COMBINED THERAPY OF PEDIATRIC BACTERIAL MENINGITIS WITH THE USE OF CORTICOSTEROIDS AND ANTIBACTERIALS: A BIBLIOGRAPHICAL REVIEW

Terapia combinada da meningite bacteriana pediátrica com o uso de corticoesteroides e antibacterianos: uma revisão bibliográfica

Anna Bárbara Ribeiro de Araújo¹
Raquel Santos Oliveira²
Folmer Quintão Torres¹
Jânio Eduardo Siqueira²
Joanilva Ribeiro Lopes³

Abstract: Bacterial meningitis in childhood is an infection that requires special care and immediate intervention, as it can cause severe sequelae in the child, which can lead to death. The idea of the use of corticosteroids and antibacterial in the combined therapy of this infection is discussed. The objective of the present article was to present a review of the literature with a detailed approach regarding the combined therapy of bacterial meningitis, through corticotherapy and its effects on the child. After analyzing the articles, it was concluded that the results of corticosteroid use in bacterial meningitis are still controversial, since there is no consensus of its benefits in the combined therapy of meningitis. There is a need for a larger number of studies to evaluate the efficacy of corticosteroids in the therapy of this infection and its action on other etiological agents, that is, the therapy should be broad-spectrum; not only for Haemophilus influenzae type B.

Keywords: Bacterial meningitis; Corticosteroid; Anti-bacterial; Combination therapy.
**Resumo:** Meningite bacteriana na infância é uma infecção que necessita de cuidados especiais e de intervenção imediata, pois pode causar sequelas graves na criança, podendo levar ao óbito. Discute-se a ideia do uso de corticoesteroide e dos antibacterianos na terapia combinada dessa infecção. O objetivo do presente artigo foi apresentar uma revisão de literatura com uma abordagem detalhada em relação à terapia combinada da meningite bacteriana, através da corticoterapia e de seus efeitos na criança. Após análise dos artigos, concluiu-se que os resultados do uso de corticoesteroide na meningite bacteriana ainda são controversos, pelo fato de não haver um consenso de seus benefícios na terapia combinada da meningite. Verifica-se a necessidade de um número maior de pesquisas para avaliar a eficácia da corticoterapia na terapêutica dessa infecção e sua ação em outros agentes etiológicos, ou seja, a terapia deve ser de amplo espectro; não somente para o *Haemophilus influenzae* tipo B.

**Palavras-chave:** Meningite bacteriana; Corticoesteroide; Antibacteriano; Terapia combinada.
INTRODUCTION

Bacterial meningitis is an infection that affects the Central Nervous System (CNS) with a prevalence of 0.9 to 2.6 per 100,000 per year in adults in developed countries and higher incidence in underdeveloped countries. *Streptococcus pneumoniae* (*pneumococcus*) is the most frequent agent of meningitis caused by bacteria acquired in the community in 70% of cases in adults. In children younger than 5 years of age, the bacterial infection is also the main cause of meningitis and, among the main pathogenic agents, gram-positive bacteria, especially, *S. pneumoniae* is responsible for about 6% of cases. Long-term sequelae, including blindness, deafness, cerebral palsy, seizures, disabilities, hydrocephalus are still high after recovery and present in approximately 25-50% of survivors.

The pathophysiology of neurological injuries is due to the severity of inflammation in the cerebrospinal fluid (CSF) which can be alleviated with the use of systemic corticosteroids. The etiology in children depends on the age, the immunity and epidemiology. Younger than 1 month to 3 months old: (Neonatal pathogens from the intestinal and maternal urinary flora): *Streptococcus agalactiae* (grupo B), *Gram-negative Bacillus* (*E. coli*, *Klebsiela*), *listeria and enterococcus*. From 3 months old: *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae type B*.

The diagnosis of this infection in children is based mainly on clinical evaluation of the patient and exams, through the analysis of the cerebrospinal fluid (CSF) except when there are contra-indications; identification of the antigen by polymerase chain reaction (PCR), computed tomography of the skull to assess the brain impairment.

In this context, due to the importance of bacterial meningitis in childhood by being an infection which needs special care and immediate intervention, besides causing serious consequences for the child, and may lead to death, the goal of this article is to present a literature review with a detailed approach in relation to the combined therapy of bacterial meningitis, through the corticotherapy and its effects on the child, from a bibliographic research of scientific articles available in the databases Virtual Library of Health, PubMed, UpToDate and JAMA.

LITERATURE REVIEW

The combination therapy of bacterial meningitis must be started from the moment it is diagnosed, as it can cause serious consequences, such as the intracranial hypertension. The antibacterials are the treatment of choice, and cephalosporins of 3° generation the most used. In addition, the corticosteroids are also used in order to avoid the progression of neurological complications, although there are controversies about its use.

The corticosteroid dexamethasone is commonly used prior to administration of the antibacterial in meningitis, because it acts in reducing the inflammatory response against bacteria killed by another therapy. The dead bacteria release pro-inflammatory cykines which may lead to a harmful reaction for the patient, however, the corticosteroid improves the prognosis and outcome of infection. Nevertheless, the corticosteroid does not have
broad spectrum for all etiological agents, as the Committee of Infectious Diseases of the American Academy of Pediatrics (AAP) claims that the treatment with dexamethasone may be beneficial in children with meningitis caused by *Haemophilus influenzae* type B (Hib) if administered before or concurrent with the first dose of antimicrobial therapy.

Ygberg et al. (2016) observed the effects of the use of Glucocorticosteroids in combination therapy of bacterial meningitis in a retrospective study of 10 years with 44 children with this infection. All children received cefotaxime as empirical antibiotic, 26 received betamethasone, 14 received dexamethasone and 4 used other Glucocorticosteroids. The children who received powerful and suitable Glucocorticosteroids - betamethasone or dexamethasone had auditory deficit significantly smaller in relation to those who used another or no corticosteroid (18% versus 50%; P = 0.032). At the end of the study, it was concluded that corticosteroids reduce hearing deficits and neurological sequelae after bacterial meningitis in all ages. On the other hand, Kaplan et al. (2014), in their work, report that in a meta-analysis of 2015 which included 2511 children it was discovered that the administration of dexamethasone did not interfere in mortality, but reduced the incidence of severe hearing loss in children with bacterial meningitis, but those whose etiological agent was the *Haemophilus influenzae* type B.

According to Ogunlesi et al. (2015), the administration of adjuvant corticosteroids reduced the risk of death among neonates with bacterial meningitis; although there is a trend toward an increase or worsening the results in relation to sensorineural deafness at two years of age, however, this difference is not statistically significant. However, dexamethasone is not indicated in the combination therapy of bacterial meningitis in infants less than six weeks or with congenital or acquired abnormalities of the central nervous system. Also, it is not indicated in combination therapy of patients in whom is suspicious of enteric, non-bacterial or gram-negative meningitis. If begun before the diagnosis, the corticotherapy should be stopped as soon as the diagnosis of enteric, non-bacterial or gram-negative meningitis is confirmed.

In addition, studies demonstrated that the corticoestroides may have toxic effects to the cultures in cortical and hippocampus neurons. The corticotherapy increases hippocampal apoptosis and leads to learning disabilities. Moreover, Engelen-Lee et al. (2016), report in their article an experimental study of pneumococcal meningitis in which was identified apoptosis in the hippocampus of rats treated with dexamethasone in association with the deficiency of learning.

**FINAL CONSIDERATIONS**

After the articles analysis, it was concluded that the results of using corticosteroid in bacterial meningitis are still controversial, due to the fact that there is no consensus of its benefits when it comes to combination therapy in meningitis. There is a need for a larger number of studies to evaluate the efficacy of corticosteroids in the therapy of this infection and its action on other etiological agents, that is, the therapy should be broad-spectrum; not only for *Haemophilus influenzae* type B.

There are no conflicts of interests.

**REFERENCES**

1. ENGELEN-LEE, J. Y. *et al.* Pneumococcal meningitis: Clinical-pathological correlations


