EVIDENCE BASED PRACTICE - COCHRANE REVIEWS

ADJUNCTIVE steroids in pulmonary TB


Background
Tuberculosis (TB) is a chronic infectious disease which causes a high mortality and morbidity burden worldwide. In 2012, approximately 1.3 million deaths and 8.6 million disease episodes were due to TB. TB is broadly classified as being pulmonary or extra-pulmonary dependent upon the site of infection. Pulmonary tuberculosis (PTB) affects the lung or lymph nodes at the site of primary infection (usually the lung and upper respiratory tract) while extra-pulmonary TB describes TB disease which affects other areas of the body.

TB infection initiates an inflammatory immune response that itself causes considerable tissue damage. Adjunctive steroid therapy may be used to counteract this, especially where inflammatory disease complicates recovery. Clinical guidance advises the use of adjunctive steroid therapy for treatment of TB meningitis and TB pericarditis (NICE 2006; WHO 2009). However, when given without anti-TB treatment, steroids can actually promote the activation of TB disease. There is also evidence that concurrent administration of anti-TB drugs and steroids causes pharmacokinetic interactions that hinder efficacy of both drugs thus impairing clinical outcomes. Approximately 79% of global TB cases are pulmonary, as such it is important to know whether or not there is a benefit from using steroids in treatment of pulmonary TB.

Objectives
To evaluate whether adjunctive corticosteroid therapy reduces mortality, accelerates clinical or microbiological recovery in people with pulmonary tuberculosis.

Search methods
At least two investigators independently assessed trial quality and collected studies indexed from 1966 up to May 2014. Randomized controlled trials and quasi-randomized control trials of recognized antimicrobial combination regimens and corticosteroid therapy of any dose or duration compared with either no corticosteroid therapy or placebo in people with pulmonary tuberculosis were included. They identified 18 trials, including 3816 participants.

Main results
When compared to taking placebo or no steroid, corticosteroids did not reduce mortality from pulmonary tuberculosis.

Compared to placebo or no steroid, adjunctive steroid therapy was associated with a significant 16% increase in clinical improvement at one month. However, there was no difference in sputum conversion at two months, sputum conversion at 6 months, failure rate or relapse rate. Significant short term clinical benefits of corticosteroid use were not maintained in the long term.

Corticosteroid use was found to increase weight gain and decrease length of hospital stay.

Authors’ conclusions
1. It is unlikely that adjunctive corticosteroid treatment provides major benefits for people with pulmonary tuberculosis.

2. Short term clinical benefits found did not appear to be maintained in the long term.
Discussion:

TB incidence has remained high in some parts of the world. One of the key drivers of TB rates over recent decades has been the HIV epidemic, yet only one trial identified was carried out amongst HIV positive pulmonary TB patients. Corticosteroids are a very cheap intervention, and might have the potential to improve TB treatment outcomes amongst those with advanced disease especially in resource poor settings, where pulmonary TB case-fatality remains high.

However, it should also be noted that corticosteroids can cause severe adverse effects, and the benefit to risk ratio of their use for pulmonary TB remains unclear. Further adequately powered, well-designed RCTs for adjunctive steroid use in HIV positive, immuno-compromised and immuno-competent patients are needed before robust conclusions upon the potential benefits of this intervention can be made.

Expert comments from CMC faculty - Steroid use in Tuberculosis

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Administrations of steroids in management of tuberculosis is a double-edged sword. It can be beneficial as well as harmful. During tuberculosis infection the host immune system mounts an inflammatory response, which is intended to kill the bacteria and control the infection. But this inflammation per se can cause considerable tissue damage and necrosis. Steroids by reducing this immune response try to control the tissue damage. But immunosuppression by steroids is a well-established risk factor for developing tuberculosis disease. Also administration of steroids with antituberculous drugs can hinder the efficacy of both drugs by pharmacokinetic interactions.

Adjunctive anti-inflammatory therapy with glucocorticosteroids is the standard of care in tuberculous meningitis. But role of steroids in management of pulmonary tuberculosis is more controversial. This Cochrane review tries to address this question. (1) What is made clear in this review is that there is no mortality benefit with administration of corticosteroids in pulmonary tuberculosis, nor there is any difference in sputum conversion rate. There are some short-term clinical benefits, which were not maintained in the long term.

Our current practice of not giving steroids in pulmonary tuberculosis is valid. But in a sick patient who is in respiratory failure or has developed Acute Respiratory Distress Syndrome (ARDS) due to tuberculosis there is a role for steroids. Short-term steroids along with ATT will help to tide over the crisis and hasten immediate clinical response. Also steroids have a role when patient develop significant Immune Reactivation Inflammatory Syndrome (IRIS) especially in patients infected with HIV. Whenever steroids are used, due attention needs to be given for the side effects especially hyperglycaemia and they have to be tapered depending on the clinical response.

Studies in tuberculous meningitis have shown that polymorphism in eicosanoid pathway is associated with the degree of inflammation and patients with pro-inflammatory genotype respond better to adjunctive steroid therapy. (2) With more research in this area we may be able to predict which subset of patients will benefit with steroids and personalized treatment can be given.

References


Anger is the fluid that love bleeds when it is cut.

C.S. Lewis