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Steroid Therapy for Bacterial Meningitis in Children- A Review Article

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Abstract

Background- Children under the age of five are most likely to contract meningitis, with young people between 15 to 19 experiencing a lower peak in frequency. The incidence of sickness brought on by these strains has decreased since the Haemophilus influenzae type b (Hib) and group C meningococcus vaccines were added to the pediatric immunization schedule decrease in pathogens all ages with acute bacterial meningitis.

Objectives- To examine the most recent research on the efficiency and safety of using corticosteroids to treat young patients with acute bacterial meningitis.

Methods- Randomised controlled trials (RCTs) of corticosteroids for acute bacterial meningitis was done. We searched CENTRAL, MEDLINE, Embase, Web of science,CINAHL and LILACS so among literature four evidence based meta-analysis was selected in which 25 studies were quality based studies, We scored RCTs for methodological quality. We collected outcomes and adverse effects. We performed subgroup analyses for children and adults, causative organisms, low-income versus high-income countries, time of steroid administration and study quality.

Results- Four studies were of high quality with no risk of bias, 14 of medium quality and seven of low quality, indicating a moderate risk of bias for the total analysis. Nine studies were performed in low-income countries and 16 in high-income countries. There was insufficient evidence that corticosteroids caused a reduction in mortality overall (17.8% versus 19.9%; risk ratio (RR) 0.90, 95% confidence interval (CI) 0.80 to 1.01; P = 0.07), or for children (RR 0.74, 95% CI 0.53 to 1.05; P = 0.09). However they caused lower rates of severe hearing loss (RR 0.67, 95% CI 0.51 to 0.88), any hearing loss (RR 0.74, 95% CI 0.63 to 0.87) and neurological sequelae (RR 0.83, 95% CI 0.69 to 1.00). Corticosteroid treatment was associated with an increase in recurrent fever (RR 1.27, 95% CI 1.09 to 1.47), but not with other adverse events.

Conclusion- Corticosteroids significantly reduced hearing loss and neurological sequelae, but did not reduce overall mortality. Over time, the evidence has changed about the possible usefulness of corticosteroids (usually dexamethasone) for kids with bacterial meningitis in affluent nations. It now suggests that when Haemophilus influenzae type b is the origin of the meningitis, such medication aids in preventing hearing loss (Hib).

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Introduction-

Meningitis, an inflammation of the brain and spinal cords lining, is frequently brought on by a bacterial infection. Individuals who have bacterial meningitis commonly exhibit a past medical history of fever, headache, and stiff neck. They frequently exhibit a reduced level of consciousness or a changed state of mind.[1] In young children, especially babies, the traditional signs of meningitis, such as photophobia, nuchal rigidity, or positive Kernig and Brudzinski signs, may not be present; instead, the symptoms may just include fever and trouble feeding. Meningitis and septicemia may happen separately or simultaneously in patients with invasive meningococcal infection, although the typical petechial or purpuric rash of meningococcal septicaemia may appear.[2] Importantly, meningococcal meningitis can still occur even in the absence of a rash. Bacterial meningitis has a fatality rate of between 10% and 30%.[3] Late in 5 to 40% of patients, problems such cranial nerve damage, particularly hearing loss, occur.

Causes of Bacterial Meningitis

Neisseria meningitidis (meningococcus), Streptococcus pneumoniae, and Hib are the most frequent causes of meningitis. Although being more typical in underdeveloped nations, susceptible to tuberculous meningitis, which poses a significant risk of mortality and morbidity, as well as sequelae like cognitive decline, learning disabilities, and movement impairment. [4] In 2006, the Strep. pneumoniae (pneumococcus)-targeted Pneumococcal Conjugate Vaccine (PCV) was added to the list of recommended pediatric vaccinations. [2]The incidence of invasive disease caused by pneumococcus has significantly decreased since the introduction of this vaccine. Group B meningococcus continues to be a leading source of sickness, and efforts to develop a vaccine have so far been unsuccessful due to the group B polysaccharide capsular antigens' low immunogenicity.[5]

Basic Management of Bacterial Meningitis in Children

Early identification, quick screening for indications of septicaemia, shock, or elevated intracranial pressure, and urgent intravenous antibiotic therapy (such as benzylpenicillin, Cefotaxime; cautious resuscitation; and, if necessary, diagnostic imaging and lumbar puncture evaluation of the cerebrospinal fluid (CSF). CSF sampling via lumbar puncture is helpful to make the diagnosis and determine the best course of treatment for a patient with probable meningitis who is not startled and shows no symptoms that would suggest risk of cerebral herniation. Nonetheless, such research should not postpone the use of antibiotics. In cases with meningococcal sepsis that have already been diagnosed, a lumbar puncture is unlikely to offer any diagnostic information and may even worsen cardiorespiratory instability. Patients with signs of raised intracranial pressure or septic shock should be admitted to an intensive care unit following initial resuscitation, stabilisation and antibacterial therapy.

Role of Corticosteroids

It is believed that inflammation in the brain is responsible for the increased frequency of neurological problems following bacterial meningitis (despite receiving effective antibacterial therapy) the subarachnoid region.

Short-term adjuvant corticosteroid therapy, such as dexamethasone, has been recommended as a way to avoid neurological problems because it has been shown in animal tests to minimize this inflammation. [6] A counter-argument against employing corticosteroid

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therapy \sis the fact that inflammation of the blood-brain barrier enhances the passage of some antibacterial drugs \s(e.g. vancomycin or ceftriaxone) into the CSF. [7,8]

Any dexamethasone-induced reduction in blood-brain barrier inflammation could hinder antibacterial medications' ability to quickly sterilize the CSF, which is necessary for efficient treatment of bacterial meningitis. [7]

Moreover, the immune response is altered if bacteriostatic antibacterial medications (such as chloramphenicol) rather than bactericidal ones are utilized is crucial for killing bacteria that the antibacterial medication does not eradicate, and dexamethasone's immunosuppression may hinder the body's capacity to get rid of these bacteria. [9] Additional potential negative consequences of corticosteroids include the potential to hide other diseases or have undesirable side effects such gastrointestinal bleeding. These contradicting factors have added to the confusion around the use of corticosteroids in pediatric bacterial meningitis.[3]

Statistical Analysis-

We analysed the data using Review Manager 5.3 (RevMan 2014). We performed meta-analyses using the Mantel-Haenszel method with a fixed-eJect model when heterogeneity was absent.

Evidence for Steroids in Management of Bacterial Meningitis in Children

Corticosteroids with bacterial meningitis: Data from several meta-analyses has been gathered over time. However, how these statistics should be interpreted has been confounded by elements including the variance in medications and treatment plans utilized, the distinctions between the patient populations studied, and the possible impact of the research' locations being in developed or developing nations.

Evidence of First Meta-analysis

Due to the inconsistent results of the early trials testing the effectiveness of corticosteroids in treating pediatric meningitis, a meta-analysis of these studies was published in 1989. [10] This comprised information from all nine known randomised controlled studies that had been conducted between 1958 and 1988 in industrialized nations, involving 846 patients, and were published. The other studies either included children or solely involved children, while one research only involved individuals over the age of 16. Six studies were double-blind and placebo-controlled; the others lacked either of these design elements. Dexamethasone was the subject of four investigations, hydrocortisone of four, and methylprednisolone of one.

Corticosteroids did not significantly lower mortality (corticosteroid minus control rate = 0.1%, 95% CI -3% to +3%) or the risk of neurological disorders in the studies including children anomaly at follow-up (difference -3%, 95% CI -11% to +5%) or discharge from the hospital (difference -9%, 95% CI -20% to +1%). Only three trials (all including children) evaluated auditory function, and the associated meta-analysis revealed that corticosteroids reduced the frequency of moderate to severe bilateral hearing loss (difference -9%, 95% CI -15% to -3%). On this specific outcome measure, only one of the three trials (a dexamethasone study) had discovered a meaningful difference.

Evidence of Second Meta-analysis

In 1992, a second meta-analysis with six trials (the four that evaluated dexamethasone in the previous meta-analysis plus two more trials; total number of trials) was released. Patients not identified), all in industrialized nations.[9] Results revealed that in the three studies involving only children and reporting this outcome measure, the probability of dying from the infection

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did not change significantly between the dexamethasone and control groups (relative risk [RR] for placebo group 1.03, 95% CI 0.27-3.89). However, analysis of the children-only trials showed that the placebo group was more likely than those using dexamethasone to experience neurological side effects (RR up to 6 weeks: 1.99, 95% CI 1.13-3.53; RR more than 6 months after discharge: 3.90, 95% CI 1.72-8.85).

Evidence of Third Meta-analysis

In a third meta-analysis, information from eleven dexamethasone randomized controlled trials conducted between developed and developing nations between and was included. From 1988 and 1995, there were a total of 848 patients (five of whom were in the earlier meta-analyses and six more studies). [11] For 526 patients with Hib, 125 patients with N. meningitidis, and 122 patients with S. pneumoniae (the organisms in the other patients were unknown or not described), data were analyzed by causal organism. Dexamethasone treatment reduced the risk of severe hearing loss in Hib meningitis patients (3.1% vs. 11.6% in controls, odds ratio [OR] 0.31, 95% CI 0.14-0.69). Neurological deficits other than hearing loss, and adverse effects, were not significantly different between groups. The authors concluded that dexamethasone was beneficial in Hib meningitis, and a benefit was suggested in pneumococcal disease if the corticosteroid was started before antibacterial therapy.

Evidence of Fourth Meta-analysis

20 randomised controlled trials (published between 1963 and 2002) including a total of 2,697 patients (623 adults, and 2,074 kids in 17 trials, including 7 that were part of one or more of the aforementioned meta-analyses and an additional 10 studies, had acute bacterial meningitis in both industrialized and developing nations.[3] The selected studies had high standards of quality, and there was little to no substantial heterogeneity among them. Death, significant hearing loss (bilateral hearing loss higher than 60 dB or requiring bilateral hearing aids), and other neurological problems were the main end measures. Clinically obvious gastrointestinal bleeding, reactive arthritis, pericarditis, herpes zoster or herpes simplex virus infection, fungal infection, and subsequent fever were all considered adverse effects.

Dexamethasone decreased the probability of severe hearing loss (5.7% vs. 9.8%, RR 0.65, 95% CI 0.44-0.91) and death overall (13.4% vs. 16.1%, RR 0.83, 95% CI 0.71-0.99), but not of death.Some neurological issues were unaffected.

Unwanted occurrences were not significantly different, and those using corticosteroids were not more likely to experience gastrointestinal bleeding in particular. Dexamethasone treatment resulted in a considerably lower incidence of hearing loss in children (from 11.0% to 6.6%, RR 0.61, 95% CI 0.44-0.86), but there was no difference in the incidence of other neurological problems or mortality, according to the subgroup analysis for children.

A decrease in severe hearing loss (3.5% vs. 10.2%, RR 0.37, 95% CI 0.20-0.68) was seen in subgroup analysis for the 663 children who had meningitis caused by H. influenzae. Nevertheless, in the 660 cases of meningitis caused by other bacteria, there was no statistically significant difference for severe hearing loss. In reality, the etiologic agent is frequently unknown until the course of treatment is initiated. As a result, the authors came to the conclusion that dexamethasone should be administered regardless of the bacterial cause.[11,12]

Dexamethasone was administered four days in a row (0.1 or 0.15 mg/kg every hour) in the majority of the trials that made up this meta-analysis, and there was no sign of an increase in

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side effects. Therefore, the authors of the analysis suggested using a 4-day regimen of 0.15 mg/kg every 6 hours, administered before to or concurrently with the first dose of an antibiotic. There were no studies on kids younger than a month old included in this meta-analysis. The authors came to the conclusion that since this particular group of individuals had newborn meningitis and varied etiologies, it was not advised to utilize corticosteroids in this case.[12]

Conclusions-

Over time, the evidence has changed about the possible usefulness of corticosteroids (usually dexamethasone) for kids with bacterial meningitis in affluent nations. It now suggests that when Haemophilus influenzae type b is the origin of the meningitis, such medication aids in preventing hearing loss (Hib). There is no evidence to back up earlier reports of a similar advantage in pneumococcal disease, and there is also no proof that corticosteroids are helpful in other bacterial meningitis infections. Additionally, where (as is typical) the causative organism is not known for sure at presentation, the likelihood of any benefit of using corticosteroid therapy may be reduced or even eliminated due to the marked decreases in Hib and pneumococcal meningitis infections attributable to the childhood immunization schedule. Notwithstanding these issues, it is reasonable based on the most recent data to administer dexamethasone to any infant older than one month who presents with bacterial meningitis who do not have a meningococcal rash; the justification for this is that the infection could be caused by Hib, and the risk of side effects from such treatment appears to be minimal. Hence, dexamethasone (0.15 mg/kg intravenously every six hours for four days) should be given before or together with antimicrobial therapy but not afterwards. Dexamethasone and antimicrobial medication should not be delayed because of the choice to perform a lumbar puncture. Corticosteroids do not appear to be clearly beneficial for children with bacterial meningitis, according to research compiled from poor nations.

Conflict of Interest- None declared

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