A Disease Modifying Treatment Protocol in Patients with Relapsing Remitting Multiple Sclerosis

S R Chandra[a], B Sree Kumar[a]

a. Department of Neurology, Faculty Block, Neuro Centre, NIMHANS, Bangalore - 29, Karnataka*

ABSTRACT

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Twenty six patients with multiple sclerosis were treated with Oral Penicillin, Atorvastatin and Azathioprine as a disease modifying treatment. Attacks were managed with Methyl Prednisolone. The frequency of relapses and severity of disability before and after were evaluated. As multiple sclerosis has a variable course, a cross over study was done.[1] Duration of follow-up is at least three years. The regime is cheap and effective in controlling relapses.

Keywords: Multiple sclerosis, Cost effectiveness, New Regime

*See End Note for complete author details

INTRODUCTION

Multiple Sclerosis came to be known to the medical profession more than one hundred years ago.[2] Its starts in early childhood and in about fifteen years patients become dependent.[3] Over a period of time steroid responsiveness comes down.[2] In India, the incidence is 0.17 to 1.33/ 1, 00,000.[4] The disease tends to have a variable course and hence there is great difficulty in predicting the course of the disease. The factors which govern the long term outcome are not clear.[2]

The treatment options available and progression monitoring recommendations are difficult to follow in the rural Medical College setup. Hence we report our experience with a rational cheap disease modifying therapy using patients before and after treatment, as their own control.

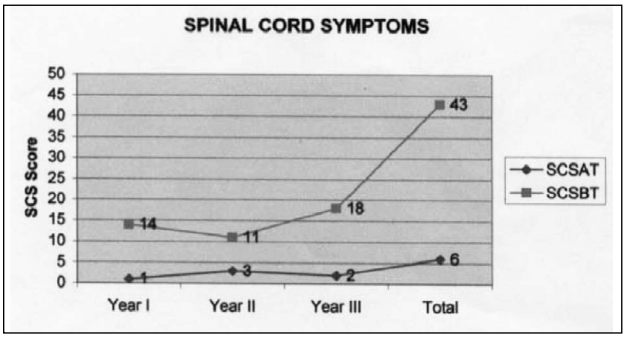
MATERIALS AND METHODS

Suspected cases of multiple sclerosis attending Government Medical College Hospitals, Alappuzha and Trivandrum from 1991 to 2007 were taken up for study. A thorough history and detailed clinical examination was done.

All of them were subjected to MRI, visual evoked responses and cerebro-spinal fluid study. However all patients could not afford Oligoclonal Band Assessment. Routine haematological tests, renal functions, hepatic functions and chest X-Rays were done for all. Diagnosis of relapsing remitting multiple sclerosis was made on clinical grounds using modified Mc Donald's diagnostic criteria.[5]

Disability was assessed using Kurtzke Expanded Disability Status Scale. Thus previous attack history

	Year I	Year II	Year III	Total
SCSAT	1	3	2	6
SCSBT	14	11	18	43



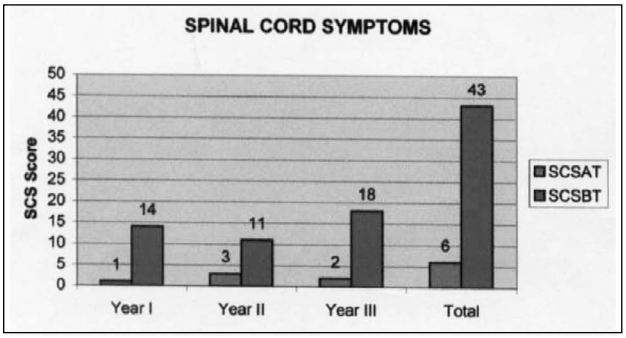


Figure 1. **Spinal Cord Symptoms**

Corresponding Author:
Dr. S R Chandra, Professor of Neurology, Faculty Block, Neuro Centre, NIMHANS, Bangalore - 29, Karnataka.
Mob: 09449106799, Res: 080-26995056, Email: drchandrasasi@yahoo.com

	Year I	Year II	Year III	Total
SSAT	3	3	2	8
SSBT	17	9	9	35

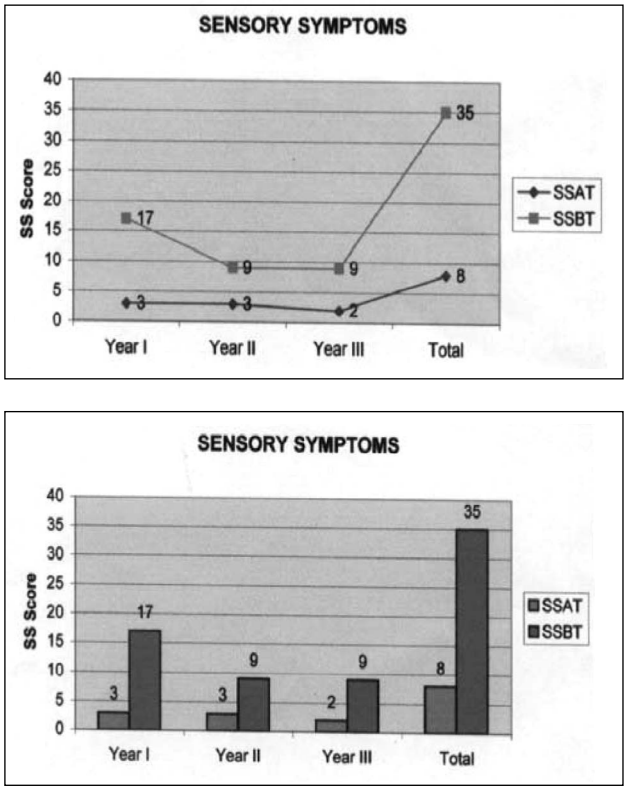


Figure 2. **Sensory Symptoms**

was documented for the longest possible time. Nature of the disease and treatment options was explained to the patients.

Patients who were willing to participate in our study were initiated into the study group. Only those with three to five years disease were included. Those who

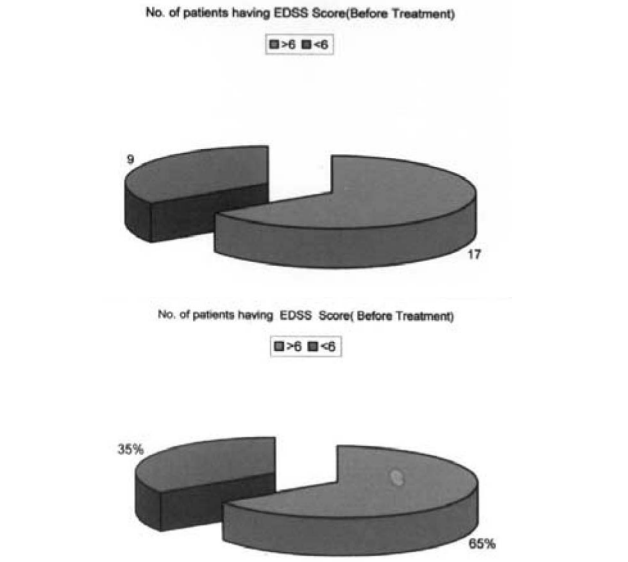


Figure 3. **Number of patients having EDSS Score (before Treatment)**

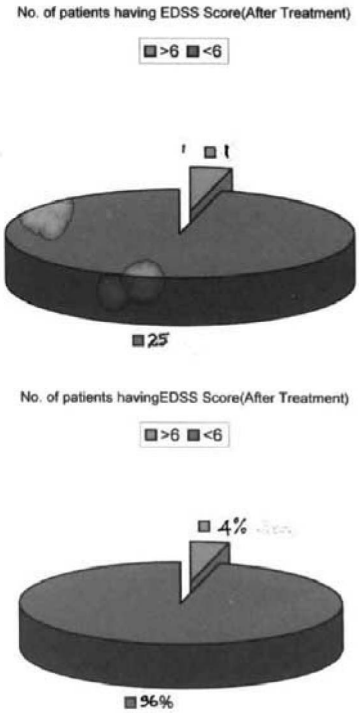


Figure 4. **Number of patients having EDSS Score (after Treatment)**

had other illnesses in addition were not included in the study group. Attacks were managed with intravenous Methyl Prednisolone for five days.

ASO titre and CRP were done during relapses. They were started off on 10 mg of Atorvostatin, 800 mg of Oral Penicillin and Azathioprine 1 mg/kg body weight. Annual EDSS scoring was done as long as the patient was available for follow-up. Adverse effect monitoring was done once in two weeks to start with and later once in three months or whenever patients had any complaint. Follow-up MRI was done in two patients at the end of two years. The disability and relapse rate every year was assessed for three years and compared with pre treatment level.

RATIONALE

Infections are suspected as a factor in triggering relapses, which is supported in our study also, by the elevated ASO, CRP during relapses. Release of inflammatory mediators breaks the Blood- Brain barrier and permits the entry of activated macrophages into Central Nervous System. Hence it was decided to add Oral Penicillin which has been proved to be safe for long term use.[6]

Multiple sclerosis is associated with T cell hyperactivity, Azathioprine action on T cell is well known. Several studies have shown that it might reduce the relapses – Type C evidence.[7]

In 1995, it was observed that survival in Cardiac Transplant patients improved when they were on Statins which did not appear to be due to its cholesterol lowering effect.[8]

Statins interfere with the production of several pro-inflammatory mediators, suppresses production of inducible Nitric oxide, TNF alpha which are important in activation of C_4T cells. It also suppress interferon gamma, inducible Major Histo compatibility complex Class II Up regulation, TCell activation of matrix metalloprotease (MMP)[9] which breaches Virchow Robin Space and also intra cellular adhesion molecule(ICAM) -1. Atorvostatin promoted differentiation of T cells to anti inflammatory Th2 Cells which protect recipient mice from experimental allergic encephalomyelitis.

The parameters which were accessed were optic nerve attacks, spinal cord attacks, brain stem cerebellar attacks, hemiplegic attacks and sensory symptoms.

STATISTICAL EVALUATION

The data collected was statistically evaluated using t-Test. The observations are for optic nerve attacks at one year, two years, three years and total number of attacks before and after treatment, the p value is less than 0.1 indicating very high significance.

For brain stem cerebellar attacks, the total score showed p value less than 0.1 indicating very high significance. However during the second year of follow-up the p value is less than 0.05.

Spinal cord attacks at one, two and three years showed a total score p valueless than 0.1.

For sensory symptoms the total p value was less than 0.1. However for the second year no significant reduction of p value and year three p value was less than 0.05.

For hemi paresis, for one two and three years the p value is not significant. However for the total score the p value is significant. This could be due to a very small number of hemiplegic attacks.

OBSERVATION AND DISCUSSION

Twenty six patients were regularly followed up for three years. Their age group varied from 19 years to 51 years. There were 17 females and 9 males; EDSS score at entry was more than six in thirty five percent of patients and less than six in sixty-five percent of patients. At the end of three years only four percent of patients had the score more than six.

Statistically, significant reduction of relapses was observed in brain stem cerebellar attacks, optic nerve and spinal cord attacks. For hemi paresis, the mean score for one two and three years did not show significant reduction. However overall attack frequency was significantly reduced. Sensory symptoms showed significant reduction at one year, three years and in the total number of scores. One Patient had leucopoenia which was corrected with drug withdrawal for one month and blood transfusion. Majority of patients complained of gastrointestinal discomforts in the form of nausea which could be easily managed. No other side effects were observed. There is significant reduction in both severity and relapse rate. Cost of treatment with beta interferon is about four to six lakhs annually and this study regime cost around five thousand rupees only. However the end point and exact dose is not clear. Longer period of follow-up and larger number of patients will answer these questions.

CONCLUSION

Our regime is effective, cheap, and safe and has a rationale. However the dose and the duration in this regime are arbitrary and needs further evaluation.

END NOTE

Author Information

1. Dr. S R Chandra, Professor of Neurology, Faculty Block, Neuro Centre, NIMHANS, Bangalore - 29, Karnataka.
   Mob : 09449106799, Res: 080-26995056.
   Email: drchandrasasi@yahoo.com

2. Dr. B Sree Kumar, Professor of Neurology, Faculty Block, Neuro Centre, NIMHANS, Bangalore - 29, Karnataka.

Conflict of Interest: None declared

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