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# Follow-Up Of The Evolution Of Neurological Status Of Newly Detected Hansen's Disease Patients On Multidrug Therapy - Results At Year 3

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## Abstract

**Background:** Leprosy causes serious functional impairment like sensory and motor neurological damage. The introduction of multidrug therapy in its treatment has helped to curb the infection and improve neurological complications.

**Goal:** The aim of this work was to identify nerve damage in patients who were taking chemotherapy and to make proposals for prevention of such complication.

**Methods:** This was a longitudinal study spread over three years (1994-1996). All new leprosy cases diagnosed between January 1st and December 31st 1994 were included and followed up for the 2 years that followed. All patients who had never received prior anti Hansen's disease chemotherapy were considered "new case". Patients already known, "found", transferred, or immigrant, admitted for relapses were not included in the study. We conducted periodic, (every 3 months), standardized neurological tests. The change in neurological status from diagnosis was specified and ranked from 0 for normal for examination to 3 in case of paralysis.

**Results:** In total 121 patients were screened, put on treatment and followed for 3 years. 87 of them were included in the study, among whom 54 (62%) were male and 33 (38%) female. The age range was from 6 to 77 years with an average of 29 years. At diagnosis, 18 patients (20.7%) had a disability at grade 1, 23 (26.4%) at grade 2 and 5 (5.7%) were considered at grade 3. During all the period of our study, 32 of the 87 patients (36.8%) experienced one or more episodes of severe leprosy reactions. Degradation of neurological status was more pronounced in male patients. So, it was found stable for 53 patients (60.9%), improved for 25 of them (28.7%) and deteriorated for 9 of cases (10.4%).

## CONCLUSION:

In this study the evolution was not related to age, neurological status at screening or its clinical form, but status was more degraded in males. And this influence of sex could be related to an intrinsic biological or genetic factor.

## INTRODUCTION

The severity of leprosy is primarily due to damage of the nerve trunks. The advent of

Multidrug therapy (MDT) has significantly reduced the duration of treatment. The overall prevalence in early 2012 was 181 941cases [1].

In Senegal, the aim of elimination of leprosy as a public health problem in 2000 was achieved in 1995 [2]. However, management of leprous neuritis remains problematic. In fact,

5-23% of leprosy patients present at diagnosis with disability at grade 2 [3]. This signifies severe neuropathy. On the other hand, it was noted that the containment of the infection by MDT was not enough to control the neuropathy and to mitigate its consequences.

Objective of our work was to study the nerve damage in leprosy patients on MDT. The goal is to propose appropriate measures for prevention.

## **PATIENTS AND METHODS**

This was a longitudinal study that lasted 3 years. It took place in four regions of Senegal (Dakar, Thies, Kaolack and Fatick). All new leprosy cases diagnosed between 1st January and 31st December 1994 were included and followed up for the 2 years that followed. All patients who had never received prior anti Hansen's disease chemotherapy were considered "new case". Patients already known, "found", transferred, or immigrant admitted for relapses were not included in the study.

MDT protocol we have adopted was the same that what WHO recommended in 1981 (amended in 1997). It included Rifampicin 600mg and Dapsone 100mg for a period of 6 months. We used the anatomical-clinical and bacteriological WHO classification. The Approach also involved the implementation of standardized quarterly neurological assessments and clinical sensitivity was evaluated by nylon filaments in the hands and feet. The use of these tools (filaments 10 grams) was consistent for all patients and in all centers. Thus, the change in neurological status from diagnosis was specified in rank, with 0 for "normal", 1 for "motor weakness or numbness", 2 in case of "motor weakness and numbness" and 3 for "paralysis". The risk of occurrence of nerve alterations during leprosy reactions was also assessed. The adopted classification was as follows: evolution of the neurological condition of the patient was considered stable if there is no difference between initial and final degree's grade. It was considered improved if the final grade is lower than the original grade. Finally, the state was degraded if the grade at the end of the follow-up is higher than the original grade.

Data were analyzed using EPI-Info 6 software and Chi<sup>2</sup> statistical tests or Fisher.

## **RESULTS**

A total of 121 patients were diagnosed and started on treatment in 1994. Of these, 87 (72%) met the inclusion criteria, 54 (62%) were male and 33 (38%) female. The age of patients ranged from 6 to 77 years with an average of 29 years. Following the distribution by age recommended by WHO for programs against leprosy, 22 patients (25%) were children (under 15 years) and 65 (75%) of adults.

Concerning classification, 46 patients (52.9%) were paucibacillary and 41 (47.1%) of multibacillary.

At diagnosis, 46 (52.9%) patients presented disability of

which 18 (20.7%) were grade 1, 23 (26.4%) grade 2 and 5 (5.7%) grade 3.

During follow-up, 32 of the 87 patients (36.8%) experienced one or more episodes of severe leprosy reactions. In these patients, severe leprosy reactions were observed at screening time in 46.9% (15/32) of cases while 17.2% (15/87) of the patients had just leprosy reaction at screening. The Type I Ridley and Jopling reaction was seen mostly in multibacillary patients (85.7%). The type II or ENL (erythema nodosum leprosum) reaction was observed in only one LL patient at screening.

All patients who had one or more episodes severe reaction received corticosteroid therapy in hospital or as outpatients when hospitalization was refused.

The neurological status when evaluated was stable in 53 patients (60.9%), improved in 25 patients (28.7%) and deteriorated in 9 patients (10.4%). In total, the development of the neurological status of the patients was satisfactory in 89.6% of patients.

## **DISCUSSION**

Leprous neuropathy is common [4,5]. It may be an isolated event as well as indicator of the infection. Despite the variability of its severity, it has full impact on the long-term prognosis of the disease. In fact, in endemic areas, 12-55% of patients show signs of neuropathy at diagnosis of leprosy [3, 6]. In our study, 52.9% of patients had a disability at the time of the screening.

In most studies, the primary cause of neurological deterioration on MDT occurs as reversal reaction. However, in our study, the neurological status of the patient was sex dependant. Thus, males were unfavorable prognosis (16.7%) compared to females (0%) [Table1]. The risk (p), being equal to 0.012 by Fisher's test bilaterally. This effect of gender on the neurological status could be due to a biological or genetic intrinsic factor. Conventionally, the main risk factors for developing neurological injury after the diagnosis of leprosy are multibacillary form, the initial presence of sensory or motor deficit, the presence of nerve hypertrophy or the occurrence of a leprosy reaction (Reversal reaction in particular). [7] Thus, the prognosis was bad in 25% of patients who had a leprosy reaction during the follow-up period. At the same time it was observed that the development of leprosy complication was not related to sex. Equally, neurological status was neither associated with age

nor the clinical form of the disease [Table 2]. However, disabilities were observed more frequently in multibacillary type patients. [8]

**Table 1**

Distribution of patients by sex and the evolution of the neurological status

Evolution of Neurological status	Sex		TOTAL
	Male	Female	
Stable or improved	45	33	78
Degraded	9	0	9
<b>TOTAL</b>	<b>54</b>	<b>33</b>	<b>87</b>

**Table 2**

Distribution of patients by age and evolution of the neurological status

Evolution of Neurological status	Age		TOTAL
	Adult	Child	
Stable or improved	58	20	78
Degraded	7	2	9
<b>TOTAL</b>	<b>65</b>	<b>22</b>	<b>87</b>

In the event of treatment without the occurrence of a reaction complication, MDT is able to control and cure some nerve damage. However, it is often inefficient or ineffective when neurological lesions are old and severe [9]. Hence, prompt management of leprosy reaction is the most important factor in the subsequent neurological status of patients.

Corticosteroids constitute the main stay of treatment as in our study [10]. However, according to Shetty [11] corticosteroids are insufficient to prevent and / or treat neuropathy. On this point, quality clinical trials are lacking but several indispensable studies have recently shown that the disability associated with neuropathy could regress without steroids. This improvement can be spontaneous or be the result of antituberculous treatment [8].

Thus, in our study, a discriminatory 90 days period was found with a risk p equal to 0.03 by Fisher's test unilateral. In fact, a reaction complication treated within 3 months of its installation resulted in a favorable outcome in 80% of our patients. And otherwise, positive developments were observed in 42% of cases. Another important factor in the evolution of the neurological condition of the patients seemed to be the nature of the affected nerve (sensory or motor). Thus, the improvement favored the motor nerve in 29.2% of cases and sensory nerve in 21% of cases. Both

nerve types were involved in 49.9% of cases. In specific terms, among patients having demonstrated a leprosy reaction, the improvement of neurological status was especially attributed to motor nerve. These differences observed in recovery time between the deficit and the beginning of the special treatment of leprosy (MDT) or corticosteroids for leprosy reaction had occurred. Electromyography (EMG) proved very reliable to the early detection of nerve damage in leprosy. In fact, 33% of the nerves examined by EMG are achieved with greater frequency and precocity of sensory functions [12]. However, we have not been able to use EMG in this study due to budget reasons. Thus, in our series, the initial sensory abnormalities were discovered during trauma such as burns or wounds. The sensory deficit was already very old when the MDT treatment was instituted. In contrast the motor deficit was a warning sign for patients allowing early treatment with a greater chance of nerve recovery. Thus, 75% of our patients have recovered from their motor deficit when treated for leprosy reaction. And improving of the sensory deficit was at 30%.

## CONCLUSION

The evolution of the neurological status of leprosy patients put under multi drug therapy is not related to age, neurological status at screening or its clinical form. The unfavorable trend in with male has a possible correlation with a genetic or physiological base. The motor deficit is a warning sign promoting early treatment.

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