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Research Article – Medicine

Role of corticosteroids in treatment of neurotuberculosis

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Introduction

Neurotuberculosis is a common neurological disorder in developing countries. Among all patients of neurotuberculosis, tubercular meningitis is an important manifestation with high morbidity and mortality[4]. Diagnosis is based on clinical features, C.S.F. changes, & imaging. Polymerage chain reaction shows promise for the future. Appropriate chemotherapeutic agents should be given as early as possible. Role of corticosteroids is controversial but should be administered to all patients presenting in stage III[1]. Surgical procedures are directed only when, hydrocephalus, focal lesions, intracranial tuberculomas, and tuberculous abscesses, are located in cerebral or cerebellar hemispheres, uncommonly in brainstem and very rarely in spinal cord but usually surgical intervention is not required. Almost all patients respond well to medical management (ATT, ATT+Corticosteroids). The patients who received ATT+steroids (oral steroids in tapering doses over a period of 4-6 weeks) showed early symptomatic & therapeutic response & the recovery was smooth over period[1].

Increasing prevalence of HIV infection, in today's scenerio, in underdeveloped countries contributes to prevelance of Neurotuberculosis[4].Other important risk factors includes over-crowding of urban population, poor nutritional status, appearance of drug-resistant strains of tuberculosis, ineffective tuberculosis control programmes, and increase in migration from countries where tuberculosis is prevalent to the developed world.

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Material and Method

The present study was carried out on 50 cases (35 males & 15 females), of various forms of neurotuberculosis, admitted in various wards of NIMS medical college & Hospital from a period of April 2012 to June 2015.Control subjects total 30 (15 males & 15 females) were in-patients with disorders other than tubercular neurological involvement.

Those patients were selected for studies that were having:-

1. Detection of antigen with clean specimens such as cerebrospinal and pleural fluids or

2. Detection of specific components of *Mycobacterium tuberculosis* by linked gas chromatography and mass spectroscopy or

3. Detection of specific DNA sequences of *M. tuberculosis* in specimens by use of labelled 'DNA sensitivity, by use of the polymerase chain reaction to amplify small amounts of the specific DNA.

4. Adenosine Deaminase (ADA): ADA is an important enzyme in purine metabolism; irreversibly deaminates adenosine to inosine. It is associated with lymphocytic proliferation and differentiation and is a marker of cell mediated immunity. Two isoforms ADA1 and ADA2 are known. ADA2 is the major contributor to the total ADA seen in TBM. Sensitivities andspecificities range from 73-100% and 71-99% respectively.

Table 1: Age at presentation and gender distribution of Neurotuberculosis

Sex	Mean age	Range	SD
Male(35)	17.6	11-48.5	0.31
Female(15)	15.4	10-45.1	0.23

Table 2: Student 'T' Test & 'P'values for two types of Therapy

	ATT ONLY			ATT + STEROIDS		
	t	df	p	t	df	p
Male Normal v/s Patients	2.29	18	>0.51	7.63	18	>0.001
Female Normal v/s Patients	3.21	16	>0.60	7.81	16	>0.001

5. *Radiological Evaluation:* Every patient with TBM was evaluated with contrast enhanced CT/MRI before the start or within 1st 48 hr of treatment. An abnormality depends on the stage of the disease.Hydrocephalus (70-85%), basal meningeal enhancement (40%), infarction (15-30%), tuberculoma (5-10%)[4].

Other non specific indicators of tuberculosis were discarded (like bromide partition test)

Clearcut diagnosed and primarily treated cases were selected for the study.All the patients admitted for any reason to ICU were NOT taken in this study.

RESULTS

The survival rate was 100%, & none patient required ICU management.These patients were hospitalised for fairly enough time for symptomatic relief, and then followed initially fornightly,then monthly till end of therapy, and finally all relevent investigation were performed to observe a satisfactory outcome before stopping their treatment & allowing them to live normal routine.

Discussion

CNS tuberculosis is secondary to disease elsewhere in the body. Mycobacteria reach the brain by hematogenous route. The disease begins with the development of small tubercular foci (Rich foci) in the brain, spinal cord or meninges. According to British Tuberculosis Society and American Tuberculosis Society duration of treatment is 9-12 months. Ethambutol should be replaced by Streptomycin. Intensive phase (2 months) — Isoniazid, Rifampicin, Pyrazinamide and Streptomycin. Continuation phase (7-9 months) – Isoniazid and Rifampicin.

Out of the 30 control individuals,the patients neighter needed ATT, or ATT with steroids or steroids for any detectable reason. And these patients responded well to the specific treatment they were given for their respective illnesses other than tuberculosis.

In patients with neurotuberculosis, male & female patients didn't show any difference in treatment variability, with two different groups. One with ATT alone & another with ATT + steroids in routine standard doses (Dexamethasone 0.4mg/kg body weight IV during hospitalisation, followed by Prednisolone orally in doses of 1mg/Kg body weight, in tapering doses over a period of 4-6 weeks).

FIRST LINE ATT: Daily Dose in Children & Adults:

Isoniazid 10-20 mg/kg= 300 mg; Rifampicin 10-20 mg/kg =450mg (<50 kg) =600mg (>50 kg); Pyrazinamide 30-35 mg/kg =1500 mg (<50 kg) =2000 mg (>50 kg); Streptomycin 20-30 mg/kg. Isoniazid in doses of 15mg/kg penetrates the CSF freely and has potent early bactericidal activity. Resistance to Isoniazid develop quickly if used as a monotherapy. Rifampicin penetrates the CSF less well, but its key role in t/t of CNS tuberculosis is very well estabilished[4].

TNF alpha play a important role in pathogenesis and leads to altered blood brain barrier permeability and CSF leukocytosis. The use of corticosteroids as adjunctive therapy in t/t of CNS tuberculosis begins as early as 1950[1]. It was proposed that steroids causes reduction of inflammation within subarachnoid space. It causes modulation of the local production of proinflammatory cytokines and chemokines by microglial cells. But the exact mechanism is not clear.

Adults (>14 years) should start treatment with dexamethasone 0.4 mg/kg/24 hr IV during hospitalization, followed by prednisolone 1mg/kg bodyweight/day orally (after meals)with a tapering course over 6-8 weeks. High CSF ADA activity has been reported in patient with lymphoma, malaria, brucellosis, pyogenic meningitis and cerebral lymphoma. The Infectious Disease Society of America, CDC and ATC recommend the use of Steroid therapy as an adjunctive therapy with standard anti tuberculosis therapy in CNS affection with mycobacterium[4].

Summary

50 cases (35 male & 15 females) of neurotuberculosis (various forms), were subjected to ATT, ATT+steroids and studied along with 30 control hospitalised patients.

Our study shows close co-relation with other authors from India in treating un-complicated various forms of neurotuberculosis,where addional benifit was found by adding steroids to ATT for initial 4-6 weeks,without causing any side-effects, except in special circumstances.

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