POLYTHERAPY IN MULTIBACILLARY LEPROSY PATIENTS IN NEPAL

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INTRODUCTION

The sulphones have been in use for nearly forty years to treat leprosy. Dapsone remains to be treatment of choice, as it is effective, inexpensive, and safe. Irregular in-take of dapsone have contributed to the emergence of secondary dapsone resistance. In any chronic mycobacterial disease use of monotherapy has not been favoured due to the development of microbial persistance. This was first reported by Pettit and Rees (1) and since then several workers have reported similar finding from different parts of the world (2-6). Furthermore, the grave danger to the contacts of secondary dapsone resistance is primary sulphone resistance. Therefore like in tuberculosis, combination of drugs in leprosy have been advocated since the WHO Fifth Expert Committee on Leprosy (7) and then subsequently at the 11th International Leprosy Congress (8).

In Nepal, the prevalence of leprosy is estimated to be 1 percent. Of those the higher proportion of patients belong to the multibacilary group, i.e. BL/LL. Because dapsone has to be taken for long periods, the patients compliance is poor. In one of the skin clinics in Nepal, the registered number of patients were over 7000 and those patients who attended the clinic regularly were around 3000. Several lepromatous leprosy patients were clinically resistant to dapsone.

For leprosy control to be effective, multibacillary patients must be motivated to be regular and drugs regimes used may be able to achieve maximal bacterial clearance.

With this background, the present pilot study has been undertaken with the following objectives:

(A) Previously untreated multibacillary leprosy patients to be admitted to hospital for health education and supervised administration of drugs.
(B) To ascertain the patient acceptability of drugs.
(C) Previously untreated paucibacillary leprosy patients to receive polytherapy under supervision.

TABLE-1 THE NUMBER OF MALE AND FEMALE LEPROSY PATIENTS ACCORDING TO CLASSIFICATION WHO ARE RECEIVING DAPSONE.

	Male	Female	Total
BL	8	1	9
LL	6	3	9
Total	14	4	18

TABLE-2 THE AVERAGE BACTERIOLOGICAL ASSESSMENTS BEFORE TREATMENT WITH DAPSONE AND THREE MONTHS AFTER TREATMENT.

	BL	MI
Pretreatment	3.51	0.96
After 3/12 dapsone administration	3.2	0.78

MATERIALS AND METHODS

One hundred and one previously untreated healthy leprosy patients were admitted to Anandaban Leprosy Hospital after explaining to them why such admission was warranted. Only those consenting were admitted. They came from all parts of Nepal and represent various ethnic groups. At the time of clinical examination the patients were classified as per Ridley Jopling classifications (13), the following investigations were undertaken.

1. Skin smears from 6 sites for BI, MI.
2. Pretreatment skin biopsy
3. Liver function tests and serum proteins
4. Chest X-ray
5. ESR, WBC, Hb.
6. Urine - Sugar/albumin

Skin smears were repeated once every two weeks. Skin biopsy and liver function tests were done after withdrawing of the campanion drug.

In a majority a black and white photograph was taken for identification and affixed in the records.

RESULTS

A.1. Use of rifampicin as a companion drug with dapsone:

600 mg of rifampicin was given orally on an empty stomach with 100mg dapsone. The patients were alloted to three different groups.

Group A. 19 multibacillary patients received rifampicin for 14 days.
Group B. 19 multibacillary patients received rifampicin for 30 days.
Group C. 9 multibacillary patients received rifampicin for 90 days.

TABLE-3: THE NUMBER OF LL AND BL LEPROSY PATIENTS WHO RECEIVED RIFAMPICIN ALONG WITH DAPSONE.

	Group A	Group B	Group C	Total
LL	11	11	6	28
BL	8	8	3	19
Total	19	19	9	47

TABLE-4: THE MALE/FEMALE PATIENT RATIO.

	Male	Female	Total
LL	20	6	26
BL	14	6	20
Total	34	12	46

Lepromatous infiltration was reduced in all patients receiving rifampicin. No liver and renal abnormalities were encountered, patients felt better and nasal ulcers healed well.

The average of BI and MI were derived by first averaging the results of the six skin smears from each patient prior to and after therapy and these ten averaged for the group of patients in A, B, C.

TABLE-5: THE RESULTS OF AVERAGE BACTERIOLOGICAL ASSESSMENT BEFORE AND AFTER THERAPY WITH COMPANION DRUG RIFAMPICIN.

		BI	MI
Group A	Pretreatment	4.0	1.92
	After 2 weeks	3.4	0.74
Group B	Pretreatment	4.2	1.36
	After 4 weeks	3.6	0.12
Group	Pretreatment	4.88	3.3
	After 90 days	3.6	0.57

A.II. Use of prothionamide as a companion drug with dapsone:

7 multibacillary patients received 500 mg of prothionamide with 100 mg dapsone daily. This was to ascertain the acceptability and to observe side effects with use of prothionamide. After 3/12 prothionamide was withdrawn and dapsone continued. Lepromatous infiltration was reduced and nasal congestion too was reduced. The following side effects were observed.

(a) 2 patients complained of nausea and abdominal discomfort.
(b) One patient developed exfoliative dermatitis.

TABLE-6: THE NUMBER OF MALE AND FEMALE MULTIBACILLARY LEPROSY PATIENTS WHO RECEIVED PROTHIONAMIDE IN ADDITION TO DAPSONE.

	Male	Female	Total
LL	4	1	5
BL	2	0	2
Total	6	1	7

TABLE-7: THE AVERAGE BACTERIOLOGICAL ASSESSMENT BEFORE AND AFTER THERAPY WITH PROTHIONAMIDE.

Pretreatment	BI	MI
Pretreatment	3.22	1.28
After 3/12	2.55	0.5

TABLE-8: THE COMPARATIVE RESULTS OF MORPHOLOGICAL INDICES.

		Group A	Group B	Total
A. I	Pretreatment	1.92	1.36	3.3
	Post treatment	0.74	0.12	0.57
A. II	Pretreatment	1.28		
	Post treatment	0.5		

B. Use of Lamprene as companion drug with dapsone for twelve months:

After giving adequate information to patients as to the side effects of Lamprene, it was administered 100 mg bi-weekly with 100 mg dapsone daily. As they are still continuing therapy, average bacteriological assessment are not reported here. However, the following side effect were noticed in 10 patients - 4BL and 6 LL.

1. Abdominal discomfort - after 3 months
2. Albumin in urine
3. Bilateral pedal oedema

TABLE-9: THE MALE AND FEMALE LEPROSY PATIENTS RECEIVING LAMPRENE ALONG WITH DAPSONE.

	Male	Female	Total
BL	14	3	17
LL	13	4	17
Total	27	7	34

The patients were admitted for three months for supervised administration of drugs after which they received the supply of drugs at the skin clinic once every three months. Five patients failed to come regularly to skin clinic (14.7%) to take drugs.

C. Polytherapy in paucibacillary patients:

Previously untreated 13 borderline tuberculoid patients received 600 mg rifampicin on empty stomach in addition to 100 mg of dapsone. After 30 days rifampicin was withdrawn. Skin biopsies were taken prior to and after 30 days of polytherapy for histopathological examination.

TABLE-10: THE NUMBER OF MALE AND FEMALE BORDER LINE TUBERCULOID PATIENTS IN THE STUDY.

	Male	Female	Total
Bt	7	6	13

Five patients were bacteriologically positive and averages are shown below:

	BI
Pretreatment	1.04
30 days	0.24

COST ANALYSIS OF COMPANION DRUGS

A.I. Rifampicin:
Group A:
per patient NC 172.50 = US$14.87 x 19 = US$282.53
Group B:
per patient NC 345.00 = US$29.74 x 19 = US$565.06
Group C:
per patient NC1036.80 = US$89.37 x 9 = US$804.33

A.II. Prothionamide:
One tablet costs Rs.1.95 x 4 = 7.80 (US$0.65)
Therefore Rs.7.80 z 90 days ... Rs.702.00 (US$58.50) x 7 = US$409.50

B. Lamprene:
Cost of one capsule of 100 mg = Rs.2.70 (US$0.225)
for year ... Rs.280.80 (US$23,3) x 24 = US$792,20
All the drugs including dapsone were purchased from U.K. by The Leprosy Mission International. The price does not include the cost of freight.

CONCLUSION

1. This preliminary report reveals that leprosy patients under our care accept and tolerate the companion drugs. Patients are able to accept Lamprene if adequate information is given regarding the side effects.
2. For intensification of leprosy control programme it is essential that polytherapy be introduced. Only 11 (10.8%) patients in the study failed to be regular on subsequent follow-up visits. The possible conclusion may be drawn to the fact that adequate health information was given prior to starting therapy.
3. Significant differences are noticed in bacteriological assessments prior to and after therapy with use of rifampicin and prothionamide, when compared with dapsone on its own. In particular, the fall in morpholotical indices in Group B patients with rifampicin for 30 days is significant.
4. The paucibacillary borderline tuberculoid patients, who received rifampicin for 30 days initially will receive dapsone for a fixed period of 3 years.
5. Polytherapy must be administered under supervision to prevent development fo resistance to companion drugs and the misuse of the drugs.
6. The benefit achieved for the patients would outweigh the additional expenditure incurred for the companion drugs.

THE FUTURE:

I. Plans are a foot to extend to conduct such a study under the supervision of the staff of the primary health care unit (HP).

II. In outpatient's clinics supervised,"intermittent therapy" has been initiated with rifampicin and Lamprene. This we feel would be more aceptable by large proportion of leprosy patients, who otherwise may find it difficult to stay as inpatients.

It is imperative that all infectious and potentially infectious patients are treated with polytherapy to reduce the reservoir of infection in the community It is therefore obvious that bold and new initiatives should be undertaken to find solutions to some of the problems facing leprosy control.

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