Occurrence of late lepra reaction in leprosy patients: subsidies for implementation of a specific care program

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SUMMARY

Leprosy would be an ordinary disease; however, it is not due to *its* reactive *episodes with risk of disability maintaining the stigma related to the leprosy. These reactions and the potential loss of the neural function may happen before, during and after treatment, through a multidrug therapy (MDT). Release from treatment results from the number of doses and regularity of the treatment,* when the *patient leaves the coefficients* of *prevalence. The aim was* to *evaluate the magnitude of late leprosy reactions and* the *operational subjects referring to the attendance quality. Charts of the 149 patients that* received *discharge* for *leprosy* from 1994 to 1999, *in CSE Jaraguá - UFU, Brazil, were revised using the Record of Inquiry of Alterations After Cure of the Brazilian Ministry of Health. Of these patients, 34 (23%) presented* late reaction, of *which* 11,76% *were paucibacillary (PB) and 88,23%* were *multibacillary (MB). An average of 3 reactive episodes* for borderline patient *and 4 episodes for lepromatous patient occurred. Of PB patients, 100% presented reversal* reaction *(RR). Among MB, 50% presented RR,* 40% erythema *nodosum leprosum (ENL), 7% isolated neuritis and 3% mixed reaction. In 91%* of the *cases, the first* reactive *episode happened in the first year after treatment.* There was a *positive correlation among medium bacillary* index *(BI)* at *diagnosis and the number of reaction episodes during* treatment *and* after *release. Among patients with late reaction,* 97% *used prednisone and 32% thalidomide, meaning 22% and 8% from* the *total, respectively. Grade of disability 2 and 3 happened in MB* patients of *the economically* active *age. It is discussed the* need of *implementing leprosy control programs for that new group* of *patients with warranty* of *treatment, personnel training for simplified monitoring of neuritis and handling of the adverse* effects *of corticosteroids therapeutics, seeking the prevention of disabilities.*

Uniterms: Leprosy. Leprosy Reaction. Leprosy control programs. Prevention of Disabilities.

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INTRODUCTION

Leprosy would be considered an ordinary disease, but it is not due to its reactive episodes with involvement of peripheral nerve trunks and risk of disabilities[1'], maintaining the stigma and the unjustified prejudice that is still associated to leprosy, which curtails citizenship rights of patients in treatment and even cured'.

These acute reactions, with potential loss of the nerve function, can occur during the natural course of the disease, during treatment and even after specific treatment 15[15,21] with a fixed-duration multi-drug therapy regimen (MDT) of 6 months for paucibacillary patients (PB), 12 or 24 months for multibacillary patients (MB), depending on the number of lesions and bacillary index[5]. The release from treatment of leprosy patients is based on the number of doses taken and regularity of the treatment, so that the patient leaves the active registry and no longer will be computed in the prevalence rates of the disease[5].

The main strategy praised by World Health Organization (WHO) to eliminate leprosy as a problem of

public health by the year 2000 was to reduce the prevalence rates of the disease to very low levels, specifically to less than one case per 10,000 inhabitants, by means of the implementation of MDT. With the very high coverage of the MDT, it is expected that the infectious foci are eliminated in elapsing of time[24].

In 1992, Brazil became signatory of the goal of leprosy elimination. The Ministry of Health elaborated an elimination plan, aiming the earlier diagnosis and treatment with MDT in all cases, which cause the prevalence rates to fall from 16.4/10,000 inhabitants in 1985 to 5.51/10,000 inhabitants in 1997[4].

To reach the elimination goal it has been used the evaluation of the ratio prevalence/detection, that determines the average time of record keeping of the leprosy patient in the active registry, with reduction of 12.7 years in 1985 to 2 years in 1997, due mainly to the "cure" at the end of MDT[4]. This indicator has been used by the Ministry of Health as argument for the control of district expenses with the assistance of leprosy patients, implementing an "operational strategy " for monitoring of the effectiveness of MDT.

The approach of cost of record keeping of the leprosy patient in active registry in the local health system, has kept an expressive contingent of patients that develop reaction after release from treatment, occupying the demand of the leprosy control program, without any guarantee of adequate and specific assistance. According to the literature, 30% of cured patients may still present reactions until about 5 years after release from treatment[6,3], with nerve damages and potential risk of permanent disabilities.

The monitoring of this group of patients who, in accordance with Opromolla[17], "no longer have an infectious disease but an immunological one", must be priority subject of the elimination and control program of leprosy proposed by the Ministry of Health, aiming the prevention and the handling of disabilities through efficient methods concerning the relation cost-benefits for patient and its application in the Unified System of Health (SUS).

The objective of this work was to evaluate the magnitude and transcendence of reactions that occur in leprosy patients after medicine discharge, and to reflect about the necessity of implementation of specific and full attention to this group, with maintenance of treatment and human resources, allowing treatment simplification and reduction the stigma related to leprosy.

Within this same proposal, it also seeks to sensitize the local district managers of the SUS in order to bring subsidies for the health centers such as: standardization of conduct protocols for treatment, handling adverse effects of the used drugs, and adequate indication of surgical intervention for prevention and rehabilitation of disabilities.

MATERIAL AND METHODS

A retrospective analytical epidemiological study was conducted through the analysis of charts of 149 patients of leprosy after medicine discharge in the period from 1994 to 1999, in the School Health Center (CSE) -)araguá - UFU, reference for leprosy treatment in the district of Uberlândia - MG, Brazil, belonging to the West Sanitary District.

As instrument of data-collection, it was used Record of Inquiry of Alterations After Cure of the Ministry of Health that contemplates the following variables: a) Identification of the patient; b) Dermato-neurological Examination; c) Clinical classification, bacilloscopy, Mitsuda's test and grade of disability; d) Treatment regimens; e) Reactive episodes during the treatment and drug therapy; f) Situation of the patient after termination of MDT (clinical examination, reactive episodes and grade of disability); g) Situation of the patient when suspected relapse or late reaction (date of the end of treatment, date of the first symptoms, clinical examination, bacilloscopy, grade of disability, clinical types, reactive episodes and drug therapy, signs and symptoms, probable diagnosis and conduct).

Statistical Analysis

For the statistical analysis between the number of reactive episodes during the treatment and the number of reactive episodes after cure and the BI at diagnosis and the number of reactive episodes during the treatment and after cure it was applied a regression analysis, and the Pearson's correlation coefficients were calculated.

RESULTS

A total of 149 patients were included in this study, 85 men (57.0%) and 64 women (42.9%) with ages ranging mostly from 15 to 54 years (80%). Accounting for the clinical type, the evaluated patients were distributed as follow: 11 (7.38%) Indeterminated (I), 21 (14.09%) Tuberculoid (T), 83 (55.70%) Borderline (B) and 34 (22.81%) Lepromatous (L). According to the operational classification, 19.4% were PB and 80.5% MB.

In terms of the disability grade, it was found that at the time of registration, 112 patients (75%) had grade zero, 24 (16%) grade 1, 10 (6.7%) grade 2 and 3 (2.0%) grade 3, with 13 (8.7%) MB patients registered as grades 2 and 3, whose majority consisted of males (76.9%) older than 15.

Considering the period of occurrence of reaction of the patients, a total of 75 (50.3%) presented leprosy reactions during treatment and 34 (23%) presented late reaction. The distribution of patients clinical types who presented reactions during treatment was: 68% L, 55% B

and 29% T. Of those presenting late reaction there were 32% L, 23% B e19% T (Table 2).

The number of reactive episodes per patient, during treatment, varied from 1 to 9 and after treatment release varied from 1 to 17 episodes. The average of reactive episodes per patient for the tuberculoid reaction was of 1.33 during treatment and 1.00 after cure. For the borderline, the average was 2.60 during treatment and 3.00 after cure. For the lepromatous, the average was 3.69 during treatment and 4.18 after cure (Table 3).

There was a significant association between the number of reactive episodes during the treatment and the number of reactive episodes after cure (r = 0,53365, p 0,05) (Table 3 and Graphic 1).

Table 1. Distribution of 149 leprosy patients after MDT, according to age, grade of disability, operational classification and sex, in CSE - Jaraguá - UFU, 1994 -1999.

Age (years)	Disability grading				
	0	1	2	3	TOTAL
		PB group- Males			
0-14	2	-	-	-	2
15-34	5	-	-	-	5
35 - 54	3	-	-	-	3
> 54	1				1
TOTAL	11	0	0	0	11
		PB group - Females			
0-14	1	-	-	-	1
15-34	7	-	-	-	7
35-54	8	-	-	-	8
>54	2	-	-	-	2
TOTAL	18	0	0	0	18
		MB group - Males			
0-14	4	1	-	-	5
15 - 34	22	6	2	1	31
35 - 54	20	7	3	1	31
>54	1	3	3	-	7
TOTAL	47	17	8	2	74
		MB group - Females			
0-14	2	-	-	-	2
15-34	15	1	-	-	16
35 - 54	13	4	1	-	18
>54	6	2	1	1	10
TOTAL	36	7	2	1	46

Operacional *Classification:* *PB = Paucibacillary; MB = Multibacillary*

Tablet. Percentage of pacients after MDT, according to clinical type and period of occurence of reaction CSE - Jaraguá - UFU, 1994 - 1999.

Classification	Patients	Treatment		Cure	
		N	%	N	%
Indeterminate	11				
Tuberculoid	21	6	29	4	19
Borderline	83	46	55	19	23
Lepromatous	34	23	68	11	32
TOTAL	149	75	50	34	23

N = Number of Patients

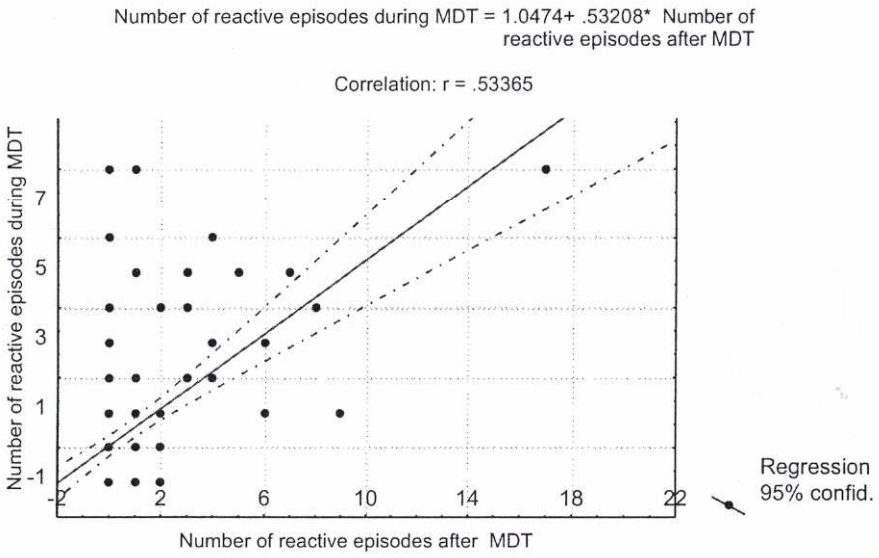
Table 3. Patients of leprosy after MDT, according to clinical type, period of occurence and number of reactive episodes, CSE - Jaraguá - UFU, 1994 - 1999.

Number of episodes	Indeterminate		Tuberculoid		Borderline		Lepromatous	
	N	%	N	%	N	%	N	%
During treatment								
0	11	100	15	71	37	45	11	32
1	-	-	4	19	15	18	4	12
2	-		2	10	11	13	7	21
3	-	-	-	-	11	13	3	9
4	-	-	-	-	1	1	2	6
5+	-	-	-	-	8	10	7	21
TOTAL	11	100	21	100	83	100	34	100
Average*	0.00		1.33		2.60		3.69	
After treatment								
0	11	100	17	81	64	77	23	68
1	-	-	4	19	7	8	4	12
2	-	-	-	-	3	4	2	6
3	-	-	-	-	3	4	1	3
4	-	-	-	-	2	2	1	3
5+	-	-	-	-	4	5	3	9
TOTAL	11	100	21	100	83	100	34	100
Average*	0.00		1.00		3.00		4.18	

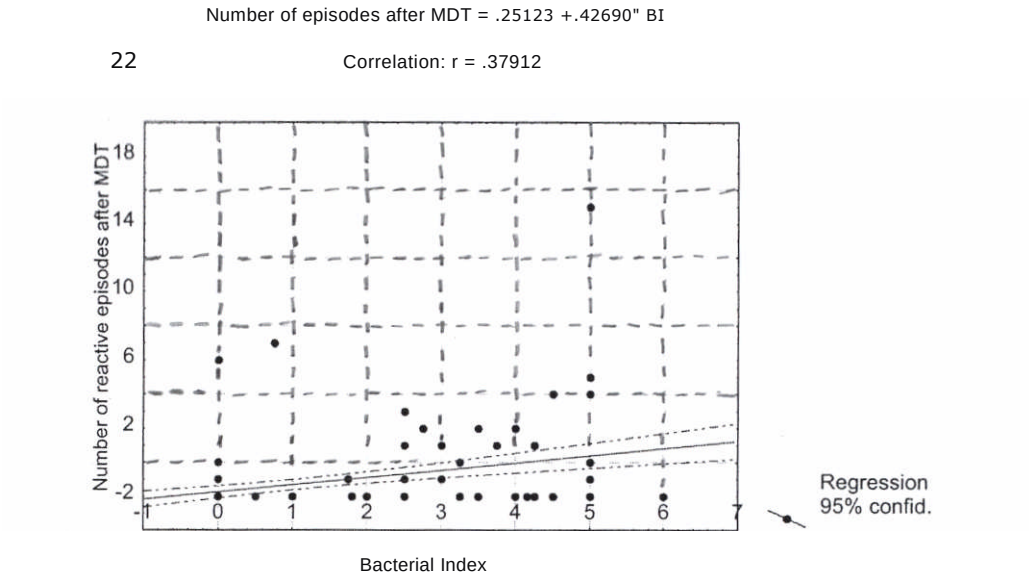
N = Number of patients

Average* = Average number of reative episodes / patient

Graphic 1. Regression analysis: Number of reactive episodes during treatment vs. Number of reactive episodes after MDT. (Casewise MD deletion).



Graphic 2. Regression analysis of the number of reactive episodes after MDT vs. Bacillary index at diagnosis (Casewise MD deletion).



Relating the bacilloscopy index (BI) at diagnosis with the number of reactive episodes during treatment and after cure, it was observed that among patients with BI zero, 67 patients (64.43%) did not present reactive episodes during treatment and 92 patients (88.46%) have presented episodes after cure (Table 4).

The patients with BI higher or equal to 2.0 at diagnosis, had presented more reactive episodes after cure, consisting of 21 (62%) out of 34 patients that experienced late reaction (Table 4).

There was a positive correlation between the BI at diagnosis and the number of reactive episodes during the treatment ($r = 0,6$, $p<0,05$) and BI at diagnosis and the number of reactive episodes after cure ($r = 0,38$, $p<0,05$) (Graphic 2).

During the period between release from treatment and the first reactive episode, it was found that 19 (56%) of the 34 patients had their first reactive episode in the first six months after the end of treatment. In 31 (91%) patients, the first reactive episode occurred in the first year after treatment (Table 5). It was observed that in the paucibacillary (PB) group the skin reaction associated to nerve involvement represented 3 (75%) cases, and there was no pure neuritis. In the multibacillary (MB) group, there was predominance of cases, with 16 (53.33%) patients, presenting only skin lesions, followed by 12 (40%) patients with skin and nerve involvement, and 2 (6.66%) cases of pure neuritis in this group (Table 5).

Table 6 shows that 4 (100%) PB patients and 15 (54%) MB patients manifested RR, 13 (47%) MB patients manifested ENL, and mixed reactions.

The treatment of choice was the administration of prednisone in 33 patients (97%) in all the reaction forms, including the treatment of a mixed reactions, 2 cases with pure neuritis, 19 cases Vti'ith RR with or without nerve involvement and 12 cases with ENL with or without nerve involvement. The use of thalidomide was required in the handling of 11 patients (32%) presenting ENL with or without nerve involvement.

It was observed that the patients with late reaction in use of prednisone and thalidomide, represented 22% and 8%, respectively, of the total cured patients (149).

DISCUSSION

In the present study a greater proportion of multibacillary clinical types (80.5%) was found among patients released from treatment between 1994 to 1999, classified as borderline and lepromatous in the beginning of treatment. Borderline leprosy spans the spectrum between lepromatous and tuberculoid poles and it is the most important part of the spectrum in terms of number of patients and severity of the nerve damage, which causes most of the disability and deformity seen in leprosy[20].

There was a slightly higher proportion of male patients. Although the occurrence of cases of leprosy tends to be equal in both sexes", the higher number of described cases among males may result from greater opportunities of exposure due to their life style[16].

Table 4. Patients of leprosy after MDT, according to bacterial index and number of reactive episodes during and after treatment, CSE - Jaraguá - UFU, 1994 — 1999.

BI	Number of Reactive Episodes						Total	%
	0	1	2	3	4	5+		
				During Treatment				
0,0	67	20	9	5	-	3	104	70
0,1 - 1,0	1	-	2	-	-	-	3	2
1,1 - 2,0	2	-	2	-	-	1	5	3
2,1 - 3,0	-	-	2	2	1	2	7	5
3,1+	4	3	5	7	2	9	30	20
Total	74	23	20	14	3	15	149	100
				After Treatment				
0,0	92	9	2	-	-	1	104	70
0,1 - 1,0	2	-	-	-	-	1	3	2
1,1 - 2,0	4	1	-	-	-	-	5	3
2,1 - 3,0	1	2	-	2	1	1	7	5
3,1+	16	3	3	2	2	4	30	20
Total	115	15	5	4	3	7	149	100

BI = Bacillary Index

Table 5. Paucibacillary (PB) and multibacillary (MB) patients that presented late reaction, according to type of manifestation and time of incidence, CSE - Jaraguá - UFU, 1994 — 1999.

Time after treatment	PB			MB			TOTAL	%
	S	S + N	N	S	S + N	N		
[0 - 31	1	1	-	7	4	-	13	38
[3 - 61	-	1	-	1	3	1	6	18
[6 - 91	-	1	-	5	2	-	8	24
[9-12[	-	-	-	1	2	1	4	12
[12 - 24[	-	-	-	1	-	-	1	3
25+	-	-	-	1	1	-	2	6
TOTAL	1	3	-	16	12	2	34	100

Type of reaction: S = skin; S+N = skin and nerve; *N = nerve*

Table 6. Paucibacillary and multibacillary patients that presented late reaction, according to type of reaction, CSE - Jaraguá - UFU, 1994 — 199

Type of Reaction	Paucibacillary		Multibacillary		Total	
	N	%	N	%	N	
RR	4	100	15	54	19	59
ENL	-	-	12	43	12	38
MIXED		-	1	4	1	3
Total	4	100	28	100	32	100

RR = *Reversal Reaction;* ENL = *Erythema Nodosum Leprosum*

It is important to stand out that 79.86% of the patients cured were part of the economically productive population (15 to 54 years), what coincides with the data presented in literatures[8,16]. Most studies of age distribution of leprosy are based on prevalence data. Further, disease occurrence is often related to age at detection rather than at onset of disease. In a chronic disease like leprosy, information based on prevalence data and data on age at onset may not fully reflect the age-specific risks[16].

During the surveillance (5 years), in terms of the WHO disability grade evaluated at the beginning of treatment, 8.72% of the patients presented grades of disability 2 and 3, representing the cases with visible deformity. Although this percentage does not represent the annual coefficient of disabilities among the new cases, it may serve as an indirect parameter to evaluate early diagnosis of the disease.

Some studies have estimated that an average of 12.5% of newly detected cases shows WHO grade 2 at the moment of diagnosis[22]. In Brazil this percentage was reduced from 15% in 1987 to 7% in 1997, for which a percentage lower than 5% indicates an early diagnosis, while a higher percentage than 10% is considered high for the parameters, indicating late diagnosis[4]. In Minas Gerais, in 1998, this percentage was of 11.1% and in Uberlândia it was of 5.6°/d[14].

The age range of patients with deformities, at the moment of the diagnosis, varied from 15 to 60 years. This data is important since leprosy is a disease that can lead to disability and that affects with higher incidence people of an economically productive age[19].

In this regard, although MDT has effectively contributed to a variety of improvements in the control of leprosy, nerve damage is still a continuing threat to managers of control programs and health personnel[22].

In the period of this study, 23% of patients (34/149) presented reaction after treatment. Results from studies held in the national centers of reference showed that 27% of patients have presented leprosy reactions after the end of treatment[3,10]. When analyzed the occurrence of late reactions in MB patients, the joined number was 25%; however, it has been reported in the literature values such as 33%[8] and 70%[1].

Of the 34 patients who presented Iate reaction, only 4 (11.76%) have not presented reaction during treatment, and it was observed a significant association between the occurrence of reactive episodes during the treatment and the occurrence of Iate reaction.

The 4 (100%) PB patients suffered from Iate reaction of type 1 or RR. Among 30 MB patients there was no statistical significance between the occurrence of reactions of type 1 (50%) and type 2 (40%). However, the discrete predominance of RR could be explained by the greater representation of the borderline group among patients with late leprosy reaction, reflecting its instability in the spectrum of the disease and therefore, its trend to manifest reactions[20].

The average of the number of reactive episodes for MB patient during treatment presented a significant association with the average of number of reactive episodes for patient after cure.

A significant association was also observed between the BI at diagnosis of the clinical types and the occurrence of reactions during and after cure, indicating that the number of reactive episodes seems to be directly proportional to the BI at diagnosis. However, in literature statistically significant difference between the BI and reactions was not found[12].

Analysis with Mitsuda's test was not possible since the Brazilian Ministry of Health does not praise its utilizations[5].

The treatment conduct adopted in patients who presented late reaction was mainly prednisone and thalidomide. Of the 34 patients, 97% had used prednisone and 32% thalidomide. These medicines were destined to the patients of the active registry, according to the forms of drugs prediction elaborated by the Technical Area of Sanitary Dermatology of the Ministry of Health. Calculation for prediction of anti-reaction drugs was observed for this group of patients that left the active registry and the prevalence rates of leprosy. This might be one of the reasons that lead to the lack of these drugs in the basic health net.

It was used Record of Inquiry of Alterations After Cure of the Ministry of Health, to evaluate its effectiveness as an instrument of follow up of the patients who returned to the health services after the end of the specific treatment of leprosy. The main objective of the creation of this record was the detection of relapses, and the differential diagnosis between relapses and late reaction. However, the record brings limitations, since there is incoherence between the information that the record requests and the procedure that the Ministry of Health standardizes. For example, BI at the end of treatment is standardize by the Ministry of Health but the record does not request. With the Mitsuda's test, the opposite occurs. However, it is important to emphasize that there was no relapses in the assessed period.

Absence of registration of other variables, such as: doses of anti-reaction drugs, side effects, indication of surgical intervention, is another limitation of the record of the Brazilian Ministry of Health, which does not allow to conduct a protocol in health services.

The treatment with corticosteroids has a limited effectiveness due to the serious adverse reactions, caused by these drugs. The corticoids induce hypercorticism,

hypopotassemia, hypertension, peptic ulcer, osteoporosis, reduction of the defenses against infections, obesity and glaucoma[13]. In the present study the survey of these side effect was not possible, once the record of the Ministry of Health does not praise such conduct; however, when revising the charts of leprosy patients cured, it was observed occurrence of diverse side effects. An absence of uniformity in the drugs regimen was also observed, and it was not possible to evaluate the number of doses taken by each of the groups of patients in reaction. It is accepted that a dose of 40 to 60 mg is sufficient to control type 1 or 2 reactions, being variable the anti-inflammatory response[17]. When the reaction has been controlled the dose is slowly tapered[9].

When nerve damage is already present, 3 to 6 months of therapy is usual, but the response rate is less then two-thirds. However, where the nerve function has been lost for over 6 months, the response to corticosteroids is generally poor, so earlier intervention and better treatments are needed[9].

In the regions where the medical doctor is the one who does the treatment of the reaction patients, the corticosteroids are more frequently utilized, including the cases in which they were not necessary. There is also the patient who knowing the drug action takes it by its own means trying to get rid of his symptoms, creating inadvertently more problems[17].

It is important to call attention for this fact, in a way to guarantee the implementation of an effective referral system for exams and procedures of increasing complexity as the assistance in service of reference of leprosy for tertiary attention, with guarantee of the internment of complications, exams for surgeries and diagnostic clarifications; evaluation of the nerve damage through neurological exams and eletroneuromiography in services of reference in neurology; prevention and rehabilitation of the disabilities with specialized procedures in services of reference of physiotherapy, and orthopedic surgery contributing for the elimination of the stigma related to the disabilities and for social reintegration of these patients.

CONCLUSION

Due to the expressive contingent of patients (23%) that presented late reaction associated to possible predisposing factors, such as Bl._2 at diagnosis and the number of reactive episodes during treatment, it is essential the structuration of a specific reference of care, progressively integrated to the basic health services with training of the local group for the management of peripheral neuropathy and side effects of the drugs available for its treatment.

In addition, it is necessary a more adequate calculation for de prediction of anti-reaction drugs to attend the demand of this new group of patients, taking in consideration that late reaction begin mostly at the first year after termination of MDT and that the main drug utilized by this patients its prednisolone.

The accompaniment of the patients by the record of the Ministry of Health, has shown itself limited though the evaluation of patients with late reaction, for which the main goal is the detection of relapses which were not observed in any patient at the present study. Thus, it is necessary to change the focus of this record in a way that in the record will be reported, with more detailed information on the conditions the patients released from treatment. Those informations will serve as a database to standardize medical conduct, aiming an early intervention to prevent disabilities.

In this sense, it is important to bring subsidies to expand the vision on the control of the disease, sensitizing the district managers of the Unified System of Health (SUS) to guarantee the assistance to this group of patients, since the strategy of decentralization and integration of the activities of leprosy have been the main element to achieve the goal of elimination of leprosy as a public health problem.

In order to attain the sustainability of the process and keep advancing toward the eradication, the concept of cure of the leprosy patient must be expanded concerning the assistance coverage to this group of patients that is out of the active registry, aiming the alteration of the negative or stigmatizing perception of the leprosy in the municipality, also because the increasing number of cured patients without disabilities is one of the indicators of improvement of the local administration and of the health conditions of the population[17].

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