Multi-drug Regimen in Leprosy and its impact on Prevalence of the Disease

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Leprosy considered as incurable for several centuries, has undergone remarkable changes in its therapy. The first drug used against leprosy was Chaulmoogra oil. The earliest record of its use was in 1914. For the next 3 decades it was the only drug known. Used by intramuscular and intradermal injections, its effect was only marginal, particularly in lepromatous cases.

With the discovery of sulphonamides, a new era began of antibiotic therapy and leprosy also got its benefit. Promin was the first sulphone shown to be effective on *M leprae* in 1943 and this discovery initiated successful chemotherapy of leprosy. Promin and other sulphones like Diasone and Sulphatrone had to be administered parenterally. However, it was found in 1950 that the parent sulphone, Diamino-diphenyl-sulphone (Dapsone) could be safely used orally with equally good results. Due to the convenience of oral usage, Dapsone was extensively applied for mass therapy.

The advent of Dapsone resulted in radical changes in the management of leprosy cases. Segregation and isolation led to domiciliary treatment and control by chemotherapy. All over the world, leprosy control programmes were carried out and Dapsone was the sheet anchor of the programme.

In India, National Leprosy Control Programme (NLCP) was initiated in 1955. This was based on the triad of Survey, Education and Treatment (SET). At that time there were an estimated 13 lakhs leprosy patients in the country. Starting with the initiation of NLCP in the first five year plan, SET work was gradually, extended to all districts. With the effective surveys and case detection programmes, 40 lakhs of leprosy cases were discovered by 1981. This was achieved by an extensive network of 720 Leprosy Control Units, 6100 SET Centres and several mobile leprosy control units. The prevalence varied in different states and in different districts. Out of the then total of 412 districts, there was a high prevalence of more than 50 per 10,000 population in 201 districts. In 140 districts, the prevalence was

moderate with 10 to 50 per 10,000. Remaining 81 districts had a low prevalence of less than 10 per 10,000.

All this time Dapsone was the only drug used. Therapeutic effect was considered very good, particularly because the comparison was with Chaulmoogra oil. By using a single drug, the development of Dapsone resistance was highly possible, but there was no way of finding it since *M leprae* is not cultivable. Also there was no other alternative drug. The experimental transmission of leprosy into the foot-pads of mice in 1960 made it possible to investigate drug resistance. Pettit and Rees in 1964 first reported Dapsone resistance in 5 among 5000 patients in Malaysia. Subsequently in 1973, Dapsone resistance among the same patients was estimated to be 25 per 10,000. Later, secondary Dapsone resistance was reported from several countries ranging from 13 to 40 per 1000 treated cases. More disturbing fact was the detection of primary resistance in Ethiopia and subsequently in India and in other countries (WHO 1982).

Fortunately a few drugs became available. Rifampicin was found to be highly bactericidal, killing 99% of the bacilli within days by a single dose. Resistance to Rifampicin could develop as one step process in patients receiving monotherapy. Usual adult dose is 600 mg daily. Another drug incidentally found effective was a Riminophenazine drug, Clofazimine. Resistance to this drug is extremely rare. Ethionamide and Prothionamide are the other alternative drugs, although not superior to Rifampicin. Recently, ofloxacin and Minocyclin have also been found to be effective bactericidal of *M leprae*.

To combat the problem of drug resistance, a combination of available drugs are to be used. Since such a combination therapy has to be applied on mass scale world wide, a standard regimen has been evolved. Leprosy has been classified under two broad groups - Paucibacillary and Multibacillary. The paucibacillary type of patient is bacteriologically negative on the skin smears and has upto 4 skin lesions with or without one

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nerve trunk involvement. The multibacillary type of patient is bacteriologically positive, or has 5 or more skin lesions or has more than one nerve trunk involvement. The schedule of multi drug therapy (MDT) for adults is as follows :

Drug	Supervised dose	Frequency	Unsupervised dose	Frequency
MB Leprosy				
-Rifampicin ..	600 mg	Once a month	--	
-Clofazimine..	300 mg	Once a month	50 mg	Daily
-Dapsone ..	100 mg	Once a month	100 mg	Daily
PB Leprosy				
-Rifampicin ..	600 mg	Once a month	--	--
-Dapsone ..	100 mg	Once a month	100 mg	Daily

Duration of therapy : MB leprosy - 12 monthly pulses in 18 months.

PB leprosy - 6 monthly pulses in 9 months.

MB - multibacillary; PB - Paucibacillary

India has given a high priority to anti-leprosy programme. As mentioned earlier, National Leprosy Control Programme, covered all the endemic districts by 1981, and monotherapy with Dapsone was carried out in all the districts. In 1982 MDT was made mandatory for treatment of leprosy. The programme was augmented as National Leprosy Eradication Programme (NLEP). International Leprosy Organisations came forth to support the Government. Drugs were made available for free distribution and there is no dearth of drugs. Drug distribution centres are so located that no patient has to walk for more than 3 kilometers. These centers are visited at monthly intervals by a mobile team which conducts treatment and documentation. The attendance in all the centres has been 85% or more.

Impact of MDT has been remarkable. The disease gets cured much faster. Lepromatous cases are cured in one year against the 5 or more years it would take under monotherapy. Similarly the paucibacillary cases are cured in 6 months as against 2 years by monotherapy. Since the advent of MDT, the pattern of leprosy has drastically changed. The cases are more towards the tuberculoid end of the spectrum. Frequency of reactions is considerably reduced.

Apart from the therapeutic benefits, NLEP with MDT has produced remarkable changes in the community. Due to sustained IEC activity and the visits of the team to all villages, leprosy consciousness in the society has increased. Consequently, patients with early leprosy present themselves for treatment. In most of the centres 40 to 50% of patients report voluntarily. Of them about 30% have a single lesion. Due to early detection and treatment, the deformity rate has become very low (2% among the new cases as against 10% in previous years).

The main objective of NLEP is to eliminate leprosy and subsequently to eradicate it. It is essential to assess how far it has been achieved. In 1985, the prevalence rate of leprosy in the country was 39 per 10,000. In 2002, the prevalence has come down to 4.2 per 10,000. Elimination is defined as the status when the prevalence falls below 1.0 per 10,000. In India, many of the states have a prevalence of 2.5 to 3.5 per 10,000. In these states, elimination could be achieved by the year 2005, the target date fixed by the Government. In 6 states, prevalence is well above 4. These states are - Jharkhand (13), Bihar (11), Chattisgarh (11), Orissa (9), Uttar Pradesh (5), West Bengal (4). It will take a longer time to achieve elimination in these states.

The presumption of fixing the elimination rate at 1.0 per 10,000 is that at this level, transmission will be interrupted. However, the real indicator of elimination is a fall in the New Case Detection Rate (NCDR). However, in all the states in India, the NCDR has remained constant at 3 to 3.5 per 10,000. It is not only in India but in all the endemic countries, there has been a marked fall in the prevalence rate but the NCDR has remained constant. The figure illustrates prevalence rate and NCDR in 32 countries in the world combined.

Fig. 1 :

This persistently constant NCDR is a very disturbing fact. It betrays the very fundamental objective of elimination of the disease. The efficacy of the drugs against the disease is beyond doubt. The problem obviously lies in the programme. Are these new cases hidden ones, which were not detected earlier? Possibly not, since many of them are early cases. Secondly, could they be cases in the incubation period, which is known to be 5 years or more in leprosy? Thirdly has the programme failed to detect and cure the infectious cases? Some of the early lepromatous cases with diffuse skin lesions could be very deceptive. Lastly and theoretically, could there be any other source of infection apart from

the infectious patient? These are problems to be addressed. Despite these set backs, there is a real optimistic feeling that this lowly infectious disease would gradually disappear in India as it has done in Europe.

References

1. Pettit JHS, Rees RJW . Sulphone resistance in leprosy, an experimental and clinical study, Lancet 1964;2:673.
2. DGHS (Govt. of India) Leprosy Division (1992) Status Report 12.
3. DGHS (Govt. of India) Leprosy Division (1992) Facts and figures 1-3.
4. DGHS (Govt. of India) Leprosy Division (2001) Mini MDT Guidelines 11-5.
5. WHO (1982) WHO expert committee on leprosy, Technical Report Series 675, 9-13.
6. WHO (1998) WHO expert committee on leprosy, Technical Report Series 874, 11-21.
7. WHO (1998) Action Programme for Elimination of leprosy, status Report 13.
8. Desikan KV. Therapeutic strategies in management of leprosy, Progress in clinical Neurosciences. Neur Soc Ind 2001;16:101-5.

MJAFI wishes its readers a Happy New Year