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Association Between Regularity in Dapsone (DDS) Treatment and Development of Deformity[1]

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In clinical practice and in mass treatment programs, it is customary for physicians and other health personnel to exhort patients to be very regular in collecting their drugs and in consuming them, for it is well known that the greater the regularity, the higher the likelihood of a favorable outcome. When doing so, they assume that regularity in drug ingestion will not have any adverse consequences that are permanent or major. In the case of dapsone (DDS), a drug used in leprosy control programs for over three decades, there have been some reports from India about the possibility of drug regularity resulting in the development of deformities ([6, 10]). The available evidence, however, has a number of limitations and is not conclusive. An opportunity to investigate the association rather more rigorously arose during the course of a retrospective assessment of the leprosy control program at the Hemerijckx leprosy control center in Polambakkam (Chingleput District) in Tamil Nadu, South India. The findings of this study are reported in this paper.

MATERIALS AND METHODS

The methodology of the retrospective assessment of the leprosy control program at Polambakkam was described in an earlier report ([8]). The analyses in the present report are based on 5746 patients who were initially not deformed from a 25% random sample of sub-centers in Uttaramerur zone (4 of 14 sub-centers) and Tindivanam zone (5 of 18 sub-centers). These patients had all been prescribed treatment with daily DDS for several years, the actual duration of treatment depending on their responses. Their clinical status was assessed at annual intervals, and on these occasions any new deformities that developed were recorded; loss of sensation was not regarded as a deformity. Characteristics of the cases, such as age, sex, type,* deformity status, bacteriological status, treatment regularity, deformity status during treatment, and outcome of treatment, were obtained from the case records by two statistical assistants working under the supervision of a senior leprologist (Dr. M. Christian).

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* The classification employed was lepromatous (L); nonlepromatous (N), consisting of tuberculoid, maculoanesthetic and polyneuritic cases; and intermediate (N?L), consisting of borderline and indeterminate cases.This is a telescoped version of the Indian classification, as reported by Dharmendra ([4]).

TABLE 1. *Development of deformities related to regularity in drug collection.*

	Percentage of drugs collected					p[a]
	<20	20–39	40–59	60–79	≥80	
0–1 year						
Total patients	1044	806	792	1033	2071	
Deformed in 1st yr (per thousand)	5.7	7.4	15.2	20.3	16.9	<0.01
Relative risk[b]	1.0	1.3	2.7	3.6	3.0	
0–2 years						
Total patients	1539	1018	916	1028	1112	
Deformed in 2nd yr (per thousand)	5.2	16.7	22.9	24.3	54.9	<0.001
Relative risk[b]	1.0	3.2	4.4	4.7	10.6	
0–3 years						
Total patients	1691	1099	920	829	754	
Deformed in 3rd yr (per thousand)	8.9	11.8	9.8	27.7	51.7	<0.001
Relative risk[b]	1.0	1.3	1.1	3.1	5.8	
0–4 years						
Total patients	1691	1142	798	706	553	
Deformed in 4th yr (per thousand)	14.8	27.1	32.6	58.1	75.9	<0.001
Relative risk[b]	1.0	1.8	2.2	3.9	5.1	
0–5 years						
Total patients	1625	1032	679	584	415	
Deformed in 5th yr (per thousand)	9.8	22.3	30.9	46.2	62.7	<0.001
Relative risk[b]	1.0	2.3	3.2	4.7	6.4	

[a] p value for the trend in the incidence of deformities.
[b] Taking "less than 20%" group as the base.

Mean regularity is defined as the number of weeks for which drugs were actually collected expressed as a percentage of the number of weeks for which drugs were due to be collected. The existence of an association between drug regularity and the development of deformities was first examined by comparing the incidence of deformity in various cohorts of patients with different degrees of drug regularity. This was followed by comparisons of the incidence of deformity in "more regular" cases and "less regular" cases in each of several subgroups according to type of leprosy and age or sex of the patient. Finally, a case-control analysis was undertaken to determine whether the deformed cases truly had significantly higher degrees of regularity before the development of the deformity than undeformed controls, after matching for several characteristics with prognostic significance.

Statistical methods employed were *t* tests for differences in means of paired observations, trend chi-square test on proportions, Cochran's test (^{2}) for combining differences in proportions from several 2 × 2 contingency tables, correlation coefficients for measuring associations, and life-table and analysis of variance techniques.

RESULTS

Of the 5746 patients with no deformity initially, 589 are known to have developed a deformity during the next 5 years: 503 at one site, 78 at two sites, 7 at three sites, and 1 at four sites. The incidence, computed using the life-table technique, was 11.1% over the 5-year period. The site of deformity was the hands in 46%, the feet in 52%, the face in 15%, and the eyes in 3%.

Incidence of deformities related to regularity in drug collection. The incidence of deformities in patients with different degrees of drug regularity is shown in Table 1. In the first year, the incidence was 5.7 per thousand in 1044 patients who collected <20% of their drugs, 7.4 per thousand in 806 who collected 20–39%, 15.2 per thousand in 792 who collected 40–59%, 20.3 per thousand in 1033 who collected 60–79%, and 16.9 per thousand in 2071 who collected at least 80% of their drugs. The increasing trend in incidence with increasing regularity was statistically significant (p <

TABLE 2. *Incidence of deformity over a 5-year period according to sex, age, and type of leprosy.*

Leprosy type	Incidence of deformity over 5-year period[a]					
	Total[b]	Male	Female	<15 yrs old	15–44 yrs old	≥45 yrs old
N	6.8% (4736)[c]	8.3% (2785)	4.7% (1931)	1.3% (1798)	8.3% (2248)	16.9% (663)
N?L	19.6% (492)	20.8% (318)	17.5% (171)	5.2% (102)	21.9% (289)	26.9% (97)
L	45.9% (450)	46.5% (359)	42.9% (89)	33.4% (30)	42.4% (325)	61.8% (90)
All types[d]	11.1% (5746)	13.5% (3516)	7.2% (2228)	2.0% (1977)	13.7% (2890)	22.8% (864)

[a] Computed using life-table technique.
[b] Including patients whose sex and age were not recorded.
[c] Numbers in parentheses denote size of cohort at start of treatment.
[d] Including patients whose type was not recorded.

0.01). Taking the <20% collection group as the base, the relative risks were 1.3, 2.7, 3.6, and 3.0 in the patients who collected 20–39%, 40–59%, 60–79%, and 80% or more of their drugs, respectively.

The findings in 0–2, 0–3, 0–4, and 0–5 years showed even stronger trends, with the risk of deformity in those who collected at least 80% of their drugs being 5 to 10 times as high as that in patients who collected <20% of their drugs.

Other characteristics associated with incidence of deformities. The incidence of deformities over a 5-year period was considerably higher in males (13.5%) than in females (7.2%) and increased substantially with age, being 2.0%, 13.7%, and 22.8% in those aged <15 years, 15–44, and 45 or more years, respectively (Table 2). It was least in nonlepromatous cases (6.8%), intermediate in N?L cases (19.6%), and highest in lepromatous cases (45.9%). The difference between the sexes and the increasing trend with age were present in all three types of leprosy cases; similarly, the difference between the types was evident in both sexes and at all ages. It is concluded that sex, age, and type of leprosy are all strongly associated with the development of deformities.

Table 3 sets out the incidence of deformity according to the year of treatment for each of the three types of leprosy. No particular pattern is evident in N and N?L patients. In the case of L patients, however, the incidence increased steadily from year to year, being 36, 72, 92, 190, and 178 per thousand in the first to the fifth years, respectively; the correlation coefficient between incidence and year of treatment was 0.94.

Study of association between regularity and deformity in different subgroups. In view of the findings above regarding the influence of type of leprosy, age, and sex on the likelihood of deformities developing during treatment, it was decided to investigate, for

TABLE 3. *Incidence of deformity according to year of treatment and type of leprosy.*[a]

Year	N cases			N?L cases			L cases		
	Population at risk	Deformed		Population at risk	Deformed		Population at risk	Deformed	
		No.	Per 1000		No.	Per 1000		No.	Per 1000
First	4736	44	9.3	492	20	40.7	450	16	35.6
Second	4644	73	15.7	469	27	57.6	432	31	71.8
Third	4413	51	11.6	428	12	28.0	390	36	92.3
Fourth	4091	78	19.1	399	21	52.6	343	65	189.5
Fifth	3659	53	14.5	356	12	33.7	269	48	178.4

[a] Excluding 68 patients for whom the type of leprosy was not recorded.

TABLE 4. *Study of the association in different subgroups (by age and sex) in N patients.*

	Drug regularity by age and sex									
	<15 years		15–44 years		≥45 years		Males		Females	
	<40%	≥40%	<40%	≥40%	<40%	≥40%	<40%	≥40%	<40%	≥40%
0–1 year										
Total patients at risk	617	1181	789	1459	238	425	936	1849	708	1223
Deformed in 1st yr										
N	0	6	5	21	4	8	5	27	4	8
Per thousand	0.0	5.1	6.3	14.4	16.8	18.8	5.3	14.6	5.6	6.5
0–2 years										
Total patients at risk	846	935	1094	1099	329	315	1292	1435	979	919
Deformed in 2nd yr										
N	1	3	12	35	6	16	14	35	5	19
Per thousand	1.2	3.2	11.0	31.8	18.2	50.8	10.8	24.4	5.1	20.7
0–3 years										
Total patients at risk	934	784	1187	892	349	249	1427	1168	1046	761
Deformed in 3rd yr										
N	0	3	7	25	7	9	10	32	4	5
Per thousand	0.0	3.8	5.9	28.0	20.1	36.1	7.0	27.4	3.8	6.6
0–4 years										
Total patients at risk	964	647	1193	730	347	195	1451	948	1056	628
Deformed in 4th yr										
N	3	3	17	23	12	20	20	29	12	17
Per thousand	3.1	4.6	14.2	31.5	34.6	102.6	13.8	30.6	11.4	27.0
0–5 years										
Total patients at risk	899	523	1151	607	317	150	1389	765	980	518
Deformed in 5th yr										
N	1	2	14	16	8	12	18	25	5	5
Per thousand	1.1	3.8	12.2	26.4	25.2	80.0	13.0	32.7	5.1	9.7
Excess incidence (per 1000) in more regular patients										
Average[a]	3.05		16.65		32.02		15.76		7.98	
p value	<0.01		<0.001		<0.001		<0.001		<0.001	

[a] Weighted average, using weights recommended by Cochran (2).

TABLE 5. *Study of the association in different subgroups (by age and sex) in N?L patients.*

	Drug regularity by age and sex									
	<15 years		15–44 years		≥45 years		Males		Females	
	<50%	≥50%	<50%	≥50%	<50%	≥50%	<50%	≥50%	<50%	≥50%
0–1 year										
Total patients at risk	34	68	75	214	22	75	81	237	51	120
Deformed in 1st yr	1	1	1	11	1	5	3	12	0	5
0–2 years										
Total patients at risk	51	48	101	175	30	60	108	193	75	90
Deformed in 2nd yr	0	1	6	13	0	7	3	12	3	9
0–3 years										
Total patients at risk	58	37	107	140	34	48	121	156	79	69
Deformed in 3rd yr	0	0	0	6	2	4	1	9	1	1
0–4 years										
Total patients at risk	59	32	114	121	38	33	127	129	85	57
Deformed in 4th yr	1	0	6	12	1	1	5	8	3	5
0–5 years										
Total patients at risk	51	31	107	102	36	28	116	113	79	48
Deformed in 5th yr	0	1	1	5	1	3	2	8	1	1
Excess incidence (per 1000) in more regular patients										
Average[a]	4.11		35.96		49.85		34.75		34.06	
p value	>0.2		<0.01		0.03		<0.01		0.01	

[a] Weighted average, using weights recommended by Cochran (2).

each type of leprosy, whether patients who were more regular had a higher incidence of deformities than the others in each age group (<15, 15–44, ≥45 years) and for each sex. Since the levels of regularity were lowest among N patients, intermediate in N?L patients, and highest among L patients (8) and since it was necessary to provide for reasonable numbers of patients for analysis in the "more regular" and "less regular" groups, different cutoff points were chosen to distinguish between the two groups. These cutoff points were 40% for N patients, 50% for N?L patients, and 60% for L patients. The findings are shown in Tables 4, 5, and 6.

Among N cases, the more regular patients had a consistently higher incidence of deformity in all three age groups and for both sexes in each year of treatment (Table 4). The excess incidence was highly significant statistically, the numerical estimates being 3, 17, and 32 per thousand in <15, 15–44, and ≥45 years of age groups, and 16 and 8 per thousand in males and females, respectively.

In N?L cases, the numbers with deformities were rather small in each year. However, on averaging the differences over the 5 years, the more regular patients had an excess incidence of deformities (Table 5). The excess was 4 per thousand in patients aged under 15 years ($p > 0.2$), 36 per thousand in those 15–44 years old ($p < 0.01$), and 50 per thousand in those aged 45 years or more ($p = 0.03$). It was highly significant ($p < 0.01$) in both males (35 per thousand) and females (34 per thousand).

In L cases, where the numbers were also relatively small, the evidence of an association was not very consistent in the various subgroups (Table 6). Thus, the excess incidence in the more regular patients was 77 per thousand in those under 15 years, 25 per thousand in the 15–44 age group, and only 1.6 per thousand in those aged 45 years or older. None of these differences is statistically significant ($p > 0.05$). There was an excess in males (35 per thousand, $p = 0.03$) but a deficit in females (3 per thousand, $p > 0.2$).

Findings of case-control study. To seek confirmation of the association between regularity and deformity, a case-control type of analysis was also employed. For this purpose, among patients who developed a de-

TABLE 6. *Study of the association in different subgroups (by age and sex) in L patients.*

	Drug regularity by age and sex									
	<15 years		15–44 years		≥45 years		Males		Females	
	<60%	≥60%	<60%	≥60%	<60%	≥60%	<60%	≥60%	<60%	≥60%
0–1 year										
Total patients at risk	5	25	90	235	24	66	90	269	30	59
Deformed in 1st yr	1	1	2	7	1	4	3	9	1	3
0–2 years										
Total patients at risk	8	20	112	203	34	50	124	222	31	53
Deformed in 2nd yr	0	1	5	16	3	4	6	18	2	4
0–3 years										
Total patients at risk	10	15	126	163	33	41	140	175	30	45
Deformed in 3rd yr	0	0	8	15	6	7	7	16	7	6
0–4 years										
Total patients at risk	10	14	119	139	26	33	132	151	24	36
Deformed in 4th yr	0	1	16	28	9	10	23	36	2	4
0–5 years										
Total patients at risk	9	13	106	102	18	20	115	102	19	33
Deformed in 5th yr	0	5	19	16	3	5	20	21	2	5
Excess incidence (per 1000) in more regular patients										
Average[a]	76.99		25.02		1.58		34.59		−3.33	
p value	0.07		0.1		>0.2		0.03		>0.2	

[a] Weighted average, using weights recommended by Cochran ([2]).

formity, those who had been clinically assessed in the immediately preceding year and found to be without deformity were identified as "cases," i.e., these were patients in whom the year of development of deformity was precisely known. Next, an undeformed matched "control" was identified for each deformed case, the characteristics for matching being the type of leprosy, sex, age, and year of starting treatment (to eliminate any cohort effect). The period over which regularity was assessed did not include the year in which the deformity developed or the subsequent years, because the regularity in that year and in subsequent years could have been affected by the development of the deformity. Finally, since it is well known that drug regularity decreases with the passage of time ([8, 9]), the period over which regularity was assessed for the control was taken to be the same as that employed for the corresponding deformed case.

The mean regularity for the cases (deformed patients) and for the matched controls (undeformed patients) was computed

TABLE 7. *Regularity of drug collection in patients who developed deformity during treatment and in matched controls.*

Leprosy type	No. of matched pairs[a]	Mean regularity[b]			p
		Deformed (case)	Not deformed (control)	Difference	
N	140	58.6%	41.7%	16.9%	<0.001
N?L	48	74.2%	51.7%	22.5%	<0.001
L	81	72.9%	65.1%	7.8%	0.04
Total[c]	269	65.7%	50.6%	15.1%	<0.001

[a] Matching undertaken by sex, age, calendar year of starting treatment, and observation period for the assessment of regularity.

[b] Percentage of drug doses collected.

[c] Excluding 27 patients for whom a matched control could not be obtained.

TABLE 8. *Analysis of variance of data on regularity from case-control study.*

Term	Source	Degree of freedom	Mean square	Variance ratio	p
a	Between pairs	268	908.53		
b	Between types (T)	2	19,596.90	25.52	<0.001
c	Between pairs of the same type	266	768.01		
d	Within pairs	269	848.98		
e	Between deformed and undeformed (D)	1	30,653.80	42.04	<0.001
f	Interaction (T × D)	2	1,876.06	2.57	0.08
g	Residual	266	729.21		

for each type of leprosy. The findings are summarized in Table 7. In general, the mean regularity of deformed patients was higher than that of matched controls—58.6% compared to 41.7% in N cases, 74.2% compared to 51.7% in N?L cases, and 72.9% compared to 65.1% in L cases. The contrast was highly significant in N and N?L cases ($p < 0.001$) but of border-line significance in L cases ($p = 0.04$).

An analysis of variance of the data on regularity from the case-control study is shown in Table 8. This demonstrates significant differences in mean regularity between a) N, N?L, and L cases (term b) and b) deformed and undeformed patients (term e). The interaction between deformity status and type of leprosy is nonsignificant (term f), i.e., the variation in the difference between deformed cases and matched controls in mean regularity—16.9% in N cases, 22.5% in N?L cases, and 7.8% in L cases—could be due to chance. However, considering that the interaction probability is border-line (0.08), and the p value for the contrast between deformed and undeformed is also border-line in L cases (0.04) unlike those in N?L cases and N cases (<0.001), it is possible that there is a difference in the strength of the association in the L cases, on the one hand, and the N and N?L cases on the other. Such an inference is consistent with the findings of the longitudinal study.

DISCUSSION

The possibility of an association between regularity in taking DDS and deformity development was first noted in 1966 by Srinivasan and Noordeen ([10]), who concluded that "DDS treatment under 'field' conditions could possibly result in increased disability in the patient population." They did add, however, that their data was from a cross-sectional one-time study only and, as such, it could not establish whether disability followed or preceded treatment. Other drawbacks in this study, as pointed out by Dharmendra ([3]), were that loss of sensation, which is a symptom of the disease, was considered as deformity, and that only 20% of the data collected by paramedical workers was cross-checked by a leprologist. Both the authors and their critic were in agreement that only a longitudinal study could clarify the issues involved.

On the basis of a general survey and a follow-up study of 2 to 6 years, Wardekar, as quoted by Dharmendra ([3]), had concluded in 1958 that practically no deformity developed in patients put on sulfone treatment in the early stages of their disease. Also, subsequent to the publication of the findings of Srinivasan and Noordeen ([10]), Wardekar ([11]) dismissed the possibility of regularity causing deformities as "completely wrong," because his longitudinal study data showed that patients with a deformity initially were more regular in collecting drugs than those who did not have an initial deformity. Wardekar's data also showed that, among patients with no initial deformity, those who developed a deformity during treatment were more regular than those who did not. He explained this by stating that the development of the deformity had induced the patients to be more regular. In 1979, Gupte ([6]) demonstrated, also in a longitudinal study, the presence of a significant positive association between regularity in clinic attendance and development of deformities. However, the period of observation was variable (i.e., from date of registration to

1972), and no effort was made, either in his study or Wardekar's, to control or allow for the impact of other relevant factors such as sex, age, or year of starting treatment (cohort effect). Furthermore, in both the studies the assessment of regularity in patients who developed deformities was based on the findings both before and after the development of the deformity. This procedure could have introduced bias if the development of deformity had some influence on the subsequent regularity pattern. Gupte did not seem to think so, for he concluded, on the basis of a test of statistical significance, that drug regularity before and after the development of deformity was similar ([6]). However, since it is well known that regularity decreases with the passage of time ([8, 9]), it could be argued that the similarity demonstrated by Gupte is consistent with the hypothesis that deformity had induced higher degrees of regularity—as inferred by Wardekar ([11])—and in the process, eliminated secular trends.

Evidence of a real association between drug regularity and the development of deformities is rather more convincing in our longitudinal study. To begin with, when all leprosy patients were considered, the incidence of deformity increased steadily and significantly with increasing regularity in each year of treatment from the first to fifth. Secondly, comparisons of deformity incidence in "more regular" and "less regular" patients pointed to significant excesses in the former in all age groups and both sexes in nonlepromatous (N) cases, who constitute the main burden of leprosy (83%) in this community (the evidence was quite strong in N?L cases also, but rather inconsistent in L cases). On the debit side, however, losses in follow-up because of migration, death, or nonattendance at the clinic were substantial (about 30%) in this study ([8]), which it may be stressed was a retrospective analysis of data collected in the leprosy control program and not a prospective study, and the possible biases arising from these are not easy to allow for. Therefore, an alternative method, retrospective in nature (namely, the case-control approach) was employed to confirm the existence of the association. The case-control study reported here eliminated the effects of sex, age, type of leprosy, and observation period for the assessment of regularity as well as any cohort effect (year of starting treatment). Even more important, the assessment of mean regularity was restricted to the period preceding the development of deformity. Thus, the possibility of the deformity itself having induced higher degrees of regularity ([11]) becomes a non-issue for the interpretation of the association in this study. This is the major difference between this study and earlier ones ([6, 10]), where the assessment of regularity included two phases, one before and the other after the development of the deformity.

The findings of the case-control study strongly confirm the presence of an association between regularity in dapsone collection and the development of deformities. Thus, in all three leprosy types (N, N?L, L), the mean regularity was significantly higher in the deformed patients than in the matched controls. The association was, however, not as strong in lepromatous cases as in the others, and was just significant ($p = 0.04$). In general, it is known that lepromatous patients run a higher risk of developing deformities than do those with other types of leprosy, suggesting that other factors also might be operating in them that lead to deformity. If this is the case, it could be argued that the role of regularity would be relatively small in lepromatous patients and, therefore, more difficult to demonstrate.

In our study as well as in earlier ones, there is a tacit assumption that drugs collected are consumed, and the inference is consequently made that regular ingestion of dapsone leads to an increased likelihood of developing deformities. However, it is well known that drugs collected are not all consumed. Thus, Asbeck-Raat and Becx-Bleumink ([1]) have stated that compliance studies, by way of urine testing for the presence of dapsone, in several countries indicate that only 40–70% of the patients had taken the drug before attending the clinic. In a community similar to that studied in this report and at a distance of about 100 km from it, Radhakrishna, *et al.* ([9]) found that only 50% of the so-called regular patients showed evidence of drug intake as determined by a DDS-creatinine ratio estimation in the urine. Nevertheless, it is common practice

to employ the regularity in collecting drugs (for self-administration) as an index of the regularity in drug intake ([6, 9–11]) in the expectation of there being a good correlation between collection and consumption. Such an assumption has been tested in South India by Gothi, *et al.*([5]) in the context of a similar chronic disease, tuberculosis, and found to be correct. They found that approximately 70% of those who collected drugs in any month consumed them, and they inferred that patients who take the trouble to collect drugs also consume a large part of them.

It could be argued that the development of a deformity is part of the healing process, and that as regular patients respond better they tend to have a higher incidence of deformities. However, the available evidence in this study does not indicate that deformed patients had responded better than the matched controls. Since Magora, *et al.* ([7]) have reported insidious deterioration of muscles in 15 lepromatous patients on maintenance dapsone for 6 years, it is possible that deformity is also drug induced. Other workers, as quoted by Gupte ([6]), have also cited neurotoxic effects of the drug. It may therefore be concluded that regular dapsone ingestion could pose some practical problems in the form of increased incidence of deformities. Since the implications of this finding on both the patient and the health administrator could be far-reaching, more research on the subject is warranted. In particular, the role of nerve involvement and reactions, which could not be elucidated in this study for want of adequate data, needs to be taken into account. A prospective study over a 5-year period, with frequent assessments of deformity status and drug regularity and with high coverages throughout the period of observation and with special attention paid to the causation chain, would be most desirable.

SUMMARY

The existence of an association between regularity in dapsone intake and the development of deformity was investigated in 5746 leprosy patients under treatment in South India. The incidence of deformity, year by year over a 5-year period, increased significantly with increasing levels of drug collection. The excess incidence in "more regular" patients was significant at all ages and in both sexes in nonlepromatous (N) cases. The same was true in intermediate (N?L) cases except in patients under 15 years of age. The evidence in lepromatous (L) cases was not so consistent. Independent confirmation of the presence of the association was sought through a matched case-control type of analysis with 140 N, 48 N?L, and 81 L cases, matching being undertaken with respect to sex, age, type of leprosy, year of starting treatment, and observation period. This showed that the mean regularity in cases (deformed patients) before the development of deformity was significantly higher than the mean regularity in the corresponding matched controls, the differences being particularly large among the N and N?L types. These findings raise the possibility of a causal link between regular dapsone intake and the development of deformity.

RESUMEN

Se investigó la asociación entre la ingestión de dapsona y el desarrollo de deformidades en 5746 pacientes con lepra en tratamiento del Sur de la India. La incidencia de deformidad, año por año, durante un periodo de 5 años, aumentó significativamente con el grado de colección de la droga. El exceso en la incidencia de deformidades en los pacientes más regulares fue significativo en todas las edades y en ambos sexos en los casos no lepromatosos (N). Lo mismo ocurrió en los casos intermedios (N?L) excepto en los pacientes menores de 15 años de edad. La evidencia en los casos lepromatosos (L) no fue tan consistente. La confirmación de la existencia de asociación se hizo estudiando a pacientes y controles apareados en un grupo de 140 casos N, 48 N?L, y 81 casos L. El apareamiento se hizo con respecto a edad, sexo, tipo de lepra, año de inicio del tratamiento, y periodo de observación. Esto demostró que la regularidad promedio en los pacientes deformados, antes del desarrollo de la deformidad, fue significativamente más alta que la regularidad promedio en los controles apareados correspondientes, siendo las diferencias particularmente grandes entre los tipos N y N?L. Estos hallazgos sugieren la posibilidad de una relación causal entre la ingestión regular de dapsona y el desarrollo de deformidad.

RÉSUMÉ

Chez 5746 malades de la lèpre traités dans le Sud de l'Inde, on a recherché l'existence d'une association entre la régularité dans la prise de dapsone et le développement des difformités. L'incidence de diffor-

mités, année par année, au cours d'une période de 5 ans, a augmenté significativement avec l'élévation des taux d'assiduité au traitement. L'incidence excessive chez les malades considérés comme "plus réguliers" était significative à tous les âges, et dans les deux sexes, chez les cas non lépromateux (N). La même constatation a été faite pour les cas intermédiaires (N?L), sauf chez les sujets âgés de moins de 15 ans. Le données recueillies chez les malades lépromateux (L) n'étaient pas aussi nettes. On a recherché alors une confirmation indépendante de cette association, en menant une étude cas-témoins de 140 malades N, 48 N?L, et 18 L, assortis à des témoins pour ce qui regarde le sexe, l'âge, le type de lèpre, l'année au cours de laquelle le traitement avait été entamé, et la durée d'observation. Cette étude a montré que, chez les cas présentant des difformités, la régularité moyenne avant l'apparition de ces difformités, était significativement plus élevé que la régularité moyenne observée dans le groupe correspondant de témoins assortis. Les différences étaient particulièrement prononcées chez les malades présentant les types N et N?L de la maladie. Ces observations suggèrent qu'il pourrait exister une relation causale entre la prise régulière de dapsone et le développement des difformités.

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