually affected. Penetrating vessels develop endarteritis whereas vessels surrounded by exudates develop periarteritis which later may produce panarteritis [9,10]. Vasculitis in TBM has been reported in 41% in an autopsy study [11].

Stroke in TBM

In TBM, stroke has been reported in up to 60% of the patients and is associated with a poor outcome [7]. The mortality is about 3 times higher in TBM patients with stroke compared to those without [12]. Therefore, prevention of ischemic stroke is great important to TBM patients. However, risk factors of stroke were not fully understood in TBM patients, especially in those young adults.

The most common vulnerable brain region is basal ganglia which has been described as 'tubercular zone'. It is comprised of head of the caudate nucleus, anteriomedial thalami and anterior limb and genu of internal capsule. In a study involving 122 TBM patients, 55 patients had stroke and 54% strokes were located in basal ganglia [13]. Another study had similar results with 49% of infarctions in basal ganglia [14]. Zhang et al found in their study, 50% of patients had stroke located in basal ganglia, which is consistent with previous studies. Strokes in 'tubercular zone' may be associated with basilar exudates. Dense fibrinocellular exudates may wrap middle cerebral trunks and their penetrating branches, which may contribute to vasculitis and cause strokes in 'tubercular zone' [15]. About a quarter of young adults with TBM have acute ischemic stroke which may be related with poor clinical outcome. Age, CSF white blood cell and basal meningeal enhancement can predict the occurrence of acute ischemic stroke in young adults with TBM [15].

Antiplatelet Therapy in TBM

Despite adequate treatment using anti-tuberculosis drugs and adjunctive corticosteroids, morbidity and mortality in patients with tuberculous meningitis remain high. Host-directed therapies, including nonsteroidal anti-inflammatory drugs such as aspirin, can be beneficial in the management of tuberculosis [16].

In the primary prevention of cardiovascular diseases, aspirin reduces deaths, ischemic strokes, and myocardial infarction [17]. However, we found no benefit of aspirin in reducing mortality among patients with tuberculous meningitis. Aspirin is commonly prescribed in two doses. The low doses of aspirin (75–150 mg) inhibit platelet aggregation and can prevent ischemic cerebrovascular diseases [18]. In contrast, the high doses of aspirin (>150 mg) have anti-inflammatory effects through the inhibition of pro-inflammatory prostaglandins and thromboxane A2 [19].

Notably, the addition of aspirin leads to a significant reduction in the risk of new infarctions among patients with tuberculous meningitis. The pooled analysis revealed that approximately 15% patients developed new infarctions in the aspirin arm compared with approximately 32% patients in the control arm. Thus, the addition of aspirin led to approximately 17% absolute risk reduction in the occurrence of new infarctions. This is equal to a number needed to treat approximately six patients, indicating that approximately six patients with tuberculous meningitis need to be treated with adjunctive aspirin to prevent the occurrence of one new infarction [16].

Aspirin use was not associated with a significant increase in adverse effects, such as allergic reactions and gastrointestinal, hepatic, cardiac, or respiratory events. No significant increase was noted in gastrointestinal or intracranial bleeding in the aspirin arm compared with that in the control arm. These estimates were available from a single trial only as the other trials did not provide a detailed breakup of adverse events. However, the safety of high-dose aspirin appears to be established to a considerable extent [3].

Conclusion

- The most common vulnerable brain region in TBM is basal ganglia which has been described as 'tubercular zone'.
- Aspirin reduces the risk of new infarctions in patients with tuberculous meningitis but does not alter the risk of death.

REFERENCES

1. Paez Espinosa EV, Murad JP, Khasawneh FT. Aspirin: Pharmacology and clinical

applications. Thrombosis 2012;2012:173124.
2. Goli RR, Contractor MM, Nathan A, Tuteja S, Kobayashi T, Giri J. Antiplatelet therapy for secondary prevention of vascular disease complications. Curr Atheroscler Rep 2017;19:56.
3. Mai NT, Dobbs N, Phu NH, Colas RA, Thao LT, Thuong NT,et al. A randomised double blind placebo controlled phase 2 trial of adjunctive aspirin for tuberculous meningitis in HIV-uninfected adults. eLife 2018;7.
4. World Health Organization. Global Tuberculosis Report 2014. Geneva, Switzerland: WHO Press; 2014. [2015-02 03]. Available from: http:// apps. who. int/ iris/ bitstream/ 10665/137094/1/9789241564809_eng. pdf?ua=1. [Last accessed on 2015 Aug 10].
5. Misra UK, Kalita J, Maurya PK. Stroke in tuberculous meningitis. J Neurol Sci 2011;303:22-30.
6. Kalita J, Prasad S, Misra UK. Predictors of paradoxical tuberculoma in tuberculous meningitis. Int J Tuberc Lung Dis 2014;18:486-91.
7. Kalita J, Misra UK, Nair PP. Predictors of stroke and its significance in the outcome of tuberculous meningitis. J Stroke Cerebrovasc Dis 2009;18:251-8.
8. Katoch VM. Managing drug-resistant tuberculosis: Experiences from India. Expert Rev Anti Infect Ther 2010;8:493-6.
9. Dalal PM. Obsevations on the involvement of cerebral vessels in tuberculous meningitis in adults. In: Goldstein M, et al, editor. Advances in Neurology, Vol. 25. New York: Raven Press; 1979. p. 149–59.
10. Lindsey L, Scholtz CL. Recent presentation of neurological tuberculosis. J Royal Soc Med 1978;71:223–7.
11. Dastur DK, Lalitha VS, Udani PM, Parekh U. The brain and meninges in tuberculous meningitis-gross pathology in 100 cases and pathogenesis. Neurol India 1970;18: 86–100.
12. Misra UK, Kalita J, Maurya PK. Stroke in tuberculous meningitis. J Neurol Sci. 2011;303:22–30.
13. Kalita J, Misra UK, Nair PP. Predictors of stroke and its significance in the outcome of tuberculous meningitis. J Stroke Cerebrovasc Dis. 2009;18:251–8.
14. Tai MS, Viswanathan S, Rahmat K, Nor HM, Kadir KA, et al. Cerebral infarction pattern in tuberculous meningitis. Sci Rep. 2016;6:38802.
15. Zhang L, Zhang X, Li H, Chen G, Zhu M. Acute ischemic stroke in young adults with tuberculous meningitis. BMC Infect Dis. 2019;19(1):362. Published 2019 Apr 30. doi:10.1186/s12879-019-4004-5
16. Rizvi I, Garg RK, Malhotra HS, Kumar N, Uniyal R. Role of Aspirin in Tuberculous Meningitis: A Systematic Review and Meta-analysis. Neurol India 2019;67:993-1002.
17. Raju N, Sobieraj-Teague M, Hirsh J, O'Donnell M, Eikelboom J. Effect of aspirin on mortality in the primary prevention of cardiovascular disease. Am J Med 2011; 124:621-9.
18. Richman IB, Owens DK. Aspirin for primary prevention. Med Clin North Am 2017; 101:713-24.
19. Botting RM. Vane's discovery of the mechanism of action of aspirin changed our understanding of its clinical pharmacology. Pharmacol Rep 2010;62:518-25.