

Relapse in MB leprosy patients treated with 24 months of MDT in South West China: a short report

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Summary This study investigates the relapse rate among multibacillary leprosy patients treated with 24 months of MDT in south west China. A retrospective relapse survey was conducted in the southwest of China. A detailed questionnaire was designed to collect the data on relapse among MB patients who completed 2 years of the WHO/MB regimen, from 1989 to 2000. The data about 2517 multibacillary leprosy patients in 27 counties in the southwest of China were collected. Among 2517 MB patients, 235 patients died or were lost to follow-up and 2374 were followed up for more than 3 years after completion of MDT. The total duration of follow-up was 20,825 person-years, with a mean duration of 8.27 years per patient. Five patients with relapse were identified with an accumulated relapse rate of 0.21/1000 person-years. Their initial BIs ranged from 1.8 to 5. The patients with relapse occurred 48–158 months after the completion of MDT. The relapse rate of MB patients treated with 24 months of the WHO/MB regimen was observed to be very low after long-term follow-up.

Introduction

Relapse is a common phenomenon among patients treated with DDS monotherapy. However, it still occurs among patients treated with WHO recommended multi-drug therapy (MDT). Because there was a report¹ that an increased relapse trend was observed from 1985 to 2002 in China and the proportion of MB cases among all newly detected cases increased in the past 10 years in China, It is necessary to assess the relapse situation among multibacillary patients treated with 2 years of MDT in China. We conducted a retrospective relapse survey in March,

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2004 among MB patients who completed a 2-year WHO/MB regimen from 1989 to 2000 in the southwest of China to assess the relapse situation.

Materials and methods

The study was carried out in 27 counties with a high leprosy prevalence. These were 16 counties in Liangshan Yi Minority Autonomous Prefecture, Sichuan Province, eight counties in Qianxinan Prefecture, Guizhou Province, two counties in Zhangjiajie City and one county in Xiangxi Tujiazu Autonomous Prefecture, Hunan Province.

From 1989 to 1996, all skin smear positive patients were classified as MB patients and from 1997 to 1998, skin smear positive patients and skin smear negative patients with six or more skin lesions or two or more nerves impaired were classified as MB. Patients previously treated with DDS monotherapy were excluded. Only MB patients newly registered between 1987 and 1998 and who completed the WHO/MB/MDT regimen between 1989 and 2000 were included in this study. MB patients were given dapsone 100 mg daily, rifampicin 600 mg monthly, clofazimine 300 mg monthly and 50 mg daily for 24 months. The monthly administration of MDT was strictly monitored by professional health workers (PHWs) either at the patient's residence or at the County Station for Leprosy Control. The daily component of MDT was self-administered by patients themselves.

The routine surveillance of leprosy was based on a computerized database and the quality of the data about leprosy patients is reliable.^{2,3} Detailed questionnaires were designed and the retrospective relapse survey was carried out in the selected counties based on the routine activity of leprosy control in March 2004 among the MB patients who met the inclusion criteria. The cut-off time of the study was set at the end of 2000 to ensure a minimum follow-up of 3 years. The information collected included the number of patients who completed treatment every year, the number of patients died or missed every year, the time and number of patients relapsed and their details including sex, year of birth, BI at the time of first diagnosis of leprosy, completed treatment and the time of diagnosis of relapse, the time of completed MDT, leprosy reaction events during MDT and clinical manifestations at relapse such as patch, nodule, plaque and infiltration.

The PHWs at county level were responsible for following up MB patients once a year for 10 years after they completed MDT as per the national guideline. The skin smear was done once a year by the PHW for patients with an initial positive BI and when that was still skin smear positive. For those with a negative skin smear, only clinical examination was performed to check the new skin lesions of relapse. However, the skin smear was done in those with skin lesions suspected of relapse and the smear sites included the suspected skin lesions and routine sites. The suspected relapse patient was carefully examined by at least two PHWs. The diagnosis of relapse after MDT was based on clear evidence and made by two experienced PHWs. In the study areas, each County Station had an experienced skin smear technician. The PHWs at county level were trained on leprosy for 3 days once every 2 or 3 years by senior PHWs at district or provincial levels.

Relapse was suspected when there was any new skin lesion or new deformity. Relapse was confirmed by reappearance of new symptoms and signs of the disease, after successful completion of appropriate treatment and either the skin smear being positive again after being negative with an increase of at least 2 units of BI at any previous site or a biopsy that showed specific histopathologic changes of leprosy with a significant number of solid acid-fast bacillus (AFB).

Results

Between 1989 and 2000, a total of 2517 new MB patients were recruited into the study to investigate relapse. Among 2517 MB patients, 2374 were followed up for more than 3 years after completion of MDT, 226 (9%) patients died and 9 (0.4%) were lost to follow-up. The total duration of follow-up was 20,825 person-years and the mean duration of follow-up was 8.27 years.

A total of five patients with relapse were confirmed. Among five patients with relapse, two occurred during the 4th year of follow-up after completion of MDT, one during the 5th year, one during the 6th year, and one during the 13th year. The cumulative relapse rate was 0.24/1,000 person-years (Table 1).

Among the five relapsed patients, four were male and one was female. The range of initial BI was from 1.8 to 5.0. At the completion of MDT, the BI ranged from 0 to 2.0. At the time of relapse, the BI of all patients was positive with BI of 1.80–5.33. The time to relapse was from 48 months to 158 months after completion of MDT. All patients showed new active skin lesions at relapse. One patient self-reported with new skin lesions and the other four patients were detected at the field visit by the PHW at county level. Two patients developed a type 2 leprosy reaction at confirmation of relapse (Table 2).

Discussion

We carried out a retrospective survey based on the routine activities of leprosy control in China. All counties had health facilities for leprosy control, leprosy PHWs at county level as they were endemic counties. The continuous detailed registers and patient medical records were kept in good condition. In addition, the cut-off time for the study was set at the end of 2000 so that relapsed patients could be detected within 3 years. Although the possibility of

Table 1. Follow-up time and number of relapse patients

Follow-up time (year)	No. of patients followed up	No. of person-years followed up	No. of relapsed patients	Relapse rate % (1000 person years)
< 1	94	52*	0	0
1	29	29	0	0
2	20	40	0	0
3	209	627	0	0
4	159	636	2	1.26
5	177	885	1	0.56
6	144	864	1	0.69
7	184	1288	0	0
8	194	1552	0	0
9	226	2034	0	0
10	216	2160	0	0
11	230	2530	0	0
12	224	2688	0	0
13	183	2379	1	0.55
14	228	3192	0	0
Total	2517	20825	5	0.2 (0.24)

*Patients died or missed within 1 year after completion of MDT.

Table 2. Details of 5 relapsed cases completed 2 year MDT from 1989 to 2000

Patients	Date of starting MDT	BI at diagnosis	Date stopped MDT	BI at stopping MDT	Time of relapse	Detection type	Skin lesions at relapse	BI at relapse	Leprosy reaction at relapse
1	Jan 1997	5.00	Jan 1999	2.0	Jan 2003	Self-report	Infiltration nodules plaques	2.75	Type two reaction
2	April 1995	3.50	May 1997	0.00	Sept 2003	Field visiting by PHW	Infiltration	5.33	No
3	Aug 1991	3.00	Aug 1993	0.33	Sept 1997	Field visiting by PHW	Infiltration, nodules plaques	5.00	Type two reaction
4	Dec 1994	1.83	Dec 1996	0.00	Sept 2001	Field visiting by PHW	Patches	1.80	No
5	Sept 1987	2.30	Sept 1989	0.00	Nov 2002	Field visiting by PHW	Infiltration nodules plaques	1.80	No

relapse among the 235 dead or missed patients could exist, these were only a very small proportion of the study population. Although the reactivation of the disease might be caused by re-infection, especially in high epidemic areas, differentiation between relapse and re-infection is very difficult in the field.

Previous studies note high relapse rates among the patients treated with 2 years of MDT,^{4,5} and Cellona⁶ reported in 2003 that there was a difference in the relapse rate between clinic patients and those in the field. Shaw reported⁷ a relapse rate of 2.2% in 46 patients with initial BI ≥ 3.0 before treatment who were treated with 2 years of MDT, with a mean follow-up of 9.26 years. Dasananjali reported⁸ that 45 MB patients were followed up for 8 years after completion of 2 years of MDT and no relapse was found. Another study of 305 MB patients found no relapse after 5 years follow-up after completion of MDT in India.⁹ Hu¹⁰ reported 12 patients with relapse (0.38/1000 person-year) among 3257 MB patients treated with 24 months of MDT and followed up for a maximum of 18 years after completion of MDT in Sichuan Province, China. In our study, the follow-up was a continuous procedure as the routine activity mainly done by PHWs at county level. The relapse rate of MB patients after 2 years of MDT in this present study was very low and similar to the results reported by many other authors.⁷⁻⁹ Our study had a small proportion of patients who were skin smear negative, however the majority was skin smear positive at diagnosis and there was a long follow-up period.

Contributors

Dr Jianping Shen organized the study group consisting of all district leprosy control program managers. He issued a document to carry out the relapse survey. He designed the questionnaire and distributed them among all study areas. He kept the close contact with all district managers during the survey including answering some questions asked by the district managers if they had. All data were again checked up by him before inputting the data into the computer at National Centre. All data were analysed by him.

Dr Musang Liu was responsible for collection of the data from all study areas and input data into the computer. The descriptive statistics of the data were performed by her.

Dr Jianhua Zhang was responsible for carrying out the survey in 16 counties in Liangshan Prefecture, Sichuan Province, People's Republic of China. He issued the formal document and distributed the questionnaire among all county stations. He was responsible for answering the questions during the survey asked by local health workers if they had. He was also responsible for collecting all forms and checked up them. At last, he sent all forms to the National Centre. After the paper was completed, he reviewed it and gave comments.

Dr Wenyi Su was responsible for carrying out the survey in eight counties in Qianxinan Prefecture, Guizhou Province. He issued the formal document and distributed the questionnaire among all county stations. He was responsible for answering the questions during the survey asked by local health workers if they had. He was also responsible for collecting all forms and checking them. Finally, he sent all forms to the National Centre. After the paper was completed, he reviewed it and made comments.

Dr Guoxing Ding was responsible for carrying out the survey in two counties in Zhangjiajie City and one county in Xiangxi Tujiazu Autonomous Prefecture, Hunan Province. He issued the formal document and distributed the questionnaire among all county stations. He was responsible for answering the questions during the survey asked by local health workers if they had. He was responsible for collecting all forms and checked up them.

At last, he sent all forms to the National Center. After the paper was completed, he reviewed it and made comments.

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