TREATMENT OUTCOME OF NEOURO TUBERCULOSIS PATIENTS PUT ON DOTS - AN OBSERVATION STUDY FROM THE FIELD

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Summary

Background: Effectiveness of intermittent Short Course Chemotherapy for Neuro Tuberculosis has not been well studied. There are only few reported studies on this issue in the world literature under filed conditions. Neurologists all over India are reluctant to accept Directly Observed Treatment Short course for neuro tuberculosis since its introduction in India.

Aim: Assessing effectiveness of Revised National TB Control Programme (RNTCP - DOTS) regimens among neuro tuberculosis patients registered under the programme.

Methods: All the neuro tuberculosis patients referred to RNTCP for treatment were included in the study. Study population included only those patients diagnosed at higher centre and referred to RNTCP during the period Jan - Dec 2002, Alappuzha District. Diagnostic Algorithm as per RNTCP guidelines was strictly followed and treatment outcome and follow-up status were taken from tuberculosis register. No pediatric age group was included in the study.

Results: A total of 32 cases registered for DOTS regimen were included in the study, of whom 29 completed the treatment and all were asymptomatic at the end of treatment (85%). All patients received treatment as DOTS, but only 70% received actual DOTS. All patients were given nine months intermittent regimen as per RNTCP guidelines. Five patients died during the treatment (14%). This result shows that DOTS under field programme conditions are efficient in curing Neuro Tuberculosis.

Conclusion: Good result was obtained with intermittent short course chemotherapy under programme conditions in neuro tuberculosis.

Key words: DOTS, Neuro-tuberculosis, TBM, Intermittent Regimen

INTRODUCTION

Neuro-tuberculosis is the most serious form of tuberculosis. It needs more intensive and prolonged therapy. Even with prompt and adequate treatment, the mortality rate goes up to 27%¹. It constitutes approximately 15% of extra-pulmonary cases or about 0.7% of all clinical tuberculosis². CNS tuberculosis may be in the form of meninitis, intracranial tuberculoma and spinal tubercular arachnoiditis and rarely tuberculous encephalopathy. Diagnosis is usually based on clinical presentation, CSF study and neuro imaging. CSF study remains the principle diagnostic tool in Tuberculous Meningitis³. CSF shows pleocytosis with lymphocytes, elevated protein ranging from 60% to 400 mg% or even higher, sugar between 20% to 40%. It is sterile on routine bacterial culture. Demonstration of tubercle bacilli by AFB staining or culture remains the most important step of CSF study but its yield is much low⁴. CSF may be normal in CNS tuberculoma and tubercular encephalopathy. Neuro imaging shows basal exudates, hydrocephalus, infarcts, tuberculoma, brain edema, etc. CT scan can also be normal. Conventionally, neuro tuberculosis is treated with initial intensive phase of four drugs – Isoniazid, Rifampicin, Ethambutol and Pyrazinamide followed by Isoniazid and Rifampicin daily for at least one year or even longer. Patients with even tuberculoma are showing good response to medical treatment, especially a Pyrazinamide containing regimen. There was no need of surgery for these cases⁵. The rate of hepatotoxicity in adults receiving Isoniazid is 1% and doubles

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with the addition of Rifampicin. Outcome of CNS tuberculosis depends on the age of the patient, duration of illness, clinical stage at time of treatment initiation, the extent of arachnoiditis, vascular complication, hydrocephalus and increased intracranial tension. The incidence of residual neurological deficits, after recovery, varies from 10% to 30%. 

With the introduction of Revised National TB Control Programme (RNTCP), Neuro Tuberculosis is categorized among extra-pulmonary seriously ill, recommending 2(HREZ)/4(HR), with extension of continuation phase for three more months (total nine months). For pediatric neuro T.B. RNTCP recommends substitution of Ethambutol with Streptomycin in the intensive phase. But neurologists and physicians are reluctant to accept the intermittent regimen, considering the seriousness of the condition and lack of published studies to prove the effectiveness of intermittent regimen in this situation.

With our best efforts, we could not find a single study in the literature proving the efficacy of fully intermittent short course therapy in Neuro TB. Thus the present study was planned.

AIM

Assessing effectiveness of RNTCP - DOTS regimen among neuro-tuberculosis patients registered under RNTCP.

SUBJECTS AND METHODS

All neuro tuberculosis patients registered for DOTS in all the four Tuberculosis Units (covering a population of five lakh each) of Alappuzha District during the period January 2002 to December 2002 were included in the study. DOTS therapy was given as per RNTCP guidelines. Diagnostic algorithm and follow-up of RNTCP were followed. Data were collected from the TB register maintained in each Treatment Unit (TU). A detailed review of case history and investigation findings were made of those patients who reported for follow-up. A detailed examination of the patient was done during their review between 6 to 12 months after completing the treatment. A co-ordinated effort of Medical Officer - Tuberculosis Control and Senior Treatment Supervisors was ensured in the evaluation.

RESULTS

Thirty-two cases were registered in all the four Tuberculosis Units of Alappuzha district during the year 2002 (Jan – Dec). This constitutes about 8% of the total of 419 extra-pulmonary TB cases registered in the district during the period. Of the patients enrolled in the study, 17 were males and 15 females. The age distribution was from 16 years to 76 years. Majority of the cases (50%) belonged to the age group 31 to 50 years.

Twenty-six patients (81%) completed the course of treatment. Among them, only 15 were later available for further follow-up between six and 12 months after the completion of treatment. Others did not respond to our call letter and their present status is not known. Thirteen of them were referred from Medical College, Alappuzha and Kottayam and two from District Hospital. Decision to start ATT by neurologist or physician with post-graduate qualification was taken.

Majority of them presented with symptoms of headache, vomiting, fever and altered sensorium. CSF study was abnormal in all, except one. The total count varied from 70 to 660 with the mean value of 272. Lymphocyte predominance was seen in eleven cases (73%). A low sugar value below 40 mg % was seen in only four cases (26%). Protein values ranged from 17 to 575 mg %. It was elevated in only 11 patients (63%). Routine Bacterial Culture was sterile in all the cases. But none was sent for AFB culture or staining. Chest X-ray was abnormal in three cases (20%). HIV screenings done in seven cases were negative. CT scan finding was suggestive only in three cases.

Of the 15 cases interviewed, only one had sequelae of hemi paresis and two were complaining of persistent mild headache. So, overall sequela in our study was negligible compared to many previous studies. There was no clinical evidence of relapse among these 15 patients.
Five patients died and one defaulted. All deaths were investigated. Among five deaths, for two cases, ATT was started empirically after surgery for intracranial space occupying lesions (SOL) by considering tuberculoma as one possible cause for space occupying lesion. Other two deaths occurred within first week of starting the treatment and the remaining one after three months’ of treatment.

DISCUSSION

India is among the nations with high incidence of TB. Usually there are 20% of extra-pulmonary cases of whom 15% will be neuro tuberculosis. So in Alappuzha alone there were 419 extra-pulmonary cases put on DOTS in 2002. Thus an expected incidence of 63 cases of Neuro TB would have occurred during study period. But the actual number of Neuro TB cases registered for DOTS was only 32 and four cases were registered for daily treatment because they were specifically requested by the referring Physician for daily treatment. Thus a total of 36 Neuro TB cases were referred to RNTCP only if patients are not affordable for the daily regimen from outside the programme. RNTCP started in Alappuzha only in 2001. Many referring physicians were unaware about regimens available from govt sector. There can be also initial screening of more serious forms (MRC grade 2 or 3) for daily regimens as these forms are having higher mortality. 22 cases received DOTS from volunteers (Aganawadi workers) and 10 from health service staff. 70% cases received actual DOTS as per criteria for RNTCP internal evaluation (At least 20 out of 24 doses of Intensive phase ingested drugs in presence of DOT provider).

Even though RNTCP recommendation is for eight – nine months’ treatment, two received treatment only for six months probably due to lack of awareness of this recommendation.

Four patients were converted to daily regimen. The reason noted for converting to daily regimen was that, three of them had clinical jaundice and one with persistent vomiting. Medical College Authority has made this alteration of regimen. There is a high incidence of hepatitis noticed in the study group and all three were 15 to 22 year age group. No other major side effect occurred necessitating change of regimen.

Eighty-one per cent treatment completion was obtained in our study, which is much higher than that in unsupervised (NTCP) regimen. A meta analysis of NTCP studies showed completion of only 50% High rate of completion seen in this study could probably due to easy availability of drugs, seriousness of disease and supervision of drug intake. The mortality rate was only 16%, which was much lower than the previously reported series. One of the known variables of mortality i.e, the stage of the disease at time of initiation of treatment could not be evaluated at the time of study.

There was only one defaulter after four days of treatment. He was later traced to have completed treatment from a private hospital. Thus the default rate was only 3% which is negligible when compared to that in unsupervised regimen which goes up to 50%

With the intermittent short course regimen, the total drug consumed by the patient is almost half that with the conventional daily regimen. The toxicity is less and cost of therapy is considerably low. So, this regimen can be universally recommended for all cases of tuberculosis including Neuro tuberculosis, especially in developing countries. Prospective studies on neuro tuberculosis should be undertaken covering all pitfalls of this study. A clear-cut diagnostic algorithm for diagnosis of Neuro T.B. should be also included in the RNTCP guidelines and training modules.

CONCLUSIONS

1. DOTS regime for Neuro tuberculosis is an effective regimen under programme conditions.
2. Default rate is negligible for this intermittent short course chemotherapy.

REFERENCES