IJS
International Journal of Sciences

Published online 03 20, 2022
ISSN 2763-5392

Changes in neural control in leprosy after high medication on cardiac autonomic modulation

Débora Rafaela Amorim Ferreira Ferraz[1]*, Relba Torquato Vasconcelos[2], Natália Fernanda Bezerra de Melo[3], Leandro Amaro da Silva[4], Paulo Rosemberg Rodrigues da Silva[5], Marília Maria da Silva[6], Loysley dos Santos[7], Maria Adrielly Almeida Nunes de Melo[8], Tacyla Rayssa Carneiro Amorim[9], Sandra Maria Correia de Santana[10], Thamires Maria de Lima[11], Giullyan Nóbrega Primo[12], Simone da Silva Andrade[13], Maria da Conceição dos Santos Lima[14], Ana Cecília Amorim de Souza[15]

1 Obstetrician nurse at Agamemnon Magalhães hospital - Specialist in obstetrics - SESAU, specialist in cardiology and hemodynamics.
2 Intensivist nurse - Specialist in orthopedics and traumatology -Nurse at the municipal Bom Jardim-PE hospital
3 Undergraduate nursing student-UNIVISA
4 Nurse regulator SES PE - Nephrologist nurse - Health service manager
5 Nurse and coordinator - SAMU- Umbuzeiro/PB - Emergency nurse
6 Undergraduate nursing student -UNIFACOL
7 Undergraduate nursing student - UNIFACOL
8 Undergraduate biomedicine – UNIVISA
9 Nurse. Intensive - resident in pulmonology at the Hospital Otávio de Freitas
10 Director of SS physiotherapy - Master in biomedical engineering - Specialist in Urogineco, Proctology and Obstetrics
11 Emergency specialist and ICU -Post-graduate studies in cardiology and hemodynamics
12 Medical specialist in cardiology - UFPE
13 Post-graduate students in general ICU
14 Postgraduation in urgency and emergency/ICU
15 Nursing and physiotherapy professor – UNIVISA

E-mail adresses: Débora Rafaela amorim Ferreira Ferraz (deborarafha19@gmail.com), Relba Torquato Vasconcelos (relba2016@hotmail.com), Natália Fernanda Bezerra de Melo (fernandaamelo93@gmail.com), Leandro Amaro da Silva (leandrobm2011@gmail.com), Paulo Rosemberg Rodrigues da Silva (paulorosemberg2007@hotmail.com), Marília Maria da Silva (fabiomarilia2016@gmail.com), Loysley dos santos(loysleysantos@gmail.com), Maria Adrielly Almeida Nunes de Melo(adrialmeida_@hotmail.com), Tacyla Rayssa Carneiro Amorim(taciamorim02@hotmail.com), Sandra Maria Correia de Santana (ss.oliveira10@hotmail.com), Thamires Maria de Lima (mariathamires1234@gmail.com), Giullyan Nóbrega Primo (giullyanprimo@gmail.com), Simone da Silva Andrade (simoneandrade1993@hotmail.com), Maria da Conceição dos Santos Lima (cg_agape@hotmail.com), Ana Cecília Amorim de Souza(anacecilia.cge@gmail.com)
*Corresponding author

To cite this article:
Ferraz, D.R.A.F.; Vasconcelos, R.T.; Melo, N.F.B.; Silva, L.A.; Silva, P.R.R.; Silva, M.M.; Santos, L.; Melo, N.A.A.N.; Amorim, T.R.C.; Santana, S.M.C.; Lima, T.M.; Primo, G.N.; Andrade, S.S.; Lima, M.C.S.; Souza, A.C.A. ***Changes in neural control in leprosy after high medication on cardiac autonomic modulation.*** *International Journal of Sciences.* Vol. 3, No. 2, 2022, pp.119-125. ISSN 2763-5392.

Received: 03 02, 2022; **Accepted:** 03 04, 2022; **Published**: 03 20, 2022

Abstract: Mycobacterium leprae infection is the main cause of non-traumatic peripheral neuropathies. To verify the effects of leprosy after high medication on linear and nonlinear indices of heart rate variability. To analyze the effects of leprosy according to degrees of disability on the Autonomic Nervous System (ANS) at the Otavio de Freitas Hospital located in the city of Recife-

PE, through the field research method in the descriptive and quantitative modalities.

Keywords: Leprosy. Autonomic Nervous System. Cardiovascular System. Physiology.

1. Introduction

Infection with *Mycobacterium leprae* (ML) infection, leprosy, is a disease with characteristics of peripheral and autonomic neurological alterations, is responsible for millions of deaths per year and affects 10% of the world population (World, 2016). Evidence indicates that ML binds and invades Schwann Cells (CS), this is the target cell of the Peripheral Nervous System (SNP) (Vital, 2012).

M. leprae infects Schwann cells of nerves that stimulate an immune response of the body that provoke infiltration with inflammatory nerve cells that lead to nerve dysfunction and nerve damage (Deepti 2012).

SC are involved in the immuno modulation of neurological injury caused by ML, thus triggering an inflammatory response to the presence of the bacterium. The cytokines that participate in this response, one of which is tumor necrosis factor (TNF-), a molecule involved in the pathogenesis of several diseases that affect the Central Nervous Systems (CNS) and peripheral (SNP) (Van brakel, 2000).

Leprosy (HS) is a chronic neurological pathology. (Lockwood, 2012) Neurophysiological studies investigate neurological impairment in leprosy. The findings provide information on the dysfunction of the affected nerves, although (Goedee, 2013). Its chronic effects on the autonomic nervous system (ANS) were investigated through heart rate variability (HRV), using traditional linear methods applied in the intervals between consecutive heartbeats (RR intervals) (Silva *et al*., 2015).

Patients with leprosy with related peripheral neuropathy and involvement of other organs may present with cardiac, respiratory and autonomic dysfunctions (Howling, 2016). Non-autonomy and side effects of drugs used for treatment can lead to multiple organ failure (Sandeep, 2011).

A cardiovascular involvement of leprosy has been mentioned in numerous reports. May cause ecg changes such as congestive heart failure (4) and ST and T wave changes, branch block, extra-systoles and a prolonged QT interval (Zawar, 1987)

Orthostatic hypotension, baroreflex dysfunction and postprandial hypotension may occur because of the influence on autonomic function (6). It has been reported that Valsalva maneuver, heart rhythm and disorders of response to foot blood pressure may develop in patients with leprosy leprosy (7). As a result of degradation as a function of the sympathetic cardiac, an increase in heart rate can be prevented by injecting high doses of atropine (4). Our patient did not present heart failure and ECG alterations and the atropine test performed to assess the sympathetic function of the heart was also positive (Howl, 2016). Autonomic function tests showed an increase in temperature with no sweating in the affected area (Deepti 2012).

However, two primary points so far remain unresolved, and their stigma and potential are incapacitating (Araújo, 2005). The prevalence of affected nerves is peripheral, and 23% of leprosy patients have a degree of disability (grades 1 and 2), however, there is evidence of reactions persisting even after drug discharge (Brasil, 2012; Deepak, 2003). Study by Nardi *et al*. (2012), reports that former patients evaluated had a higher percentage of disability after drug discharge, which can be concluded that leprosy alterations may occur even after drug discharge. With regard to autonomic alterations, the rupture of the vascular reflex arch, where it leads to a relative tissue anoxia, because circulation does not accommodate tissue needs (Brasil, 2008).

According to Valentini, *et al*., (1999), tests were performed with leprosy to assess the integrity of the autonomic nervous system (histamine test = incomplete and pilocarpine = absence of sweating) and were altered in 6 patients. This alteration confirms the involvement of this system in leprosy, even outside dermatological lesions, since it was performed in areas with edema, without apparent dermatological lesion (Valentini *et al*., 1999).

Leprosy treatment consists of multidrug therapy consisting of rifampicin, clofazimine and dapsone. Leprosy reactions are managed by steroids and other immunosuppressants (Deepti 2012); (Pinheiro, 2011).

2. Methodology

Study population

We analyzed subjects in treatment and post-treatment of Multi Bacillary leprosy (MB) with grade 3 neural disability, of both sexes aged 20 to 20 years, a sample of 19 patients characterized as a cohort-type comparative epidemiological study, where they were selected through the rehabilitation group of the Otavio de Freitas Hospital (HOF), where the researchers must have obtained pathology treatment in the HOF and be participants in the rehabilitation program of the hospital located in the city of Recife-PE.

The inclusion criteria were patients who were medicated with prednisone, thalidomide and azathioprine as well as vef1 <50% of the predicted with a degree of moderate to severe obstruction and who did not present coronary artery disease, arterial hypertension, diabetic neuropathy. Those of exclusion were patients after high neurological disorders and other known impairments that prevented the subject from performing the procedures. All volunteers were informed about the procedures and objectives of the study and, after agreeing, they will sign a free and informed consent form. The project is under submission by the Research Ethics Committee of the Hospital da Restauração de Pernambuco, Recife - PE and followed resolution No. 244 of the National Health

Council of 12/12/2012.

Initial evaluation

Before the beginning of the experimental procedure, the volunteers identified themselves by collecting the following information: age, gender, weight, height and body mass index (BMI). Anthropometric measurements were obtained according to the recommendations described by Lohman *et al*. (1988). Body mass index (BMI) was calculated using the following formula: weight (kg)/height $(m)^2$.

Analysis of linear indexes of heart rate variability

For the analysis of HRV indices, heart rate was recorded beat by beat throughout the experimental protocol with a sampling rate of 1000 Hz. From the period of greatest signal stability, an interval of five minutes was selected, and only series with more than 1000 RR intervals will be used for analysis (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996).

In these series, digital and manual filtrations were performed to eliminate premature ectopic beats and artifacts, and only those with more than 95% of sinus beats will be included in the study (Vanderlei *et al*, 2008). For HRV analysis in the frequency domain, low frequency spectral components (LF: 0.04-015 Hz) and high frequency (HF: 0.15-0.40 Hz) were used in ^{ms2} and standard units. Spectral analysis was calculated using the Fourier Fast Transform algorithm.

On the other, the analysis in the time domain was performed using the SDNN (standard deviation of the mean of the normal RR intervals) and RMSSD (square root of the square mean of the differences between the adjacent normal RR intervals). Hrv analysis software (Niskanen *et al*., 2004) will be used to analyze linear indices in the frequency and time domains.

Experimental protocols

Data collection was performed in a room with temperature between 21°C and 25°C and humidity between 50 and 60% and volunteers will be consulted if they did not drink alcoholic beverages and caffeine in the 24 hours prior to the evaluation. The collection will be performed individually, between 8:00 am and 12:00 AM to minimize the interference of circadian rhythm, and volunteers will be instructed to remain at rest, avoiding conversations during collection.

After the initial evaluation, the capture belt and, in the wrist, the Polar RS800CX heart rate receptor (Polar Electro, Finland), equipment previously validated for the capture of the heartbeat and the use of its data for HRV analysis, is positioned in the chest of the volunteers, in the region of the distal third of the sternum. After placing the brace and monitor, volunteers will be positioned in the sitting position with their feet supported, 90-degree position and will remain at rest for 10 minutes without hemodialysis.

Manual pressure test (*handgrip*): The subjects were instructed to perform handgrip to obtain maximum force. The maximum strength of each individual will be obtained by means of the mean. In the test, the individual will perform manual isometric grip with 30% of the maximum force for 90 seconds (Delaney *et al*., 2010). This protocol will be based on evaluation in just one day. After 10 minutes of registration at rest, the patient was submitted to manual pressure test (*handgrip*). After the end of manual pressure, 10 minutes of heart rate recording (Table 1).

Table 1. Procedures performed in the protocol

0 - 10 minutes	90 seconds (90")	10 - 20 minutes
HrV registration in rest.	Pressure test manual (***handgrid***)	Post-test HRV record.

Statistical analysis

For data analysis, a database was constructed in the Microsoft Excel electronic chart, and the Shapiro-Wilk normality test was applied to evaluate the statistical distribution. To compare HRV indices between before the Handgrip Test, during the test and, after the Test, we applied the unidirectional variance analysis (ANOVA) for the repeated measurement test followed by the Bonferroni post-test for parametric distributions. For nonparametric distributions, we used the Friedman test followed by Dunn's test. We use Biostat 2009 Professional 5.8.4 software for statistical analysis.

For data analysis between groups: under treatment and after treatment the database was exported to the SPSS software, summer 18, where the analysis was performed. Foi used the mean statistic and standard deviation to measure HRV through the scores of the performance parameters. The normality of quantitative variables was evaluated using the Shapiro-Wilk test. In cases where normality was indicated, the student's t-test was applied to compare the performances of patients submitted to type 1 treatment with the performance of patients submitted to treatment type 2. In cases where normality was not indicated, the Mann-Whitney test was applied to make the performance comparations of the two groups. All conclusions were drawn considering the significance level of 5%.

3. Results and Discussion

Table 2. Age, height, weight, BMI, HR and mean RR intervals of the volunteers. Mean ± standard deviation, minimum-maximum.

Variables	Mean ± standard deviation
Age (years)	24.94±16.38
(Min-max)	(15-42)
Height (m)	1.60±0.06
(Min-max)	(1.48-1.71)
Weight (kg)	68.88± 14.33
(Min-max)	(47.30-87.70)
BMI ($kg/^{m2}$)	24.94± 4.54

(Min-max)	(17.99-33.42)
FC (bpm)	91.75±12.37
(Min-max)	(65.43-115.47)
Average RR (ms)	668.45±94.70
(Min-max)	(520.30-925.00)

m: meters; ms: milliseconds; kg: kilograms; bpm: beats per minute; min-max: minimum-maximum.

Table 3 shows the descriptive analysis of gender, age, BMI and waist circumference of the patients evaluated. It was verified that most patients in treatment group 1 and treatment 2 are male (63.6% and 66.7%, respectively). Furthermore, it is observed that the homogeneity test was not significant (p-value = 1.000, indicating that the distribution of sex in the two treatment groups are similar. Regarding age, BMI and waist circumference, on average, the group of patients in type 2 treatment presented higher mean than the group of patients submitted to type 1 treatment (49.2 years; 27.2 kg/m² and 99.1cm, respectively), however, the mean/distribution comparison test was not significant in any of these measures evaluated (p-value = 0.666 for age, p-value = 0.991 for BMI and p-value = 0.879 for WC, respectively), indicating that the two groups are similar in relation to age, BMI and WC.

Table 3 Descriptive analysis of gender, age, BMI and waist circumference of the patients evaluated, according to the treatment group.

Factor evaluated	**Rated group**		**p-value**
	Treatment	**After Treatment**	
Sex			
Male	7(63,6%)	6(66,7%)	1,000[1]
Female	4(36,4%)	3(33,3%)	
Age	46.7±10.6	49.2±14.8	0.666[2]
BMI	27.1±4.9	27.2±4.1	0.991[2]
CA	95.6±23.7	99.1±14.9	0.879[3]

[1]p-fisher exact value (if p-value <0.05 the distribution of the evaluated factor differs between treatment groups 1 and treatment 2). Student t-test [2]p-value for independent samples (if p-value < 0.05 the mean of the evaluated factor differs between treatment groups 1 and treatment 2). Mann-Whitney test [3]p-value.

Table 4. Media and the standard deviation of the indices in the time domain between T1, T2 and T3. Dez minutes at rest, manual grip test antes (T1); 30 seconds of handgrip (T2); minutes at rest after handgrip (T3).

Indices	**T1**	**T2**	**T3**	**p**
SDNN (ms)	40.02±17.78	40.45±18.61	39.55±16.41	0,6437
PNN50 NN50	9.23±14.89	8.28±13.67	6.68±11.44	0,1831
RMSSD (ms)	24.81±18.26	23.05±16.94	20.73±15.99	0.7663

ms - milliseconds. SDNN - standard deviation of all normal RR intervals. pNN50 - percentage of adjacent RR intervals with duration difference greater than 50 milliseconds. RMSSD - square root of the square mean of the differences between adjacent normal RR intervals.

In table 5 we have the Mean and standard deviation of the score of the evaluated parameters. It was verified that in the 1st moment of evaluation the group of patients who received type 1 treatment presented higher mean in all parameters evaluated, except in RR, HF (ms2) and HF (naked), in which the type 2 treatment group presented higher mean score. Even though differences were found in the means of the parameters evaluated, the mean/distribution comparison test was significant only in the following parameters: LF (nude) (p-value = 0.031), HF (naked) (p-value = 0.029) and LF/HF (p-value = 0.017), indicating that the group of type 1 patients presented a relevantly higher mean of LF (naked) and LF/HF than the type 2 treatment group; and that the type 2 treatment group presented a significantly higher mean of HF (naked) than the group of patients who received type 1 treatment.

In the 2nd moment of evaluation, the group of patients who received type 1 treatment presented a higher mean score in the following parameters: RR, RMSSD, NN50 and pNN50. The group of patients who received type 2 treatment presented the highest mean score in the parameters: SDNN, HR, STD HR, triangular RR, TINN, LF (ms2), HF (ms2) and LF/HF. In the LF (nude) and HF (nude) parameters, the mean scores were the same in the two groups of treatments evaluated. Furthermore, it is observed that even though differences were found in the mean values of the parameters evaluated between the group of patients who received type 1 treatment and type 2 treatment, the mean/distribution comparison test was not significant in any of the parameters (all p-values were greater than 0.05), indicating that there is no difference in the parameters between the types of treatment used.

In the 3rd moment of evaluation, the group of patients who received type 1 treatment presented higher mean in all parameters evaluated, except in RR, STD HR, RMSSD and HF (naked), in which the type 2 treatment group presented the highest mean score, and in the HR parameter in which the mean of the two groups was identical. Even though differences were found in the mean values of the parameters evaluated between the group of patients who received type 1 treatment and type 2 treatment, the mean/distribution comparison test was significant in none of the parameters (all p-values were greater than 0.05), indicating that there is no difference in the parameters between the types of treatment used.

Table 5. Mean and standard deviation of the score of the evaluated parameters.

Paramt	MOMENT 1			MOMENT 2			MOMENT 3		
	Trat 1	Trat 2	p	Trat 1	Trat 2	p	Trat 1	Trat 2	p
RR	813.9±159.8	911.3±156.1	0.187[1]	743.4±100.4	741.9±107.4	0.975[1]	846.8±122.6	867.4±188.6	0.771[1]
SDNN	43.9±16.0	36.8±15.2	0.327[1]	46.9±29.4	66.4±48.6	0.305[2]	40.5±12.3	33.7±16.2	0.300[1]
HR	77.1±17.9	58.9±19.2	0.063[2]	82.6±11.8	83.3±12.8	0.621[2]	72.5±11.3	72.5±16.9	0.996[1]
STD HR	4.5±3.6	2.7±1.3	0.087[2]	5.5±2.4	6.7±3.8	0.421[1]	3.4±0.8	10.0±22.1	0.425[2]
RMSSD	31.1±19.7	27.2±9.5	0.909[2]	29.2±22.3	21.5±15.3	0.390[1]	33.1±17.9	24.0±12.0	0.210[1]
NN50	81.7±104.7	50.3±47.4	0.761[2]	3.5±4.0	2.7±3.7	0.613[2]	93.7±104.4	45.0±53.9	0.270[2]
PNN50	12.7±16.4	7.9±6.9	0.820[2]	8.9±9.7	6.8±9.3	0.669[2]	14.7±16.9	6.9±8.2	0.342[2]
Triangular RR	10.4±3.3	9.6±3.5	0.565[1]	6.6±1.8	7.9±2.7	0.201[1]	10.2±3.4	9.3±4.8	0.628[1]
TINN	187.7±50.4	130.6±93.2	0.125[1]	167.7±77.7	172.2±90.1	0.906[1]	171.8±45.2	131.7±11 0.7	0.285[1]

[1]p-student t-test value for independent samples (if p-value < 0.05 the mean of the evaluated parameter differs between treatment groups 1 and after treatment 2. [2]p-value of the Mann-Whitney test.

Leprosy is a chronic granulomatous and infectious disease that affects the skin, various organs and tissues, and in particular, somatic and autonomic nerves. Secondary complications of neuropathy may result in deformity and disability. Dermato-neurological signs and symptoms are the primary manifestations. However, secondary complications of neuropathy may result in deformity and disability (Correa *et al*., 2012).

In the studies analyzed and evaluated, it is clear and noticeable that this pathology causes several skin lesions, as well as neuropathy, some secondary complications of it can result in deformity and disability, being a stigmatizing disease (Cabalar *et al*., 2014). Already according to Osvaldo (2013) and Vagner *et al*. (2014), the different clinical presentations of the disease are determined by the quality of the host immunity response, and this disease is also an important health problem worldwide.

However, Deepak, *et al* (2014), reinforces that leprosy is one of the main causes of severe neuropathies in developing countries and that in many times its diagnosis can be a huge challenge, especially neuritic leprosy, with this it is possible to observe that it is a major global and social problem.

The great importance of nerve conduction studies, which provide a noninvasive modality, to estimate the involvement of peripheral nerves in leprosy and contribute to the evaluation of those assisted with peripheral neuropathy, evaluate and also monitor the evolution of the disease and therapeutic intervention having as the only disadvantage the cost factor that is high and the knowledge that is involved in conducting an investigation of this nature.

Vital *et al*., (2012), in their study, describes that in the patients analyzed nerve conduction was recovered in most nerves, but in most cases in the radial, median, and common peroneal nerve, however no conduction was obtained from 13 sural and three nerves. Mohanty (2002), points out that it was in 1998 that studies of leprosy present on the skin were taken at the College Hospital Medical VSS and in 1996 diagnosed clinically, he also pointed out that cases with clinical impairment of sensory function or motor nerve were selected for presentation.

The common neurological manifestations of peripheral neuropathy in this pathology, such as local sensory deficiency, asymmetric, the preferential involvement of several intrinsic muscles of the hand and also of the feet, nerve enlargement and tenderness to obtain an early diagnosis of this disabling and avoidable deforming specific neuropathy (SKACEL *et al*., 2000) . It is possible to point out that mono neuritis is the most common form of exposure of this great evil, and may occur with other clinical manifestations including even skin lesions and that its diagnosis is only achieved by neuropathological study of skin lesions and peripheral nerve, evidenced by the assimilation of the bacillus.

Neurophysiological and imaging studies can be used to investigate neurological impairment in leprosy (LUGAO, 2016)

The authors concluded that leprosy patients may present abnormal nerve anatomy with preserved nerve function and vice versa (LUGAO, 2016)

Several studies have focused on understanding even higher basic aspects such as genetics. They contribute in a great way to better understanding, elucidation and understanding of physicians and to better planning of nursing professionals and how they should proceed to avoid adverse events (Veiga *et al*., 2015).

Nervous system dysfunction in Leprosy is accompanied by autonomic nervous system dysfunction and has a predominance of sympathetic autonomic modulation (Calabar, *et al*., 2014). In this study, when evaluating skin sympathetic responses (SSR) and RR interval variations, it was observed that, after clinical, motor examination and sensory analyses of nerve conduction, sympathetic skin responses and RRIV interval variations were performed in patients with chronic leprosy and that electrodiagnostic findings at the beginning of the disease elucidate demyelinated characteristics, such as cooling conduction activity and stretching latencies, but as the disease progresses secondary axonal injury commonly ensues.

Sandeep 2011, Anesthetic consideration is mainly focused on complications related to leprosy, such as non-cardiac or respiratory autonomy, autonomic dysfunctions and side effects that are related to drug therapy and are challenging. The involvement of the cardiovascular system in leprosy characterized by non-leading bradycardia bradycardia cardiac autonomy, hypotension, cardiac arrest, various arrhythmias and other ecg changes, or lack of response to various perioperative manipulations such as intubation, extubation, or anticholinergic drugs that require careful intraoperative surveillance. All of these are more

pronounced in patients with longer duration of leprosy. (Repercussion of anesthesia in surgery with hansen's patient). Autonomic Neuropathy may present and manifest as orthostatic hypotension, altered baroreceptor reflexes and inadequate response to Valsalva maneuver. Fortunately, our PAC patient ruled out no cardiac and respiratory autonomy and autonomic involvement, but we were prepared with adequate monitoring for possible complications and their management. As leprosy patients may present with non-cardiac, respiratory autonomy and autonomic involvement.

Due to side effects of drugs and non-autonomy are prone to multiple organ failure. Proper evaluation and optimization of the CAP with the intraoperative period, adequate monitoring and preparation is essential when managing leprosy patients.

It is also observed that it is a disease of extreme importance and deserves more attention, causes physical disability of high severity, although it has a very low prevalence, the involvement of the peripheral and autonomic nerve is frequent and severe in several cases, including in our research. According to several experts in the field, there are three diagnostic signs that is hypopigmentation of the skin with loss of sensitivity, the second is the thickening of peripheral nerves and finally the positive skin-smear for ADR, it is also important to remember that indeterminate leprosy lesions are not always indetermined by the thickness of the anesthetic peripheral nerve and can also be localized in different neurological diseases.

References

[1] Accorsi-mendonça, D. (2007). Urethane inhibits the GABAergic eurotransmission in the nucleus of the solm itary tract of rat brain stem slices. Am J Physiol Regul Integr Comp Physiol, v. 292, n. 1, p. R396-402, Jan.

[2] Araújo, M. G. (2005). Evolução e estado atual da quimioterapia da hanseníase. A Bras Dermatol. 80(2):199-202.

[3] Bernardi L, *et al*. (2009). Dynamic interactions between musical, cardiovascular and cerebral rhythms in humans. Circulation, v. 30, n. 3, p. 3171-3180, Mar.

[4] Brasil. (2008). Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Manual de prevenção de incapacidades. 3º ed. Brasília: Disponível em: http://bvsms.saude.gov.br/bvs/publicacoes/manual_prevencao_incapacidades.pdf Acesso: 02 jan. 20013

[5] Brunetto, A.F. *et al*. (2005). Limiar ventilatório e variabilidade de frequência cardíaca em adolescentes. Rev. Bras. Med. Esporte., v. 11, n. 1, p. 22-27, jan.

[6] Cabalar M, Yayla V, Ulutas S, Senadim S, Oktar AC. The clinical & neurophysiological study of leprosy. Pak J Med Sci. 2014. 30(3):501-506.

[7] Cardoso FM, de Freitas MRG, Escada TM, Nevares T, Nascimento OJ. Late onset neuropathy in leprosy patients. Late onset neuropathy in

[8] Cashion, A. K. *et al*. (2005). Heart Rate Variability and Mortality in Patients with End Stage Renal Disease. Nephorology Nursing Journal, v. 32, n. 2, p. 173-184, mar.-abr.

[9] Colombari, E. *et al*. (2001). Role of the medulla oblongata in hypertension. Hypertension, v. 38, n. 3, p. 549-554, Sept.

[10] Deepak V, Arjun LD, Sanjeev S. Nerve conduction studies in leprosy tuberculoid early. Indian Dermatol Online. 2014; 5(Suppl 2): S71–S75.

[11] Deepak, S. (2003). Answering the rehabilitation needs of leprosy affected persons in integrated setting through primary health care services and community-based rehabilitation. Indian J Lepr. 75(2):127-42.

[12] Deepti G, Reshma G, Chitra N. síndrome de dor regional complexa secundária à lepra. Analgésico. 2012; 13: 1067-1071.

[13] Deligiannis, A.; Kouidi, E.; Tourkakantonis, A. (1999). Effects of physicl training on heart rate variability in patients on hemodialysis. American Journal of Cardiology, v. 84, p. 197-202, jun.

[14] Fite GL .(1941). The vascular lesions of leprosy . Int J Lepr . 9:193–202

[15] Fukuta, H. *et al*. (2007). Prognostic value of Herat rate variability in patients with end-stage renal disease on chronic haemodialysis. Nephrology Dialysis Transplantation, v. 18, p. 318-325.

[16] Gamelin, F. X. *et al*. (2006). Validity of the polar S810 heart rate monitor to measure R-R intervals at rest. Med. Sci. Sports Exerc., v. 38, n. 5, p. 887-93.

[17] Garbino JA, Marques Jr W, Barreto JA, *et al*. Primary neural leprosy: systematic review. Arq Neuropsiquiatr 2013; 71:397-340.

[18] Goedee HS, Brekelmans GJF, van Asseldonk JTH, Beekman R, Mess WH, Visser LH. High resolution sonography in the evaluation of the peripheral nervous system in polyneuropathy—a review of the literature. J Ultrassound Med. 2009; 28: 1201-9.

[19] Goldberger, A. L. *et al*. (1941). PhysioBank, PhysioToolkit, and PhysioNet: Components of a new research resource for complex physiologic signals. Circulation, v. 101, n. 23, p. E215-E220, June 2000.

[20] Grassi, G. *et al*. (2009). Sympathetic activation in cardiovascular and renal disease. J Nephrol 22:190-5.

[21] Hansen, G. A; LOOFT C . (1973). Leprosy in its Clinical and Pathological Aspects, 1895. Translated by Norman Walker. Bristol, London: John Wright & Co.

[22] Jena S, Mishra S, Mohanty G. (2002). neuropatia silenciosa na hanseníase. Indiana J Dermatol Venereol Leprol. 68: 84-5.

[23] Julius, S. *et al*. (1996). Sympathetic overactivity in hypertension. A moving target. Am. J. Hypertens., v. 9, n. 11, p. 120

[24] Khaled, A. S. *et al*. (2006). Employing time-domain methods and poincaré plot of heart rate variability signals to detect congestive heart failure. BIME J., v. 6, n. 1, p. 35-41.

[25] Le prell, C. G. *et al*. (2011). Evidence of hearing loss in a 'normally-hearing' college-student population. Int. J. Audiol. 2011. 50(1): S21-31.

[26] leprosy patients released from treatment: not all due to reactions? Lepr Rev 2013;84:

[27] Lockwood DNJ, Saunderson PR. Nerve damage in leprosy: a continuing challenge to scientists, clinicians and service providers. Int Health. Royal Society of Tropical Medicine and Hygiene; 2012; 4(2):77–85.

[28] Lohman, T. G. *et al*. (1988) Champaign: Human Kinetics Books. Anthropometric Standardization Reference Manual.

[29] Lugão HB, MHN Barbosa, Wilson Marques Jr, Norma Tiraboschi Foss, Marco Andrey Cipriani Frade. Asymmetric Nerve Enlargement: A Characteristic of Leprosy Neuropathy Demonstrated by Ultrasonography. PLoS negl Trop Dis . 2015. 9 (12): e0004276.

[30] Mainardi, L. T. *et al*. (2005). Analysis of scaling behavior of ECG signal during atrial fibrillation. Comp. Cardiol., v. 32, n. 4, p. 627-630.

[31] Makikallio, T. H. *et al*. (1999). For the Trace Investigators. Fractal analysis of heart rate dynamics as a predictor of mortality in patients with depressed left ventricular function after acute myocardial infarction. Am. J. Cardiol., v. 83, n. 6, p. 836-839.

[32] Mancia, G. (1997). Bjorn Folkow Award Lecture: the sympathetic nervous system in hypertension. J. Hypertens., v. 15, n. 12, p. 1553-1565.

[33] Mark, A. L. (1996). The sympathetic nervous system in hypertension: a potential long-term role of arterial pressure. J. Hypertens., v. 14, n. 2, p. 165, Feb.

[34] Murat, C.; *et al*. The clinical & neurophysiological study of leprosy. Pak J Med Sci. 2014. 30(3) :501-506.

[35] Nardi, S. M. T. *et al*. (2012). Leprosy-related disabilities after release from multidrug treatment: prevalence and spatial distribution. Rev. Saúde Pública. 2012.46 (6): 969-977.

[36] Nascimento OJM, de Freitas MRG, Escada T, *et al*. Leprosy lateonset neuropathy: an uncommon presentation of leprosy. Arq Neuropsiquiatr. 2012; 70:404-406.

[37] Niskanen, J. P. *et al*. (2006). Software for advanced HRV analysis. Comp. Met. Progr. Biomed., v. 76, n. 1, p. 73-81.

[38] Osvaldo JMN. Leprosy neuropathy: clinical presentations. Arq Neuropsiquiatr. 2013. 71(9-B) :661-666.

[39] Paschoal, M. A. *et al*. (2006). Variabilidade da Frequência Cardíaca em diferentes Faixas Etárias. Revista Brasileira de Fisioterapia, v. 10, n.4, p. 413-419.

[40] Penne, E.L. *et al*. (2009). Sympathetic hyperactivity and clinical outcome in chronic kidney disease patients during standard treatment. J Nephrol, 22:208-15.

[41] Pinheiro Ro De Souza Salles J Sarno EM Sampaio EP Interações de Mycobacterium leprae-célula-hospedeiro e determinantes genéticos na hanseníase: Uma visão geral Futuro Microbiol 2011; 6(2):217 - 30.

[42] Rubinger, D. *et al*. (1999). Heart rate variability during chronic hemodialysis and after renal transplantation: Studies in patients without a with systemic amyloidosis. Journal of the American Society of Nephrology, v. 10, p. 1971-1981.

[43] Sandeep S, Vipin G, Sanjay D, Kamal K, Singh PK. Um caso muito comum torna-se raro: Considerações anestésicas da lepra lepromatosa. Anestesia: Ensaios e Pesquisas. 2011; 5: 207-10.

[44] Skacel M, et, al. (2000). The diagnosis of leprosy among patients with symptoms of peripheral neuropathy no skin lesions. Arq Neuropsiquiatr, 58(3-B):800-807.

[45] Storm, F. *et al*. (2006). Die Heilkraft bestimmter Musikstile. In: STORM, F. (Ed.). Heilen mit Tönen. Stuttgart: Lüchow-edition, p. 17-47.

[46] Tamura, K. *et al*. (1998). Determinants of Herat rate variability in chronic hemodialysis patients. American Journal of Kidney Diseases, v. 31, n. 4, p. 602-606.

[47] Task force of the european society of cardiology and the north american society of pacing and electrophysiology. (1996). Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation, v. 93, n. 5, p. 1043-1065,

[48] Tory, K. *et al*. (2003). Autonomic dysfunction in uremia assessed by heart rate variability. Pediatric Nephrol, v.18, p.1167-1171, sep.

[49] Tulppo, M. P. *et al*. (1998). Vagal modulation of heart rate during exercise: effects of age and physical fitness. Am. J. Physiol., v. 274, n. 2, p. H424-9, Feb.

[50] Uçar M , Şanlı M , Özkan AS, Demiroz D, Erdoğan MA , Durmuş M. Regional Anaesthesia Management in a Patient with Leprosy: Rare Case with Rare Application. Turk J Anaesthesiol Reanim . 2016. 44 (1): 37-39.

[51] Vagner WBS. (2015). Primary Motor Cortex Representation of Handgrip Muscles in Patients with Leprosy. PLOS Neglected Tropical Diseases,

[52] Valentini, A. *et al*. (2008). Edema in leprosy: clinical and therapeutical aspects. Rev. Soc. Bras. Med. Trop. vol.32 n.2

[53] Van brakel, W.H. (2000). Peripheral neuropathy in leprosy and its consequences. Lepr. Rev. 71(Suppl.):S146–53.

[54] Vanderlei, L. C. *et al*. (2009). Basic notions of heart rate variability and its clinical applicability. Revista Brasileira de Circulações Cardiovasculares, v. 24, n. 2, p. 205-217, Feb.

[55] VanderleI, L. C. M. *et al*. (2008). Comparison of the Polar S810i monitor and the ECG for the analysis of heart rate variability in the time and frequency domains. Braz. J. Med. Biol. Res., v. 41, n. 10, p. 854-859, Oct.

[56] Veiga A, Costa A, Taipa R, Guimarães Um, Pires MM. Hansen Neuropathy: Still a Possible Diagnosis in the Investigation of a Peripheral Neuropathy. Hansen neuropathy. Acta Med Port. 2015. 28(3):329-332.

[57] Vital RT, Illarramendi X, Nascimento O, Hacker MA, Sarno PT, Jardim MR. Progression of Leprosy Neuropathy: A Case Series Study. Brain and Behavior. 2012. 2(3):249–255.

[58] World Health Organization. (2010). Global leprosy situation. Wkly Epidemiol Rec. 85(35):337-48.

[59] Zawar PB, Chawhan RN, Swami RM. Alterações eletrocardiográficas na reação lepra. Lepr Índia. 1983; 55: 197-9.