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Serological response of chemoprophylaxis on high risk contacts of new leprosy cases in Nyaungdon Township

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This study was carried out in one of the leprosy endemic townships, Nyaungdon Township, Ayeyawady Division. The aim was to study the serological response of chemoprophylaxis by using a single dose of ROM (rifampicin, ofloxacin and minocycline), which is WHO recommended regime for single lesion of leprosy, on high risk extended contacts of new leprosy cases. The blood samples were collected from extended contacts two times before and six months after the chemoprophylaxis. Indirect NTP-BSA ELISA test was carried out on samples. Determination of the baseline seropositivity rate of extended contacts of new leprosy case was also carried out. Seropositive contacts were assumed as high risk group. In the baseline study, the seropositivity rate is significantly higher in household contacts of multibacillary (MB) leprosy cases. The seropositivity rate of children contacts under 15 years of age is higher than that of adult contacts, χ^2= 31.58, p<0.001. The difference of mean OD titers in treated group before and after chemoprophylaxis is significantly reduced compared to non-treated group in adult, p=0.004. However, it is not significant in children. The difference of seropositivity rate before and six months after chemoprophylaxis is not significantly reduced in treated group compared to non-treated group.

INTRODUCTION

Leprosy elimination was achieved at the national level at the end of January 2003 in Myanmar (prevalence rate <1/10,000) [1]. In Myanmar, WHO Multi Drug Therapy had been introduced since 1986. At that time the prevalence rate was 59.3/10,000 population. In 1990, the prevalence came down to 27.6/10,000. In 1995, Multi Drug Therapy service reached every village making 100% geographical coverage by integrating into Basic Health Services in Myanmar. From 1997 to now, National Health Plan has been carried out by integrated effort by all departments in Ministry of Health and collaboration with health related departments [2]. Up to June 2003, the new case detection rate (NCDR) was more than 4/10,000 population in 70 townships mainly from Ayeyawady, Bago, Magwe, Mandalay, Sagaing Divisions and Southern Shan State [3]. Although effective elimination program using MDT was carried out, the incidence is still high possibly because of the long incubation period of the disease in the role of healthy carriers in transmission of *Mycobacterium leprae*. ROM (rifampicin, ofloxacin and minocycline) was given as a single dose for adults with single skin lesion in WHO recommended MDT regimen for paucibacillary (PB) leprosy [4].

Household contacts and social contacts of leprosy cases are at high risk to develop the disease within a few years in endemic area. It was found that the risk of developing leprosy increased progressively with increasing phenolic glycolipid-1 antibody (antiPGL-1) levels indicating the risk of

developing leprosy in the next few years [5]. To control leprosy and to accelerate achievement of the goal of leprosy elimination and sustaining of this elimination as a public health problem, chemoprophylaxis would be needed to carry out on high risk group in high prevalence area [6]. Thus, it would be needed to screen the high risk group of healthy carriers for chemoprophylaxis for decreasing the incidence and preventing in transmission of *M. leprae* [7]. Therefore, this study was carried out to assess the efficacy of chemoprophylaxis after six months on high risk extended contacts of new leprosy cases using a single dose of ROM in endemic area of Myanmar.

Objectives

- To determine the baseline seropositivity rate of extended contacts of new leprosy cases in Nyaungdon Township
- To determine the antibody response and seropositivity rate among treated and non-treated groups

MATERIALS & METHODS

This study was a community-based prospective study. Nyaungdon Township, Ayeyawady Division (prevalence rate - 1.52/10,000) was selected for study area. Extended contacts of all new leprosy cases in Nyaungdon Township (n=490) were assumed as study population. Two milliliter of blood was taken out after obtaining informed consent. The samples were transported under cold storage to Immunology Research Division, Department of Medical Research (Lower Myanmar). NTP-BSA ELISA was used to determine antiPGL-1 antibody levels in the subjects' sera. The high risk group of leprosy was identified from cut-off point of controls (apparently healthy blood donors of National Blood Bank, Yangon). After baseline study, all seropositive extended contacts (n=156) were determined as high risk contacts and were enrolled in the chemoprophylaxis study. Subjects with possibility of pregnancy, liver disease, renal disease and subjects who are taking antiTB treatment were excluded from the chemoprophylaxis study.

Therefore, 152 contacts were enrolled in the study of chemoprophylaxis. These subjects were randomly allocated into treatment and non-treatment of 76 subjects. Each subject in treatment group was given ROM (rifampicin, ofloxacin and minocycline) for >15 years of age (adult) group and RMP (rifampicin alone) with the dose of 25 mg/kg for <15 years of age (children) group. Subjects in non-treatment group were given vitamins as placebo. The forms (capsules, caplet or tablet) and colors of drugs containing vitamins were similar to the drugs containing ROM.

Among 76 subjects of each group, there were 42 of each in adult group and 34 in children group, respectively. To study the serological response of chemoprophylaxis, blood samples were collected again after six months. Among them, 31 subjects dropped out from the study. Sixteen dropouts of the remaining subjects were from the treatment group and 15 subjects were from non-treatment group. Among 121 subjects, totally 9 subjects, 3 subjects from treatment group and 6 subjects from non-treatment group, were still seropositive.

Statistical analysis

Frequency distribution and cross tabulation of variables were constructed by using SPSS (version 11.5). The high risk individuals (seropositive) were compared in study Rural Health Centers. Seropositivity rate and mean antibody titer among exposed (treatment) and non-exposed (non-treatment) groups were analyzed using Wilcoxon Signed Rank Test and Chi Square Test. A comparison was made on all these groups for the study period.

RESULTS

Twenty-one new leprosy cases including 13 multibacillary (MB) and 8 paucibacillary (PB) were detected in Nyaungdon Township. Among 490 extended contacts (65 households and 425 neighbours), 306 were

contacts of MB cases and 184 were that of PB cases. Baseline seropositivity of these overall contacts was 31.84% (Fig.1). The seropositivity rate in children contacts was higher than that of adult contacts (50.72% vs. 24.43%, χ^2 =31.58, P<0.001). The seropositivity rate was not different by gender (29.41% vs. 34.13%).

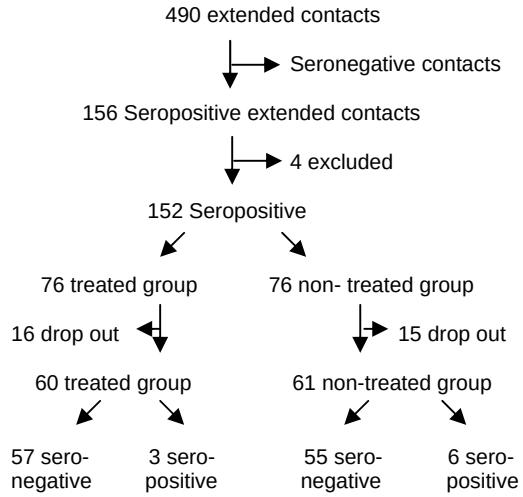

Fig.1. Serological response of extended contacts to chemoprophylaxis

The seropositivity rates of overall contacts of MB and PB cases were 36.27% and 24.46%, respectively. The seropositivity rates of household contacts of MB and PB cases were 42.50% and 40%, respectively, and that of neighbour contacts of MB and PB cases were 35.34% and 22.01%, respectively. The seropositivity rate of household contacts of MB cases was the highest in all different types of contacts and followed by the household contacts of PB cases, the neighbour contacts of MB cases and the last of neighbour contacts of PB cases. Number of seropositive extended contacts distributed by age group was the highest in the age group of 11 to 20 years (Fig. 2).

The mean OD titers were significantly reduced after the chemoprophylaxis in both treatment and non-treatment groups for both adults and children (Table 1). The difference of mean OD titers before and after chemoprophylaxis in treatment group was significantly reduced compared to non-treatment group adults, but was not significant in children (Table 2).

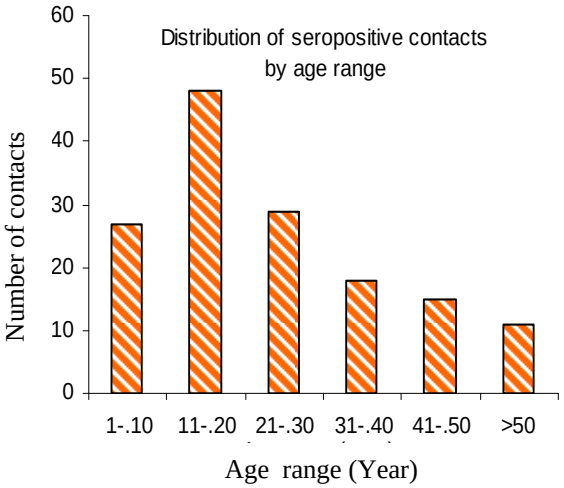

Fig. 2. Numberof seropositives among extended contacts of new cases of leprosy by age range in Nyaungdon Township

Table 1. Mean OD titers before and after chemoprophylaxis of treatment and non-treatment groups

Type of contacts	Optical density titer (Mean±SD)					
	Treatment group			Non-treatment group		
	Before	After	p value	Before	After	p value
Adult (n=35)	0.28 ± 0.08	0.13 ± 0.06	0.005*	0.27 ± 0.06	0.17 ± 0.06	0.007*
Child (n=25)	0.29 ± 0.08	0.15 ± 0.06	0.005*	0.27 ± 0.08	0.16 ± 0.06	0.006 *

*Wilcoxon Signed Rank Test, *P<0.05 = significant

Table 2. The difference of mean OD titers before and after chemoprophylaxis in treatment and non-treatment groups

Type of contacts		Mean optical density titer difference between before and after		
		Treatment group	Non-treatment group	p value
Adult (n=35)	Mean OD	0.15	0.1	0.004
	SD	0.09	0.08	
Child (n=25)	Mean OD	0.14	0.11	0.18 (NS)
	SD	0.09	0.08	

*Wilcoxon Signed Rank Test, *P<0.05 = significant, NS = not significant

DISCUSSION

The epidemiological significance of presumably many people who are infected with

leprosy but without clinical symptoms is still to be investigated. Improving their understanding of the natural history of leprosy, and ability to recognize infection might ultimately have important implications for leprosy control, particularly if it would permit the definition of targets in the population for immunoprophylactic and therapeutic strategies [8].

Therefore, in this study, to reduce the subclinical infection leading to decrease new case detection rate of leprosy, the high risk group of extended contacts of new cases in Nyaungdon Township, Ayeyawady Division, was determined using NTP-BSA ELISA test and chemoprophylaxis was carried out using ROM on these high risk group of contacts.

It has been suggested that the screening of the sera of apparently healthy individuals may permit the identification of subclinical disease. There have been few prospective studies in which antibody levels to PGL-1 have been related to the subsequent risk of leprosy. If such cases could be detected and treated, it is theoretically possible that their infectivity for others would be curtailed, with a significant impact on the overall incidence of leprosy [5]. From July 1997 to October 1998, two rounds of screening and chemoprophylaxis using ROM were carried out in Kiribati, Pacific Ocean. About 92% of the population has been screened and there is 85% reduction in number of new cases [9].

In Federated States of Micronesia, new case detection rate was significantly reduced after chemoprophylaxis consisted of ROM for adults and rifampicin alone for children <15 years [10]. These observations suggested that subclinical infection with *M. leprae* is common in endemic communities and that PGL-1 seropositivity is a marker of subclinical infection. Detection of subclinical infection may confound control strategies that use screening tests to identify asymptomatic highly infectious cases for earlier therapy [8].

In this study, household contacts of MB cases are the highest risk. Age is found to be a potential risk factor for contacts to develop leprosy. Among the household contacts of MB cases, the risk for children under 14 years of age was substantially higher than that for adults [11]. The sero-positivity rate was higher in children than adult contacts in the present study. When considering gender, there have been conflicting findings. Vijayakumaran *et al.*, found no gender differences which is consistent with the study of Rao *et al.* [12]. In Malawi, it was found that the risk was significantly greater for males than for females [11]. The sero-positivity rate had no difference by gender in this study. The difference of seropositivity rate before and after six months of chemoprophylaxis was not significantly reduced in treatment group compared to non-treatment group. The mean OD values were significantly reduced after six month of chemoprophylaxis. The difference of mean OD values (antibody titer) in treatment group was significantly reduced compared to non-treatment group in adults after six months.

This study revealed that ROM treated adult contacts have significant reduction of mean OD value of antiPGL-1 level. However, a significant reduction of seropositive rate in treatment group was not clearly observed. Evidence-based clinical trial could be recommended for the importance of chemoprophylaxis in interrupting the transmission of subclinical leprosy.

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