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Monitoring dapsone self-administration in a multidrug therapy programme

ANNE-MARIE VAN ASBECK-RAAT*
& MARIJKE BECX-BLEUMINK†
* *Elective medical student, Erasmus University Rotterdam, Netherlands*; † *Director of ALERT Leprosy Control, Addis Ababa, Ethiopia*

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Summary In the ALERT Leprosy Control Programme implementation of multidrug therapy (MDT) started in January 1983. The majority of the patients had received dapsone monotherapy prior to MDT. To assess the intake of dapsone in the MDT programme the urine spot test is done in all the paucibacillary patients during the 4th and 6th supervised treatment day; with the multibacillary patients during the 4th, 6th, 12th, 18th and 24th supervised treatment. Results of the 4th and 6th treatment round are presented and discussed.

Of the 721 patients tested the overall percentage of patients with a positive test was 90·9%. Patients with a previous duration of treatment of more than 3 years were found to be significantly less compliant than others. Determinants like age, sex, disability grade or having a leprosy contact in the family did not influence compliance in a significant way.

Introduction

In leprosy control programmes patients on dapsone monotherapy are regarded as regular attenders if they have collected 75% or more of the tablets they were expected to collect during a year. The collection of drugs for self-administration (attendance) is generally used as a measure for drug intake (compliance) by the patients. However compliance studies by way of urine testing for the presence of dapsone in several countries showed that only 40–70% of the patients had taken the drug before attending the clinic.[1–14] One of the reasons for treatment failure with dapsone has been the irregularity of drug intake.

In the ALERT MDT programme the WHO recommended regimens have been introduced.[15] These are:

Paucibacillary leprosy—rifampicin 600 mg once a month, supervised, for 6

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months; and dapsone 100 mg daily for 6 months, self-administered.
Multibacillary leprosy—rifampicin 600 mg once a month, supervised; dapsone 100 mg daily, self-administered; and clofazimine 300 mg once monthly, supervised, and 50 mg daily, self-administered.

For paucibacillary patients the attendance for supervised treatment is the most important factor to determine whether a patient should be regarded as cured. They can be released from chemotherapy after having collected 6 doses of supervised treatment and the 6 months of dapsone for daily self-administration within a period of 9 months.[16] Multibacillary patients have to continue MDT for at least 2 years and until their skin smears are negative.[15] They have to collect the 24 doses of supervised treatment and the daily dapsone and clofazimine for self-administration within a period of 36 months.[16]

For the group of patients who received monotherapy prior to MDT, the regularity of attendance is the important criterium for release, as the majority of them will have had negative skin smears already at the start of MDT. Compliance in MDT is even more critical than in dapsone monotherapy because irregularity of drug intake may result in unmanageable situations, i.e. multiple resistance. The WHO Studygroup stresses that 'to maintain regular drug intake has now become a managerial task par excellence and needs priority attention'.[15] The International Federation of Anti-Leprosy Associations (ILEP) asks, in its publication *The introduction of multidrug therapy in leprosy*[17] for special evaluation studies, among which is the testing of compliance to monitor the intake of the drugs prescribed.

Objectives of this study

The objectives of this study are: to get information on whether or not patients take the unsupervised component (dapsone) of MDT; and to obtain determinants of patients' compliance behaviour.

At ALERT the spot test has been introduced to detect dapsone in urine. It was described in 1965 by de Castro and recommended by WHO in 1966 but has, despite its simplicity, not been used widely in the field, apart from India.[12,13,21–25] The test was found insensitive by some[20] but more recently a good correlation with the dapsone/creatinine method was reported.[13,24,25]

For clofazimine, the second unsupervised drug in multibacillary leprosy, no satisfactory test has been developed yet. However, we may probably assume that in most cases dapsone intake means clofazimine intake as well, especially because many leprosy patients have lost faith in dapsone and show a tendency to consume capsules.[18] Therefore it is likely that clofazimine has been taken when the urine test is positive for dapsone.[19] Furthermore our impression was that the vast majority of patients showed a distinct clofazimine discoloration of the skin, of

which only a few have complained so far. In the MDT programme the spot test is done during the 4th, 6th, 12th, 18th and 24th supervised treatment round. This publication gives the results of the 4th and 6th treatment round and is the first to report on compliance testing by way of the urine spot test in an MDT programme.

Patients and methods

All patients who started MDT in the 13 Addis Ababa town clinics during the period May–July 1984 and in the 11 clinics of Yerer & Kereyu area during June and July 1984 were included. Surprise home visits were not done as they are not feasible in the field and moreover were not found to render significantly different results as compared to routine clinic visits.[11]

The urine of 721 patients was tested on the 4th and 6th supervised treatment round. Patients who did not attend during the scheduled clinic days were not included. However, most patients who did not attend during the scheduled day, came one or more days later. Also excluded were patients who were absent in the treatment round prior to the test (18), and patients who had a dapsone allergy (2) or could not pass urine (3). The spot test is done by pipetting a drop of fresh urine on filter paper impregnated with modified Ehrlich's reagent. When dapsone is present, an inner spot of orange to yellow colour appears; a yellow ring in the periphery is due to urea. A very faint orange spot was recorded as $\pm$ but considered as positive. In the case of a negative test a drop of 1N HCl was added to the urine specimen and the test was repeated to exclude false negatives. Because of instability of the solution a positive control could not always be included. However, we did not experience any problem in reading the results. Recently a stable positive control solution was developed.[19] We may reasonably assume that our + and $\pm$ group is identical with the positive category as indicated by the positive control solution mentioned.

A positive test means that on average dapsone was taken 4 days ago but probably no more during the last 3 days before testing. A negative test indicates that dapsone was not taken according to schedule and possibly so long ago that the blood level has fallen below the MIC.[19]

Information was collected from each patient about sex, age, classification, leprosy contact in the family, disability grade and duration of previous treatment.

Table 1. Attendance rates and urine test results in 13 Addis Ababa town clinics.

Treatment round	Patients expected	Patients attended	%	Urine tested	Urine pos.	%	Urine ±	%	Urine neg.	%
4th	568	500	88·0	494	415	84·0	44	8·9	35	7·1
6th	582	481	82·6	473	396	83·7	22	4·7	55	11·6

Results and discussion

Tables 1 and 2 show the test results. On average, 85·0% of the patients who were expected during the supervised treatment day attended. The percentage of attenders with a positive test ranged from 88·4 to 93. When nonattenders are included in the denominator the minimal range of positive tests still varies

Table 2. Attendance rates and urine test results in 11 clinics in Yerer & Kereyu area.

Treatment round	Patients expected	Patients attended	%	Urine tested	Urine pos.	%	Urine ±	%	Urine neg.	%
4th	148	121	81·8	114	98	86·0	8	7·0	8	7·0
6th	165	142	86	142	126	88·7	3	2·1	13	9·2

Table 3. Data of patients with a positive and negative urine test

	Addis Ababa				Yerer/Kereyu			
	Positive		Negative		Positive		Negative	
	n	(%)	n	(%)	n	(%)	n	(%)
Classification								
Multibacillary	286	(60·3)	60	(73·2)	94	(64·8)	12	(60)
Paucibacillary	188	(39·7)	22	(26·8)	51	(35·2)	8	(40)
Total	474	(100)	82	(100)	145	(100)	20	(100)
Sex								
Female	247	(52·1)	41	(50)	44	(30·3)	8	(40)
Male	227	(47·9)	41	(50)	101	(69·7)	12	(60)
Total	474	(100)	82	(100)	145	(100)	20	(100)
Age								
<15	21	(4·4)	5	(6·1)	5	(3·4)	0	
15–45	361	(76·2)	62	(75·6)	100	(69·0)	16	(80)
45+	92	(19·4)	15	(18·3)	40	(27·6)	4	(20)
Total	474	(100)	82	(100)	145	(100)	20	(100)
Disability grade								
0–1	339	(71·5)	55	(67·1)	100	(69·0)	14	(70)
2–3	135	(28·5)	27	(32·9)	45	(31·0)	6	(30)
Total	474	(100)	82	(100)	145	(100)	20	(100)
Contact in family	47	(9·9)	10	(12·2)	19	(13·1)	1	(5)

Table 4. Duration of treatment in relation to compliance (Addis Ababa and Yerer & Kereyu combined).

Duration of treatment	Positive test n	%	Negative test n	%
less than 1 year	46	(7·5)	3	(2·9)
1–3 yr	188	(30·6)	16	(15·7)
3–5 yr	115	(18·7)	29	(28·4)
5+ yr	265	(43·2)	54	(52·9)
Total	614	(100)	102	(100)

between 72 and 81%. Tables 3 and 4 contain general data on compliant patients, as well as data for the patients who were negative once (92) or twice (10). A statistically significant relationship was found between noncompliance and duration of treatment prior to MDT longer than 3 years ($p < 0{\cdot}01$ in χ^2 test). Paucibacillary patients were more compliant than multibacillary patients ($p = 0{\cdot}10$). A significantly reduced compliance in patients under the age of 15 or above 45 was not observed, nor did we find a correlation between compliance and sex, disabilities or having a leprosy contact in the family.

A number of studies have dealt with the relationship between patients' variables and compliance.[3,9,11–13,24,26] The picture emerging from it is not uniform, but most authors have agreed on the following conclusions, of which the first was confirmed also in this study:

1 Patients with a long duration of treatment are less compliant. Associated with this is the observation that patients on the lepromatous side of the spectrum (who tend to have been treated longer) are less compliant than those on the tuberculoid side.
2 Patients younger than 15 years and older than about 45 are less compliant.

Some authors found a negative relationship between compliance and having a leprosy contact, having disabilities and being a female, while others could not confirm this.

Conclusions and recommendations

The intake of dapsone in the ALERT MDT programme as measured by way of the urine spot test appears to be very encouraging, especially when compared to

the 60% compliance in the monotherapy era.[10] Among others it indicates the enthusiasm of both patients and staff for the new programme.

The relationship between noncompliance and a long history of treatment has been confirmed in this study. Sex, age, disability grade and a contact in the family were not found to be important determinants. It is recommended that feedback of the test results is given to the patients afterwards. In the ALERT programme this was done by the supervisors in the health education talk and this was very satisfactory. Individual feedback was occasionally given, mostly to the patients who had been negative twice.

The urine spot test will be incorporated in the routine work of the field staff during the next treatment rounds. This is highly recommended also for other control programmes. The spot test is sufficiently sensitive, it is cheap ($0·2/100 tests), but above all it is simple enough to perform on the spot in the field.

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