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Rational Use of Dexamethasone in Tuberculous Meningitis

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Abstract:

Rational use of drugs is to ensure right drug given to right patient in right dose, at right time using right route. Tuberculous meningitis (TBM) is one of the life threatening forms of tuberculosis with high morbidity, mortality and complication rate. It affects all ages and socio-economic classes. It is caused by *Mycobacterium tuberculosis.* Clinical features include fever, headache, meningism, vomiting, malaise, decreased consciousness, fits, cranial nerve palsies, and strokes. Investigations are done using CSF for lab tests, and CT and MRI. Management includes Anti-TB drugs & steroids. The rationale behind the use of adjuvant corticosteroids lies in reducing the harmful effects of inflammation as the antibiotics kill the organisms. During treatment I/V Dexamethasone is given as adjuvant therapy and after discharge, Prednisolone is prescribed orally. Dose tapering is done to avoid complications of withdrawal symptoms. Shunt Surgery may be prescribed if patient is not responding to the therapy.

Key words: *TBM, management of TBM, Dexamethasone, Rational use, Steroid.*

Introduction:

Tuberculous meningitis is the most serious form of tuberculosis and carries a high mortality and morbidity despite the availability of effective chemotherapeutic agents. Poor response to therapy or death is often due to failure to begin appropriate therapy in the early stages of the disease.[1] TB meningitis normally begins with vague, non-specific symptoms of aches and pains, low-grade fever, generally feeling unwell, tired, irritable, not being able to sleep or eat properly, and gradually worsening headache.[2] HIV infection appears to have little impact on the findings and in-hospital mortality of tuberculous meningitis, With the exception of an increased incidence of intracerebral mass lesions in HIV-infected individuals.[3] Vaccinated and unvaccinated group of patients have no difference in terms of severity of clinical presentation and outcome. No significant differences in CT or MRI findings between the 2 groups were present except for tuberculomas on MRI, which were significantly higher in the non—bacille Calmette-Guerin vaccinated group. Bacille Calmette-Guerin vaccination appears to translate into less tuberculoma formation on MRI. [4] In adults with suspected bacterial meningitis without the described risk factors, performing immediate spinal tap and blood culture is likely the best management. In the presence of baseline risk factors, management should be blood culture (which may be positive even when spinal cultures are negative), intravenous antibiotics, and then CT scan, followed by spinal tap unless the CT scan indicates increased risk for cerebral herniation. [5] Hydrocephalus is one of the commonest complications of tuberculous meningitis (TBM). It is more severe in children than in adults. It could be either of the communicating type or the obstructive type with the former being more frequently seen. The management of hydrocephalus can include medical therapy with dehydrating agents and steroids for patients in good grades and those with communicating hydrocephalus. However, surgery is required for patients with obstructive hydrocephalus and those in poor grades. [6] Antituberculosis therapy should be promptly initiated in any young infant with a clinical impression of meningitis in the context of cerebrospinal fluid white cell count of less than 500 cells/mm3 and lymphocytic predominance, hyponatremia, and hydrocephalus.[7] Use of adjunctive corticosteroids has shown benefit in reducing mortality and morbidity for certain pathogens in developed countries. But dexamethasone should be reserved for patients for whom rapid confirmation of bacterial meningitis is possible. [8] Corticosteroids are recommended if the patient is mentally confused, has neurologic signs, or is comatose (Stages II and III). In patients with moderate disease (Stage II), corticosteroids appear to

improve neurologic sequelae and survival. Dexamethasone 6 to 12 mg per day and prednisone 60 to 80 mg per day tapered over 4 to 8 weeks has been used. Symptoms of central nervous system (CNS) inflammation may recur if the corticosteroid taper is implemented too soon or too fast. Steroids and diuretics such as furosemide and acetazolamide are sometimes used to treat hydrocephalus. Ventriculoperitoneal or ventriculoatrial shunting may be required to relieve signs and symptoms of hydrocephalus. [9] The lysis of bacteria with the release of bacterial cell-wall components in the subarachnoid space induces meningeal inflammation by stimulating the production of inflammatory cytokines. The presence of inflammatory cytokines in the subarachnoid space leads to several pathophysiologic consequences. Inflammatory cytokines recruit polymorphonuclear leukocytes from the bloodstream that cause vasculitis-induced stroke. Inflammatory cytokines also increase the permeability of the blood-brain barrier, allowing leakage of serum proteins and formation of an inflammatory exudate and obstructive hydrocephalus. Dexamethasone exerts its beneficial effect by inhibiting synthesis of the inflammatory cytokines and by decreasing CSF outflow resistance and stabilizing the blood-brain barrier. The goal of adjunctive therapy with dexamethasone in bacterial and mycobacterial meningitis is to attenuate the inflammatory response. The recommended dose of dexamethasone for adults with bacterial meningitis is 0.15 mg/kg every 6 hours intravenously for 4 days. [10] Dexamethasone may affect outcome from tuberculous meningitis by reducing hydrocephalus and preventing infarction. The effect may have been under-estimated because the most severe patients could not be scanned. [11] Treatment guidelines must be applied to the individual patient, considering the patient's initial condition, likelihood of drug resistance, and HIV coinfection. Steroids are also useful in patients with TM alone who respond to treatment but who have a paradoxical expansion of existing tuberculomas or who develop new tuberculomas. [12]

Materials and Methods:

Fourty patients with complaints of Tuberculous meningitis of Medical wards of Mayo Hospital Lahore and Services Hospital Lahore from 14 June to 2 July 2010 were studied. A questionnaire was designed to get all the important and relevant information from the patient or their relative about disease. After detailed history, patient's medical history and all the important data was collected including complications, diagnosis, tests done and the treatment prescribed to the patient according to his condition. Side effects of the treatment with antibiotics and steroids if any were also observed. The ratio was very low as dose tapering with steroids and dose calculation of Antibiotics and Antituberculour drugs was done. Occasionally, some patients were prescribed Surgery if they are not responding to the treatment.

Result:

Important factors related to rational use of Dexamethasone were observed and some other important disease parameters were also noted, some are in form of graphs as follows:

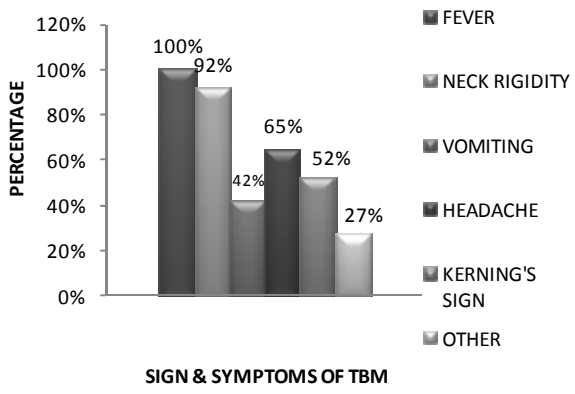

Fig.1. Graph showing frequency of sign & symptoms of TBM in patients. (Fever 100%, neck rigidity 92%, headache 65%)

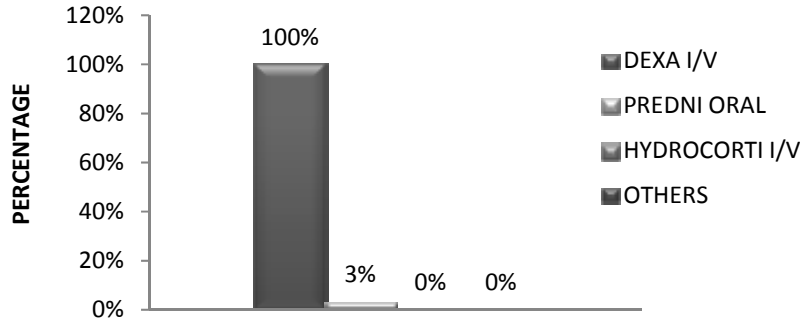

Fig.2 Graph showing ratio of Steroid used in TBM treatment. (Dexamethasone 100%)

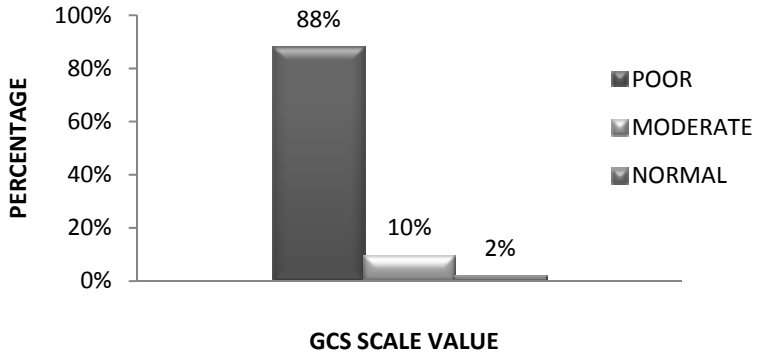

Fig.3. Graph showing GCS value for TBM patients. (88% patients were unconscious)

Discussion:

Tuberculosis is a serious disease of global importance with a rising incidence in the developing as well as developed countries in the recent years. Although it affects both males and females equally but it is observed in our study that 58% patients were females. .

Tuberculous meningitis is associated with a high morbidity and mortality if there is a delay in diagnosis and if treatment is started late. This is mostly because patients are brought to the hospital late, when the disease is already advanced. Various factors like ignorance, poverty and many socio-cultural aspects apart from non-specific clinical features of the disease cause delay in presentation to the hospital leading to increased risks.

Family history of TB was found in 40% patients only. Considering the fact that TB is a common infection in our region it may be because it is still considered as a social stigma and people hide the contact history.

Most common clinical features at presentations found in our study were headache, fever, neck stiffness and altered mental state, respectively.

CSF examination is still the gold standard and most important investigation to diagnose TBM. CSF analysis including leukocyte count, proteins & glucose levels was done for all the TBM patients, showing higher TLC, proteins and low glucose levels in CSF of TBM patients.

Normal Chest X-ray is a common finding in TBM. In our study, 60% patients showed Abnormality in chest radiograph suggesting pulmonary TB.

In our study 70% of the patients developed cranial nerve abnormalities and 58% had hydrocephalus, 42% of the patients with TBM had cerebral edema found in our study. 88% patients have poor GCS value, 10% have moderate GCS value & only 2% have normal value of GCS.

It has been observed that typical CSF findings, clinical features and CT scan findings are quite sensitive in the early diagnosis of TBM. The mortality rate due to TBM was very low but the reasons for the mortality might be longer duration of illness, late presentation with advanced stage or delay in the start of treatment.

The early clinical features of TBM may be non specific, resulting in delayed diagnosis, so a high index of suspicion is required in order to avoid delay in diagnosis which may influence treatment outcome. Immediate treatment with Antituberculour drugs and adjunctive use of corticosteroids can minimize the morbidity & mortality.

For a disease like TBM, which carries high morbidity, mortality and complication rates, prevention is the best measure to control. Efficacy of BCG vaccination is controversial but it is well established that patients vaccinated with BCG who developed TBM, had less complications and low mortality.

Conclusion:

In conclusion, management of infectious diseases is constantly changing because of new discoveries in management and the emergence of resistant bacteria. Conditions in certain areas may be different and guidelines made in one country are not necessarily applicable in other settings due to difference in susceptibility patterns and resources available. Thus local data is essential to provide a rational approach to the management of bacterial meningitis in children. TBM is treatable and outcomes are more positive if early diagnosed and treatment is started early without waiting for detailed reports of CSF analysis. Dexamethasone is used in all TBM patients irrespective of the stage of disease, in doses 2-2.5ml t.d.s. (I/V). Treatment had no serious side effects as supportive therapy and compensatory therapy was also given to avoid or minimize Side-effects of Dexamethasone. Dose tapering was also done to avoid withdrawal symptoms and oral Prednisolone was prescribed after discharging the patient from the hospital.

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