

ASSESSMENT OF ULNAR NEUROLYSIS IN LEPROUS NEUROPATHY

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SUMMARY

In this study, the authors assess the results of 35 surgical ulnar nerve decompression procedures performed on 28 leprous patients. The parameters employed included the visual analogue scale, the behavioral scale, the muscle strength evaluation, the esthesiometry and the evaluation of the effect of the procedure on decreasing postoperative corticoid

therapy doses. Early resolution of pain was seen after surgery, muscle strength increased in half of the patients, sensitivity increased in half of the patients, with ongoing and significant decrease of prednisone doses after surgery.

Keywords: *Leprosy; Ulnar neuropathies; Surgical operative procedures.*

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INTRODUCTION

Mycobacterium leprae is a resistant alcohol-acid bacillus, and a mandatory intracellular parasite, measuring 0.3-0.5 x 4-7 micrometers, preferably affecting Schwann's cells and the skin.

Its growth is slow, with a generation time of 12-14 days, with an incubation period of two – four years, presenting better growth at 30 degrees centigrade, thus typically affecting colder areas of the body, culminating with the chronic evolution of the disease.

This bacterium may remain viable for several days *ex vivo*. The Gram-positive type of the cell wall is highly complex and contains proteins, phenolic glycolipids, arabinoglycan, peptidoglycan, and mycolic acid, the latter potentially responsible for its resistant alcohol-acid nature⁽¹⁾.

Leprosy pathogenesis involves interactions between the *Mycobacterium leprae* and a certain dysfunction of the host's immune system. *M. leprae* is highly infectious, but poorly pathogenic and virulent^(1,2). Most people are resistant to the bacillus, so that its presence in human body will not necessarily mean disease.

The clinical presentations of leprosy are associated to distinct immunologic patterns, ranging from an immune response mediated by cells to *M. leprae* to the absence of cell response to the antigens of *M. leprae*. In tuberculoid lesions, TCD4+ cells and Th1(IL-2,IFN-gamma) cytokines are prevalent. IFN-gamma activates the macrophage and IL-2 stimulates the growth of antigen-specific T-cells, resulting in a milder disease or cure. In virchowian lesions, there is a prevalence of CD8 suppressive T-cells and Th2(IL-4,IL-5,IL-10) cytokines, which increase humoral response. IL-4 stimulates IgE and IL-4 production, and IL-10 stimulate B-cells and inhibit macrophage activation, resulting in progressive infection^(2,3).

Patients having the multibacillar forms are regarded as the main infection source, although men are not the unique natural reservoir of the bacillus. Armadillos and non-human primates may be naturally infected and might play a role on the disease epidemiology⁽⁴⁾.

The main transmission form is the inter-human one, and the persons at higher risk are those who live in the same house as the carrier of the bacillus⁽⁵⁾. People having close contact with leprous patients are at a high risk of developing the disease. The age at contact, the index

rating of the disease, the physical and genetic distance are independent factors associated to the risk of acquiring leprosy⁽⁶⁾.

Upper respiratory tract is the access and elimination port for the bacillus; eventually, cracked skin can also serve as access port^(2,4). In our country, there is an increasing trend towards global endemics, higher than the population growth rate. In the Northeastern region, the mean rate is 5.96% / year. There is an increased number of cases with the paucibacillar forms (which reflect the increased number of circulating bacillus and the higher exposure of the non-susceptible to risk) with corresponding reduction of multibacillar forms⁽⁷⁾.

This trend of incidence increase, associated to the modification of the distribution of clinical forms, is the basis on which we can suppose that leprosy endemic is being widely spread in the country⁽⁷⁾. Leprosy is an inflammatory disease primarily affecting the skin, peripheral nerves, upper respiratory tract and eyes.

Skin manifestations are basically due to: (1) bacterial load; (2) host's immune responses; (3) peripheral nerves injury due to bacterial load and to the host's immune responses, and (4) predictable secondary deformities, largely responsible for most of the disease stigma.

Systemic symptoms may vary. New distant lesions arise, and with more often neuritis, which can be the only clinical manifestation. Neuritis can be insidious, where the functional damage of the nerve becomes patent without any clinical picture of pain and nerve thickening.

The most compromised nerves are the ulnar and medial on upper limbs; fibular and posterior tibial on lower limbs, and; facial and the great auricular on cephalic segment.

Neuritis constitutes an inflammatory process of the nerve caused by the leprosy bacillus, either directly or indirectly. It occurs as a response to bacillus invasion and constitutes an inflammatory response with severe edema and/ or neural abscess formation, with resultant compression of the affected nerve at certain anatomical sites, ultimately leading to degeneration and nerves death. It may be chronic or acute (hypersensitivity), the latter constituting a medical emergency due to its swift progression to function loss.

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Neuritis treatment is dependent on its current stage: (1) treatment of early stages is provided with anti-inflammatory agents, anti-reaction drugs and clinical follow-up; (2) neurological deficit unresolved with short-term medication requiring surgical release, and (3) treatment of the sequels, irreversible lesion.

The most frequently affected nerve in leprous neuritis is the ulnar nerve, with a critical area around the elbow⁽⁸⁾.

A compressive syndrome results from neural edema associated to the infectious inflammatory process generated by bacillus invasion and immune response, combined to epineural thickening, which is not elastic and permeable, associated to the path through ulnar sulcus of the medial epicondyle. There is an increased intraneural pressure, compressing its axon^(8,9).

The treatment of choice for this syndrome at the compressive stage II is external ulnar neurolysis^(8,10).

This procedure can be effectively performed with an outpatient technique under local anesthesia without garrote⁽⁸⁾.

The objective of our study is to assess the results of surgical decompression of the ulnar nerve in leprous patients using the visual analogous scale, behavioral scale, assessment of the muscle strength, esthesiometry, and assessment of the effect of the procedure on the reduction of postoperative corticoid therapy.

CASE SERIES AND METHODS

This study was conducted after the evaluation and recommendation of the Committee of Ethics of Hospital Santa Izabel, Santa Casa de Misericórdia de Salvador (Bahia).

Between January 2003 and April 2005, 35 ulnar nerve decompression procedures were performed on 28 patients with leprous ulnar neuropathy who signed an informed consent form prior to the surgery at Hospital Especializado Dom Rodrigo de Menezes (HEDRM –Bahia State Health Department, in Salvador, Bahia (Table 1).

There was a prevalence of male patients (24), accounting for 85.71% of the total patients. Age ranged from 14 to 47 years (mean: 31.7). Of the total, 21 patients (75%) were unilaterally approached (nine on the left side and twelve on the right side), while seven were operated bilaterally. Paucibacillar (PB) forms were found in eight patients (28.6%) and the multibacillar ones (MB) in 20 patients (71.4%). The form of the disease was tuberculoid in two cases (7.14%), the tuberculoid dimorphous was present in six cases (21.43%), the dimorphous dimorphous (central) in eight cases (28.5%), the virchowian dimorphous in five cases (17.9%) and the virchowian in seven cases (25%).

They were also assessed for pain status by the visual analogous scale (VAS), behavioral scale (BS), sensitivity test with the use of Semmes-Weinstein's monofilaments, and motor strength according to the BMC scale.

After evaluation, the patients were submitted to surgical treatment (external neurolysis) of the ulnar nerve, when meeting the following criteria:

- Patient contraindicated to the use of corticoids.
- Nerve abscess.
- Patient with neuropathy not responding to clinical treatment of neuritis within 4 weeks.
- Patient with sub entrant neuropathy (neuritis).
- Patient with uncontrolled and/ or chronic pain.

Surgical technique

The technique employed was described by Jambeiro et al.⁽¹¹⁾.

Preoperative care included: clinical evaluation, laboratory tests, electrocardiogram, and chest X-ray images. For ulnar nerve external neurolysis procedure, an outpatient technique was used with local anesthesia and without using a garrote.

The arm of the patient was positioned in abduction and external rotation in order to enable an easier access. Then, local-regional anesthesia was provided (nerve blockage, supplemented by skin and subcutaneous infusion) with 10 ml 2% lidocaine for intraneu-

ral infusion and 10 ml 1% lidocaine for skin and subcutaneous infusion.

Subsequently, an incision was performed on the posteromedial elbow region, starting seven centimeters above the medial epicondyle, at distal orientation, ahead of the epicondyle, following the skin projection of the ulnar nerve path. The skin and subcutaneous portions were dissected, enabling the identification of the origin of the flexor muscles of the wrist and the ulnar nerve sulcus at the level of the medial epicondyle. By careful dissection, the ulnar nerve was released from that sulcus, identifying its branches to the deep flexor m. of the fingers and the ulnar flexor muscle of the carpus in order to obtain a better mobilization of the main stem. Each and every fibrocatricial tissue that could compress the nerve was excised. When necessary, epineurotomy was included in the procedure, which consists on opening the epineurium with delicate scissors all the way through de compromised nerve.

After release, the canal was sutured along its entire extension, with chromed catgut 2-0 in order to prevent the nerve from occupying its original position and becoming compressed again. The subcutaneous closing was made with plain catgut 3-0, and the skin was sutured with non-absorbable wire (mononylon 4-0).

After closing, a compressive smooth dressing was placed, and the limb was kept on slings with the elbow flexed at 90° for 15 days, after which the stitches were removed and elbow mobilization was started.

Postoperative assessment

After procedure, the patients were clinically assessed again, according to the parameters presented for pain, muscle strength, esthesiometry, and corticoid dosage administered at 30, 90, and 180 days postoperatively.

RESULTS

The aspects assessed were the following:

1. Pain evaluation with the Visual Analogous Scale (VAS)
2. Pain evaluation with the Behavioral Scale (BS)
3. Motor strength evaluation
4. Esthesiometry
5. Amount of corticoids prescribed

The first four aspects were assessed at an individual nerve basis, while the last one at an individual patient basis.

Each of these aspects was assessed at four different moments. Only the first moment occurred before the procedure. The comparison between two different moments for each aspect enables the characterization of patients' evolution. Particularly, the comparison between the first measurement and the last one shows the end result of the surgical procedure.

We also assessed the effects of age, gender, kind and form of leprosy, time elapsed from disease onset and neurolysis procedure.

Pain assessment with the visual analogous scale

In the pain visual analogous scale (VAS), patients evaluate their pain. The zero level corresponds to absence of pain while level ten corresponds to the worst possible pain.

We realized that the average level in this scale is immediately reduced after surgery. This reduction remains through the postoperative assessment moments (Figure 1).

Paired hypotheses tests between the preoperative moment and the postoperative moments 1, 2 and 3 resulted in p values of $6.41 \cdot 10^{-9}$, $2.38 \cdot 10^{-14}$, $1.29 \cdot 10^{-15}$, respectively. In each case, the null hypothesis is ruled out. It is clear that surgery reduces the level of pain assessed by the visual analogous scale.

On the histogram comparing the last moment and the first preoperative moment, only one patient showed a worse score on the visual analogous scale. All the others showed improvement. This corroborates the conclusion that surgery is beneficial for VAS scores (Figure 2).

	Age	Gender	Leprosy Kind	Leprosy Form	Disease onset	Treatment onset	End of Treatment	Date of Left Neurolysis	Date of Right Neurolysis
1	30	2	1	2	May/00	Sep/00	Mar/01	Feb/03	
2	31	1	2	4	Oct/01	July/02	June/03	Apr/05	Feb/03
3	44	1	2	5	Dec/98	Dec/98	Dec/00	Mar/03	
4	20	1	1	1	Sep/01	Sep/01	Sep/02	Apr/03	
5	30	1	2	3	Feb/00	Dec/00	Aug/02	May/03	Aug/03
6	29	2	2	5	May/01	May/01	May/02	May/03	Oct/03
7	14	2	2	5	June/02	June/02	June/03		May/03
8	35	1	2	4	Aug/97	Aug/97	Aug/98	July/03	
9	34	2	1	1	Nov/01	Dec/01	Dec/02	July/03	
10	44	1	2	3	Mar/95	Mar/95	Mar/97		Sep/03
11	47	1	1	3	Mar/02	July/02	Feb/03		Sep/03
12	40	1	2	3	Jan/02	June/02	June/03		Oct/03
13	18	1	2	3	Feb/03	Apr/03	Apr/04		Nov/03
14	37	1	2	3	June/02	Aug/03	Aug/04		Nov/03
15	37	1	2	4	Nov/99	June/00	June/02	Dec/03	Jan/04
16	23	1	1	2	June/01	Nov/01	Apr/02	Dec/03	Feb/04
17	24	1	2	5	Aug/97	Aug/99	Mar/03	Jan/04	Feb/04
18	47	1	2	3	June/02	June/02	June/04		Feb/04
19	28	1	2	4	Apr/96	Apr/96	Apr/98		Mar/04
20	44	1	2	5	May/01	May/01	Aug/02	Apr/04	
21	40	1	2	3	July/00	Feb/02	Feb/03		Apr/04
22	23	1	1	2	Feb/02	June/02	Jan/03		May/04
23	36	1	1	2	Feb/00	Feb/02	Aug/02	Oct/04	
24	22	1	2	5	Nov/00	Nov/03	Nov/04	Dec/04	Oct/04
25	24	1	2	2	Sep/02	Sep/04	Sep/05		Nov/04
26	24	1	1	2	July/04	Sep/04	Feb/05	Dec/04	
27	37	1	2	5	May/99	June/03	June/04		Dec/04
28	25	1	2	4	Aug/01	Sep/01	Sep/02	Apr/05	

Gender: 1=male, 2=female

Clinical Form: 1= tuberculoid leprosy, 2= dimorphous tuberculoid leprosy, 3= Dimorphous dimorphous leprosy (central), 4= Dimorphous virchowian leprosy, 5= virchowian leprosy

Type of polychemotherapeutic treatment: 1=PB, 2=MB.

Table 1. Leprous patients, assessed according to age, gender, clinical form and type of polychemotherapeutic treatment.

Pain assessment with the behavioral scale

On the behavioral scale (BS), the patient evaluates his/ her pain and behavior. The zero level corresponds to absence of pain, while level ten corresponds to persistent pain, even at rest and with the use of medication, impairing his/ her daily basic activities, including eating and hygiene.

We realized that the average pain level on the behavioral scale also shows reduced scores immediately after surgery. Such reduction remains during postoperative assessment moments (Figure 3).

The paired hypotheses tests between the preoperative moment and the postoperative moments 1, 2 and 3 resulted in p values of $2.84 \cdot 10^{-7}$, $8,76 \cdot 10^{-18}$, $1,75 \cdot 10^{-21}$, respectively. In all cases, the null hypothesis is ruled out. It is clear that surgery reduces the pain as assessed by the behavioral scale, as occurs on the visual analog scale.

On the histogram comparing the last postoperative moment with the preoperative one, all patients showed improvement. This corroborates the conclusion that surgery is beneficial for BS scores (Figure 4).

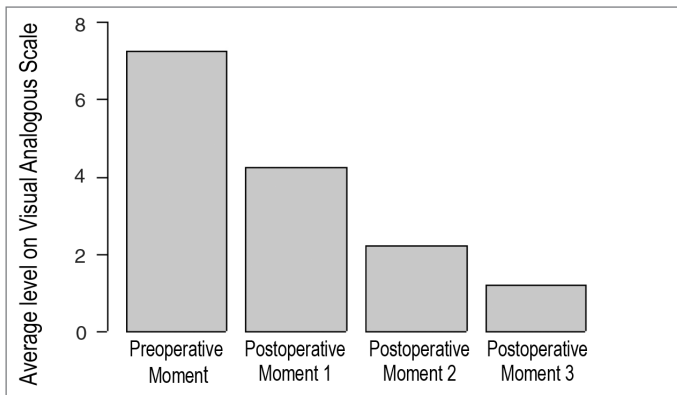


Figure 1 – Visual analogous scale over time.

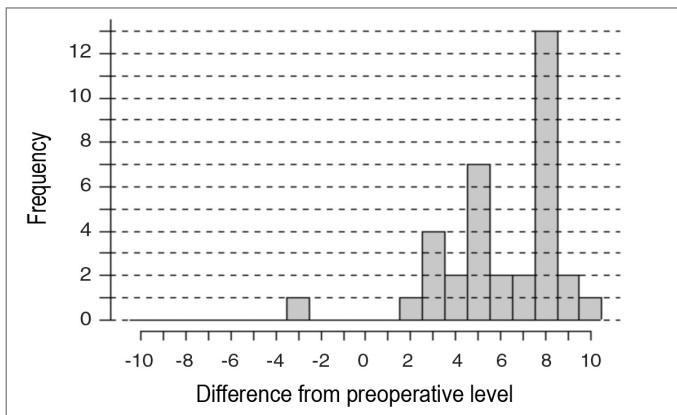


Figure 2 – Histogram of the difference of the visual analogous scale.

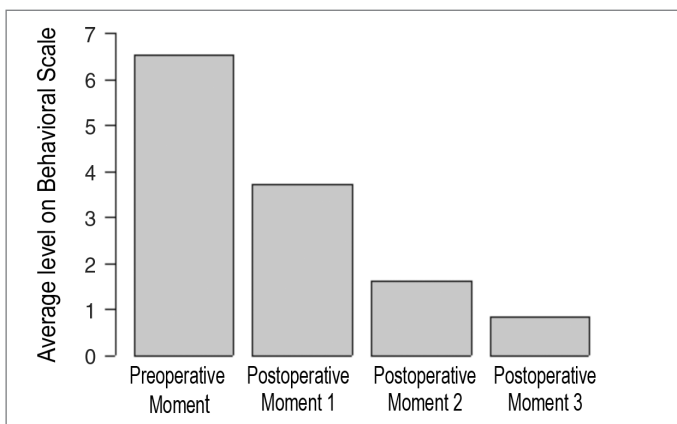


Figure 3 – Behavioral scale over time.

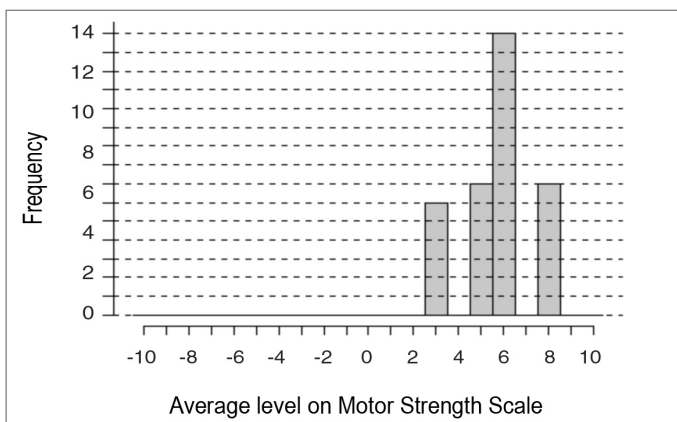


Figure 4 – Histogram of the difference on the behavioral scale.

Muscular Strength Assessment

Motor strength is assessed by the Motor Strength Scale. Level zero corresponds to total inability to move (palsy), while level five corresponds to absolute normality.

We realized that the average motor strength level is increased soon after surgery and remains improving (Figure 5).

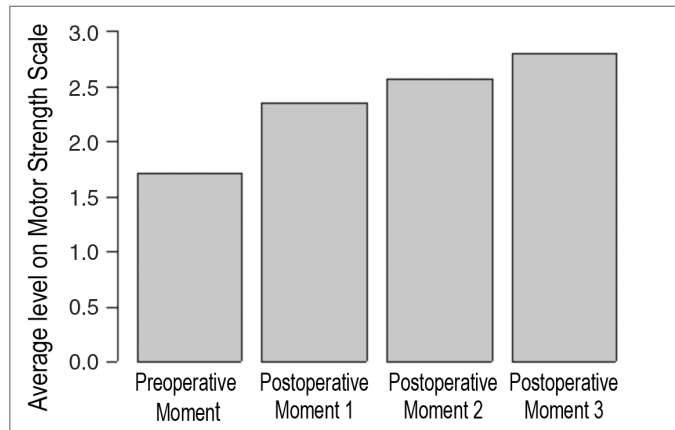


Figure 5 – Motor strength over time.

The paired hypotheses tests between the preoperative moment and the postoperative moments 1, 2 and 3 resulted in p values of $4.93 \cdot 10^{-4}$, $7.40 \cdot 10^{-6}$ and $2.05 \cdot 10^{-6}$, respectively. These values are enough for ruling out the h_0 =null hypothesis on a 5% significance level. We can conclude that surgery improves motor strength.

Let's see a histogram comparing the last postoperative assessment moment to the preoperative one. No patient presented worse motor strength, while 60% of them showed improvement (Figure 6).

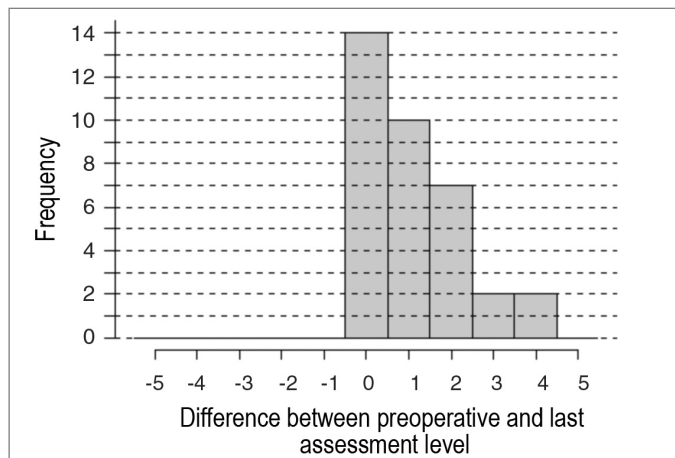


Figure 6 – Histogram of the difference on motor strength.

Sensitivity Assessment

Sensitivity is assessed by esthesiometry. Level zero corresponds to total lack of sensitivity (anesthesia), while level 5 corresponds to absolute normality.

We realized that the average sensitivity level is increased soon after surgery, and remains growing (Figure 7).

The paired hypotheses tests between the preoperative moment and the postoperative moments 1, 2 and 3 resulted in p values of $5.49 \cdot 10^{-2}$, $2.96 \cdot 10^{-4}$ and $3.33 \cdot 10^{-5}$, respectively. We cannot rule out the null hypothesis when comparing the first postoperative evaluation to the previous one. However, other values are enough to rule out the null hypothesis on 5% significance level. We can conclude that surgery enhances sensitivity.

On the histogram comparing the last postoperative evaluation to the preoperative one, only two patients showed worse sensitivity, while 60% of them showed improvement (Figure 8).

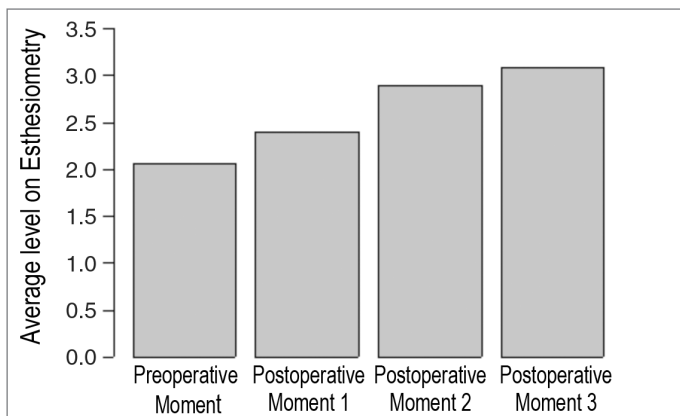


Figure 7 – Esthesiometry over time.

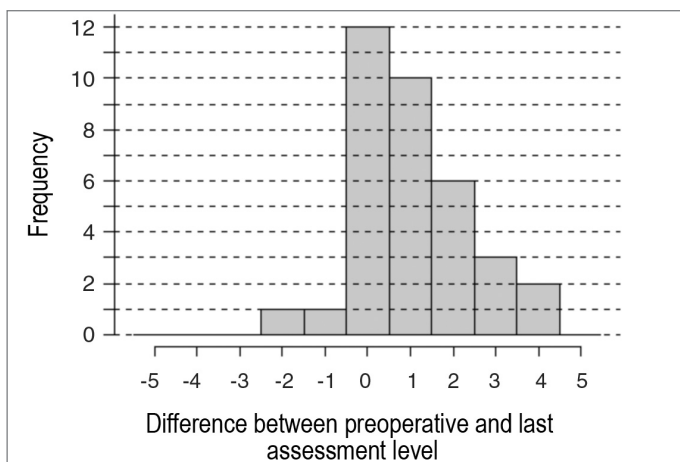


Figure 8 – Histogram of the difference on esthesiometry.

Effects on the Amount of Corticoids Prescribed

We found a subtle reduction of the average cortisone use soon after surgery and sharp drops later postoperatively (Figure 9).

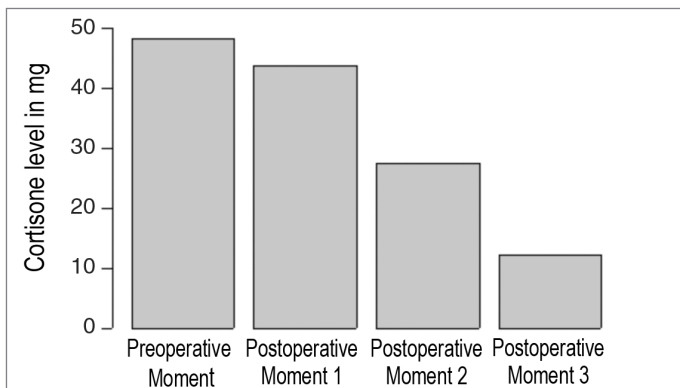


Figure 9 – Average cortisone level over time.

In order to validate our hypothesis that the use of cortisone was reduced, we conducted tests comparing each of the three postoperative moments to the preoperative one. As in each of these comparisons we have a 'before and after' kind of comparison, we will use paired hypotheses tests.

The test involving the "Postoperative moment 1" resulted in a p value of 0.02. This does not allow us draw an absolute conclusion, but we could rule out the null hypothesis on 5% significance level.

The histogram of the difference in the cortisone use between the preoperative and the first postoperative assessment moment (Figure 10)

shows an increased level of cortisone only for two patients, while nine patients showed reduction. However, most of the patients presented the same cortisone levels as prior to surgery.

The test involving the "Postoperative moment 2" resulted in a p value of $2.34 \cdot 10^{-8}$. The null hypothesis is, thus, ruled out. The benefits of surgery are proven as early as the second evaluation.

The histogram of the difference in the use of cortisone between the preoperative moment and the second postoperative one confirms this conclusion (Figure 11). The fact that no patient had a raise of the level of cortisone is relevant.

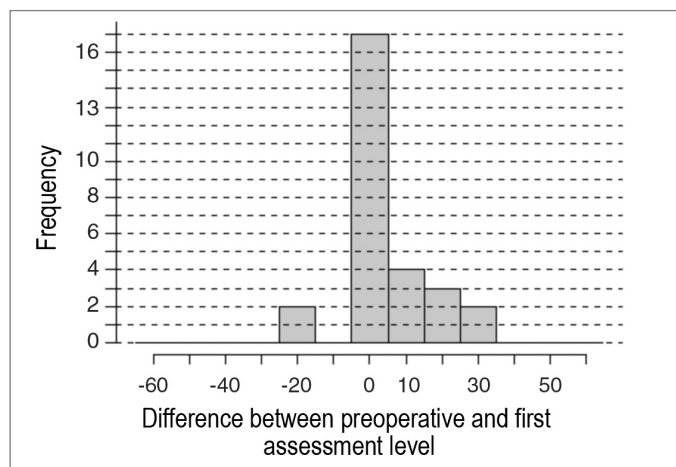


Figure 10 – Histogram of the difference of cortisone use on the first assessment after surgery.

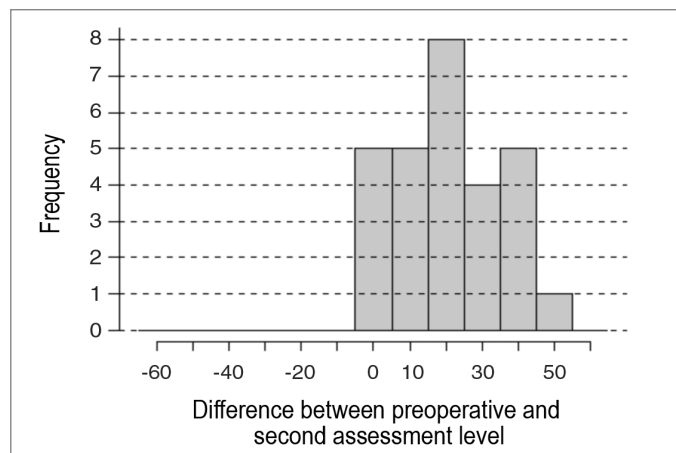


Figure 11 – Histogram of the difference of cortisone use on the second assessment after surgery.

Although in the second evaluation we had proven the reduction of the cortisone levels, a drawback could still occur. However, the test involving the "Postoperative moment 3" resulted in a p value of $1.16 \cdot 10^{-11}$. The null hypothesis is, therefore, ruled out. The maintenance of the benefits of surgery is proven.

The histogram of the difference in the use of cortisone between the preoperative moment and the third postoperative one (Figure 12) confirms this conclusion. Only one patient showed no reduction of the cortisone level.

Influence of patients' characteristics

We employed linear regression models in an attempt to unveil the influence of the variables: age, gender, kind of leprosy, form of leprosy, and time elapsed since the onset of the disease and the neurolysis procedure on VAS, BS, motor strength and sensitivity.

The results achieved with the statistical software R clearly showed the fact that when leprosy has a Virchowian form the benefit of the surgery for sensitivity is reduced.

We confirmed this result with histograms. The first one includes only non-Virchowian cases (Figure 13); the second includes Virchowian cases (Figure 14).

However, we verified that Virchowian leprosy patients had an increased sensitivity over the other patients even before surgery. Thus, there was less opportunity for improvement (Figures 15 and 16).

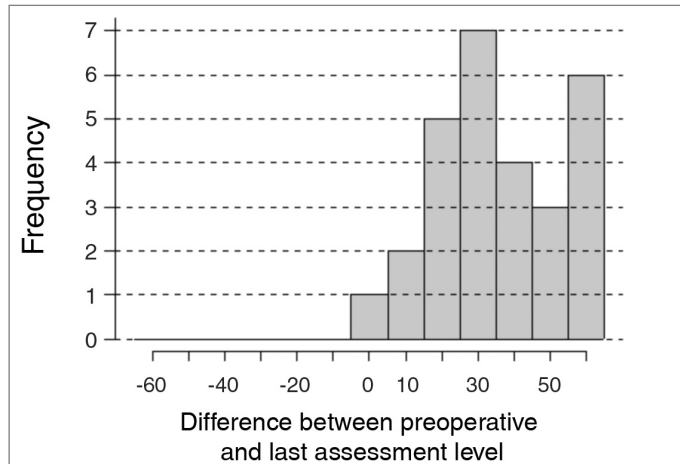


Figure 12 – Histogram of the difference of cortisone use on the last assessment after surgery.

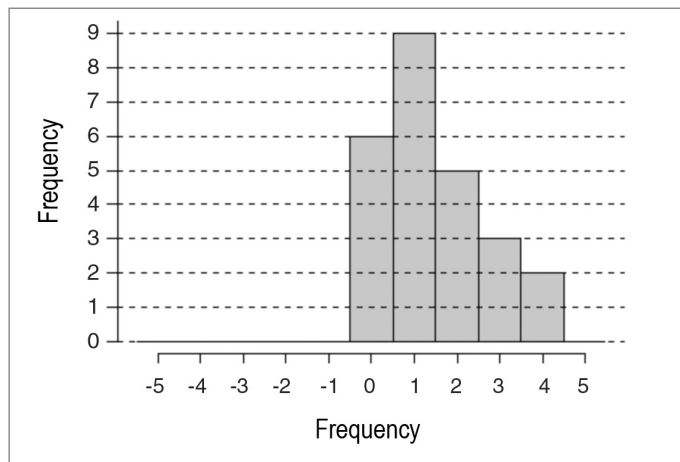


Figure 13 – Difference on sensitivity for the non-Virchowian form.

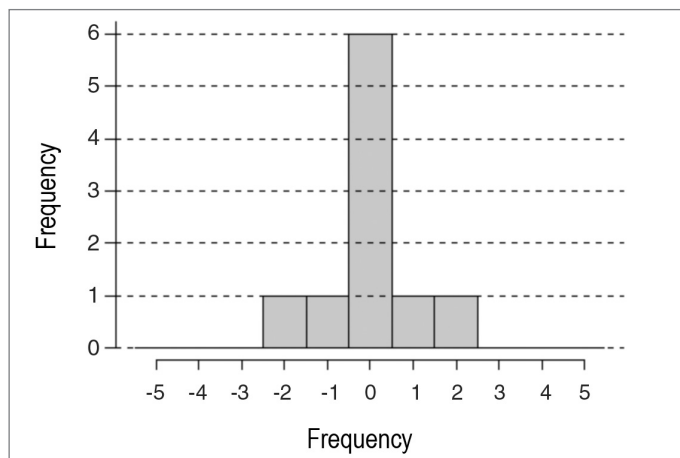


Figure 14 - Difference on sensitivity for the Virchowian form.

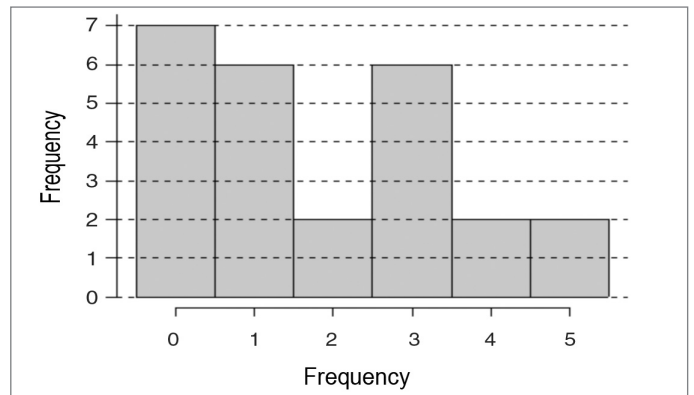


Figure 15 – Initial sensitivity level for the non-Virchowian form.

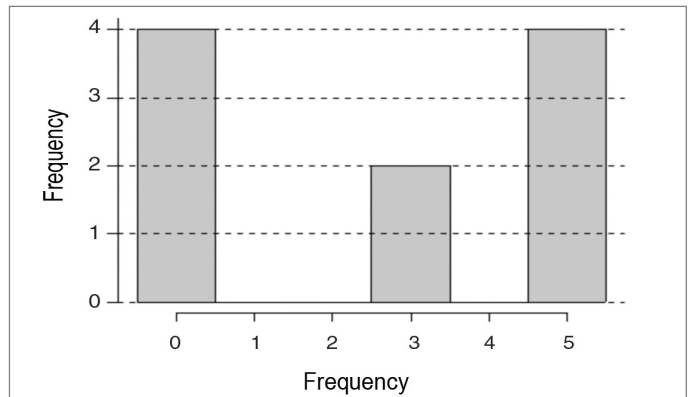


Figure 16 - Initial sensitivity level for the Virchowian form.

DISCUSSION

Leprosy is a neuroectodermal disease with serious consequences associated to the locomotive apparatus, where cure or even eradication does not mean absence of injured and sequelled patients, because it is estimated that 2,400,000 surgeries would be required to treat and fix affected patients. Despite of recent advancements in immunopathogenesis, epidemiology and prognostic factors of neural lesions, several aspects of the disease concerned to neural involvement remain unclear⁽¹²⁾.

Neural involvement in leprosy, previously faced as a simple diagnostic aspect of the disease and as a treatment complication, represents a phase and factor that are essential in the infection and reinfection cycle by *Mycobacterium leprae*⁽¹³⁾, additionally to constitute one of the determinant factors of the immunologic spectrum seen in leprosy⁽¹⁴⁾.

Leprous neuritis is an inflammatory process caused either directly or indirectly by the invasion of *Mycobacterium leprae* into peripheral nerve, with the ulnar nerve being most frequently affected. This suggests that the early identification of the bacillus could be helped by the detection of early stages of neural compression⁽¹⁵⁾. Such process triggers the intrinsic and extrinsic neural compression, presenting as three basic stages: irritative (stage I), characterized by pain, paresthesia, and hyperesthesia; compressive (stage II), characterized by hypoesthesia and paresthesia, and; deficitting (stage III), characterized by anesthesia, palsy and atrophy.

On stages II and III, surgical treatment (external ulnar neurolysis) is believed to be an alternative providing more promising outcomes, especially on stage II, where the patient can partially or totally recover his/ her sensorial-motor loss. As for stage III, external neurolysis inhibits the intraneural degenerative process; however, clinical regression will rarely happen, requiring its combination with rehabilitation-nature surgeries. The external ulnar neurolysis performed in outpatient facilities and without garrote constitutes an effective, fast and low-cost procedure.

The fact that we found, in our case series, a higher prevalence of ulnar nerve neuropathy (6:1) is consistent with literature reports. Concerning kind, we noticed that even the paucibacillar forms previously treated with multiple chemotherapy regimens may lead to neural lesions, with the dimorphous form (tuberculoid, dimorphous and virchowian) being the ones most affecting nerves, accounting for 67.6% of the operated patients, which is consistent to previously described findings. Polychemotherapy is effective in blocking the disease process progression, as well as in reducing the viable bacterial load, both in multibacillar and paucibacillar patients. However, the presence of *M.leprae* antigens on neural lesions in all multibacillar cases treated with polychemotherapy and in the majority of paucibacillar cases also treated, suggests that antigens remain for a long time. Thus, the risk of an immune response and insidious neural lesion associated to antigens, may remain even after most of the bacillus load are killed. Such fact indicated that, in leprosy, most neural lesions are due to bacterial antigens⁽¹⁶⁾.

The effects of surgery concerning the visual analogous scale and the pain behavioral scale are strong, and this can be noticed in the early postoperative period. The analysis of the histogram confirms the conclusion that surgery brings benefits on pain relief and behavior changes.

We noticed an improved motor strength in 50% of the patients, while for the other 50%, no worsening was seen. These data suggest that ulnar neurolysis can either produce neurological improvement or can prevent further neural damages when this is significant.

Concerning the sensitivity assessment with esthesiometry, it is important to emphasize that the outcomes achieved with the use of the statistical software R clearly showed only the fact that the virchowian form of leprosy (intranural disease) is less benefited regarding sensitivity improvement (comparative histograms).

Prednisone is administered for the treatment of leprosy neuropathy at

a 1mg/kg/day dosage, with 60mg/day being the maximum dosage. The use criteria are: pain, neural thickening, reduced motor strength and sensitivity. Prednisone was prescribed by another doctor according to the usual criteria. The worse the patient's status, the higher the amount of cortisone required.

The secondary effects of cortisone use for long periods of time are widely known (generalized osteoporosis and its consequences, Cushing syndrome, diabetes, obesity, cellulites, striae, among others).

The reduction of prednisone dosage after surgery was consistent and significant in each of the postoperative moments. This suggests that the therapy with high-dosage corticoids established previously to surgery would be beyond the needs of a patient who, in fact, showed symptoms related to the mechanical compression of the ulnar nerve.

CONCLUSIONS

- Surgical decompression (neurolysis) is the method indicated and urgent to resolve compressive leprosy neuropathy.
- Neurolysis can be performed on an outpatient basis under local anesthesia, without the use of garrote.
- Pain relief was immediately achieved after surgery.
- The reduced use of prednisone after surgery suggests that the long-term use of high-dosage corticoids should be discussed, because of the risks of sequels or diseases associated to that practice.
- Surgery promoted personal satisfaction and improved self-esteem for all patients.
- Motor strength and sensitivity may be preserved or improved with timely surgery.
- Surgery and the use of corticoids are methods not competing with each other or excluding one another.

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