ESJ Natural/Life/Medical Sciences

Low-Level Laser Therapy At The Healing Process Of Grade I And II Ulcers In Patients With Diabetic Foot

Gustavo Argenis, (M.I.M.)
Ahtziry Aguilar, (P.S.S. Ft.)
Karen Najar, (P.S.S. Ft.)
Universidad Autónoma de Querétaro, México
Hospital General de Querétaro – SESEQ, México
Sistema Universitario de Atención en Fisioterapia – SUAF-UAQ, México

Doi:10.19044/esj.2022.v18n17p78

Submitted: 24 November 2021
Accepted: 09 February 2022
Published: 31 May 2022

Cite As:
Argenis G., Aguilar A.., & Najar K.,(2022). *Low-Level Laser Therapy At The Healing Process Of Grade I And II Ulcers In Patients With Diabetic Foot* European Scientific Journal, ESJ, 18 (17), 78.
https://doi.org/10.19044/esj.2022.v18n17p78

Abstract

Background: Chronic nonhealing ulcers are one of the major causes of morbidity and disability in people with diabetes mellitus (DM), which represents the most frequent cause of hospital admission in this group of DM. In terms of the acceptability, availability, and minor adverse effects, the effect of low-level laser therapy (LLLT) on diabetic foot ulcers (DFUs) has been highly documented in scientific literature. **Purpose:** The present study had the aim to evaluate the effectiveness of LLLT to promote the healing of diabetic foot ulcers. **Methods:** A quasi-experimental test-retest study was performed with a sample of 12 subjects. Before executing the research, it was submitted for review and approval by the Research Subcommittee of the Physiotherapy Degree, as well as the Research Committees of the Hospital General de Querétaro. **Results:** The average area at the beginning of the physical examination of the DFUs was 7.98cm2 (SD= 8.13), and the average area after the intervention was 0.93cm2 (SD= 1.64) revealing an average difference of -7.05cm2 (SD= 8.1) at the end of the intervention with LLLT. The Student's t-test was then used for related samples with a calculated value of t= 3.00 and significance of P=0.012 which shows at 95%, a significant difference in the reduction of the area in square centimeters of the ulcers after the application

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

of therapeutic low-intensity laser. **Conclusions:** The effects and efficiency of the LLLT were demonstrated, although further study with a numerically larger sample is suggested.

Keywords: low-level laser therapy, diabetic foot ulcer, healing process.

Introduction

Worldwide between 15% to 25% of patients with DM develop diabetic foot. Within these, 1% to 4% develop diabetic foot ulcers, producing between 40% and 70% of lower limb amputations, with evidence of incidences of new episodes after an amputation (Cisneros et al., 2015).

According to International Diabetes Federation (2019), Mexico occupies the sixth position with diabetic people worldwide, with a figure of 13 million, where most of them have diabetic foot syndrome (DFS).

DFS is considered as the presence of ulceration, infection, and/or gangrene of the foot associated with diabetic neuropathy and different degrees of peripheral vascular disease, resulting from the complex interaction of different factors induced by sustained hyperglycemia (González et al., 2018).

As stated by Obeso et at., (2021), DFUs generally inflict a prolonged, recurrent hospital stay; causing in most cases the amputation of the limb. This causes a high economic and social cost and a decrease in the quality of life and lifespan of patients.

Texas wound classification system determines that a grade I ulcer is a superficial skin injury that does not involve tendons, capsules, or bone without or with infection and ischemia, and a grade II ulcer already compromises tendons or capsules without or with infection and ischemia (Pereira et al., 2018).

The management of the DFUs is a public health problem due to the frequency with which cases occur, and the burden that is generated on the health system and on the economy (ENSANUT, 2016). Conventional treatment of diabetic foot ulcers uses drugs, wound cleansing, surgical intervention, and hyperbaric oxygenation. However, these have the disadvantage of high costs and long attention spans (CENETEC, 2020).

Laser therapy is an efficient and low-cost therapeutic resource proven in the treatment of ulcers due to its ability to accelerate the repair process in different tissues through the use of low-power light sources. Its biomodular action on the tissues allows faster tissue recovery, added to an effective action to relieve pain, especially in the first fifteen days of treatment (Perea & Navarro, 2019).

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

The LLLT boosts the reduction of the inflammatory phase, promoting angiogenesis and the production of components of the extracellular matrix, as well as its organization. In addition to reducing the area of the lesion and accelerating the healing process, laser therapy has the advantage of being easily administered (Sandoval, 2014).

In a clinical trial carried out with 2 control groups, Mathur (2017) demonstrated a positive effect was obtained in the group treated with laser regarding the reduction of ulcers, improving significantly more than those patients who have not been treated with this therapy, which indicates that it is an effective modality to facilitate wound contraction in patients suffering from diabetes and can be used as an adjunct to the conventional mode of treatment (dressing and debridement) for diabetic wound healing.

Carvalho et al., (2016), in an experimental, randomized, controlled and prospective clinical trial; with a sample of 32 patients, proved that after 30 days it was possible to observe how the patients who had been treated with laser therapy had practically healed ulcers.

Gebala et al., (2016) found that laser increased cell proliferation and increased type I collagen content, cell migration, proliferation, and viability in fibroblasts, noting that a group treated with low-level therapy had a significant reduction in ulcer area compared to patients on conventional therapy alone.

De la Cruz et al., (2011) concluded in their study that "laser therapy as a biostimulator that promotes the hyperpolarization of the cell membrane, the acceleration of metabolic processes and the increase in the exchange of nutritional substances, which contributes to strengthening the action of immune cells".

The results in the study by Hernández et al., (2015) showed complete healing or reduction in the area of the ulcers in approximately 50% of their initial surface and in more than 50% of the patients.

The objective's study was to evaluate the effectiveness of LLLT aplication to promote healing of diabetic foot ulcers.

Methods

Protocol and type of study

A quasi-experimental study was performed with a sample of n=12 subjects in an age range between 30 and 60 years (SD=6.99). To carry out the research, it was submitted for review and approval by the Research Subcommittee of the Physiotherapy Degree, as well as to the Bioethics Committee of Universidad Autónoma de Querétaro; it was also submitted for review, presentation, and approval to the Research Committee of the Hospital General de Querétaro.

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

Criteria Selection

The patients included in the study were selected meeting the inclusion criteria: patients who were in an age range of 30 to 60 years of age; subjects who presented grade (0 to II) ulcers according to the classification scale of the University of Texas and who did not present infection in the ulcerated area; and patients who agreed to sign the informed consent once they were informed in detail about the nature of the study.

Induction to study participants

During the induction to the research project, they were instructed and made clear that the end of the project intervention was the evolution of the ulcer until its closure, reduction, and/or that it presented favorable conditions to be treated conventionally or by means of partial-thickness skin grafts, as long as a minimum of 12 attendances were met for the methodological effect of the research project itself.

Measurements and scheduling

Measurements were taken (length and width of the area) by means of a ruler graduated in centimeters of the international system of units (SI), emptying the data obtained to the app "Geometry" version 2.8.4 ARPAPLUS of the Android system that allowed the calculation of the area and perimeter of the lesion; this made possible to evaluate the evolution of the ulcer after the application of the initial and final treatment; photographic capture was made as well for the follow-up of the ulcer in each session.

The treatment program consisted of a total of 12 sessions, divided into 3 sessions per week, alternately, which took a total of 4 weeks per patient; in the other hand, for bioethical reasons and of passion for the subjects participating in the research, he dedicated himself to continuing with the application of the therapeutic laser until a total closure of the lesion was presented or a reduction greater than 50% of it was observed.

All subjects in the study group attended their scheduled sessions without absences, cancellations, setbacks, or appointment changes. It is worth mentioning that none of the subjects had secondary symptoms or adverse effects developed during or at the end of treatment; however, based on the elimination criteria, one subject was discharged due to poor glycemic control.

Medical equipment, dosage, and application methodology

The intervention was applied with medical-grade equipment that emits a low-intensity therapeutic laser with a power of 50mW and a diode applicator with a wavelength of 785nm. The dosage was 10 J/cm2, at a frequency of 3000

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

Hz, applying it for 6 seconds per point, keeping the applicator 1cm away from the perimeter of the skin surrounding the outer edges of the ulcer.

Data analysis

A test-retest, the Student's t-test, and Wilcoxon signed-rank test analysis were used to process the information and determine the results. The variables considered were the area (cm2) of the ulcers before and after the intervention, their perimeters (cm), as well as the grade and stage according to the "Texas Scale", also both before and after the LLLT intervention.

Results

As a result of the statistical analysis, it was observed that the average area at the beginning of the assessment was 7.98cm2 (SD= 8.13), and the average area after the intervention was 0.93cm2 (SD= 1.64), revealing an average difference of -7.05 cm2 (SD= 8.1) at the end of the intervention with laser therapy (Table No.1). The Student's t-test was subsequently used for related samples with a calculated value of t= 3.00 and significance of P=0.012, which shows (CI=95%), a significant difference in the reduction of the area in square centimeters of the ulcers after the application of LLLT.

In the analysis of the measurements of the perimeter of the ulcers before and after, statistics were also performed, showing that the average perimeter at the time of the initial assessment was 9.59 cm (SD= 6.17), the final average perimeter was 2.52 cm (SD= 4.09), obtaining a final difference of -7.26cm of average reduction (SD= 6.29), as shown in Table No. 2. In the same way, the Student's t-test was used for samples related to a value of t= 3.99 and significance P= 0.002, which states that with a (CI=95%), there was a significant difference in the reduction of the perimeter of the ulcers after the application of laser therapy.

Table No.1.- Statistical analysis of the before and after of the area of the ulcers.

Measurements	Area (cm2) BEFORE	Area (cm2) AFTER	Area differences (cm2)
Sample (n)	12	12	12
Average ($\bar{X}$)	7.98	0.93	-7.05
Standard Deviation (SD)	8.13	1.64	8.1

Source: self-made.

Table No.2.- Statistical analysis of the before and after of the perimeter of the ulcers.

Measurements	Perimeter (cm) BEFORE	Perimeter (cm) AFTER	Perimeter differences (cm)
Sample (n)	12	12	12
Average ($\bar{X}$)	9.59	2.52	-7.26

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

Standard Deviation (SD)	6.17	4.09	6.29

Source: self-made.

On the other hand, according to the degree and stage of the "Texas Scale" of the ulcers before and after the intervention with therapeutic laser therapy, a non-parametric test was used, so an analysis was carried out for related samples through the Wilcoxon test, obtaining a degree of significance of (P= 0.002) with a (Z= -3.07), which clearly shows that there was a decrease in the degrees of ulcers after the intervention. Likewise, with the stage of the ulcers, a result was also obtained with the Wilcoxon test (P value = 0.016) with a (Z= -2.4), which also indicates a significant decrease in the general stages of the ulcers at the end of the intervention with laser therapy compared to the initial evaluation. Based on a random selection of photographic evidence, some of them are shown below

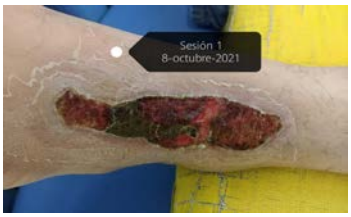
Figure 1.

Case 1 before LLLT

Figure 2.

Case 1 at seventh session

Figure 3.



Case 3 before LLLT

Figure 4.

Case 3 at twelfth session

Figure 5.

Case 11 before LLLT

Figure 6.

Case 11 at nineteenth session

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

Case 9.

Case 9 before LLLT

Case 9 at twenty-ninth session

Discussion

It is convenient to observe the statistical consistency with respect to the results obtained, which provides validity to the methodology used. Also, it is necessary to make it clear that a substantially larger sample would obviously be required to have more representative reliability.

The importance of this study is in the strength of the methodology, the care of the processes involved, as well as in the details related to the infrastructure, the technology used, the object of the study focused on the before and after based on measurements of the (SI), the parameters of the therapeutic laser, the determination of the dose, in the administrative, bioethical and regulatory aspects.

Although the subject matter of LLLT is very extensive in the scientific literature and in the main scientific search engines, recent systematic review and meta-analysis studies have shown that many of them lack methodological support. In this sense, fortunately, it was possible to identify the best available sources, and based on the results of the study, it can be established that there is a high affinity in terms of the effectiveness and benefits of therapeutic laser associated with the DFUs healing process.

The limitations of the project are mainly focused on the size of the sample, which was circumscribed according to the time it took to develop the research; this has an impact on the fact that other statistical tests could even be performed that can further reinforce the importance of the efficacy of the LLLT.

Conclusions

Regardless of the limitations in terms of sample proportion, the results are considered to confirm the importance and effectiveness of low-power laser therapy applied mainly to people suffering from diabetic foot ulcers.

As reflected in the scientific literature, it can be affirmed that LLLT has positive and certainly rapid effects on the repair process of DFUs in

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

comparison with the recommendations and conventional treatments in the management of such conditions.

It is important to highlight that the tissue repair process can surely be related to the healthy lifestyle of patients as well as to the specific care that DM entails (glycemia level), both with that of the DFUs in terms of repair processes as carried performed by professionals, with due procedure, local hygiene, antisepsis, postures and movements that promote correct peripheral circulation, ventilation, oxygenation, venous return, lymphatic drainage, and others.

It is also concluded that the Texas scale is a meaningful reference that allows for a verification margin in terms of a more objective measurement of DFUs. In the present study, significant degrees and stage reduction were observed in both parameters, and that contrasted with the area and perimeter reductions, it is established that it is a reference scale for the study and analysis of such kinds of ulcers.

This type of study has the nobility of motivating to carry out extensive interventions even to have more consistent results, but it also has the virtue to inspire to carry out more educational and awareness campaigns about the UFDs, which allows having an impact on the prevention of these health conditions.

Also, the advantage of this study results in the fact of the importance of having an explicit methodology, but mainly in the sense of the technologies or parameters used as well as the doses that prove to be effective in order to have greater reproducibility, which translates into the prevention of progression of ulcers and therefore, prevention of diabetic foot amputations.

Due to the alarming epidemiological representativeness that DM, DFS, and UFDs entail, this type of technology and intervention can easily justify its implementation in the health system that even allows the development of cost-benefit research in terms of people's health, as well as in administrative and economics, both in the short and long term.

Evidently, the recommendation extends that the application must be carried out by a competent and qualified health professional, as well as making use of medical-grade equipment and/or technologies within pertinent regulations and procedures. Although laser therapy has few adverse effects in its correct application, there are serious precautions concerning its handling and use.

Acknowledgments

To the Research Committee of the Hospital General de Querétaroand its staff, as well as the Dean of the degree in physiotherapy; to the Sistema

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

Universitario de Atención en Fisioterapia and its staff. To the commitment and participation of the study participants. To all person involved and encorauged us in this project.

Human Studies

The research protocol was submitted for review and approval before its aplication by the Research Subcommittee of the Physiotherapy Degree, as well as the Bioethics Committee of the Universidad Autónoma de Querétaro; it was also submitted for review, presentation and approval to the Research Committee of the Hospital General de Querétaro.

Conflicts of Interests

None at all.

Author contributions

Acordin to the standards of the International Committee of Medical Journal Editors (ICMJE):

G. A. design of the study, process monitoring, data analysis and interpretation, writing the manuscript, and final approval.

A. A. study proposal, literature review, design of the study, scientific presentation, study intervention, data collection, writing the manuscript.

K. N. study proposal, literature review, design of the study, study intervention, data collection, writing the manuscript.

References:

1. American Diabetes Association (2018). 4. Lifestyle Management: Standards of Medical Care in Diabetes-2018. Diabetes care, 41(Suppl 1), S38–S50. https://doi.org/10.2337/dc18-S004
2. Albornoz, M., Maya, J., & Toledo, J. (2016). Electroterapia práctica. Avances en investigación clínica. In Elsevier.
3. Alves, A. C., Vieira, R., Leal-Junior, E., dos Santos, S., Ligeiro, A. P., Albertini, R., Junior, J., & de Carvalho, P. (2013). Effect of low-level laser therapy on the expression of inflammatory mediators and on neutrophils and macrophages in acute joint inflammation. Arthritis research & therapy, 15(5), R116. https://doi.org/10.1186/ar4296
4. Apelqvist, J., Bakker, K., van Houtum, W. H., Nabuurs-Franssen, M. H., & Schaper, N. C. (2000). International consensus and practical guidelines on the management and the prevention of the diabetic foot. International Working Group on the Diabetic Foot. Diabetes/metabolism research and reviews, 16 Suppl 1, S84–

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

S92. https://doi.org/10.1002/1520-7560(200009/10)16:1+<::aid-dmrr113>3.0.co;2-s

5. Botas Velasco, M., Cervell Rodríguez, D., Rodríguez Montalbán, A. I., Vicente Jiménez, S., & Fernández de Valderrama Martínez, I. (2017). Actualización en el diagnóstico, tratamiento y prevención de la neuropatía diabética periférica. Angiología, 69(3), 174–181. https://doi.org/10.1016/j.angio.2016.06.005
6. Cameron MH. (2009). Agentes físicos en rehabilitación. De la investigación a la práctica. 3.ª ed. Barcelona: Elsevier. pp. 346-69.
7. Carvalho, AFM., Coelho, NPMF., Rebêlo, VCN., Castro, JG., Sousa, PRG., et al. (2016). Lowlevel laser therapy and Calendula officinalis in repairing diabetic foot ulcers. Revista da escola de enfermagem USP. Vol. 50, nº4, p. 628-634. DOI: http://dx.doi.org/10.1590/S0080-623420160000500013.
8. Castro-Sande, Noelia, Arantón-Areosa, Luis, & Rumbo-Prieto, JM. (2020). La terapia láser como tratamiento de elección en la onicomicosis del pie diabético. Revisión de alcance. Enfermería dermatológica, 14(40), e01–e10. https://doi.org/10.5281/zenodo.4032365
9. CENETEC. (2017). Diagnóstico y tratamiento de la neuropatía diabética en adultos. Guía de Práctica Clínica: Guía de Evidencias y Recomendaciones. Cenetec. Retrieved November 15 2021, from: http://www.cenetec. salud.gob.mx/contenidos/gpc/catalogoMaestroGPC.html.
10. Ceylan, Y., Hizmetli, S., & Siliğ, Y. (2004). The effects of infrared laser and medical treatments on pain and serotonin degradation products in patients with myofascial pain syndrome. A controlled trial. Rheumatology International, 24(5), 260–263. https://doi.org/10.1007/s00296-003-0348-6
11. Cisneros, N., Ascencio, IJ., Libreros, VN., Rodríguez, H., Campos, Á., Dávila, J., Kumate, J., Borja, VH. (2016). Índice de amputaciones de extremidades inferiores en pacientes con diabetes. Rev Med Inst Mex Seg Soc; 54(4):472-9.
12. Couselo, I., & Rumbo, J.M.. (2018). Riesgo de pie diabético y déficit de autocuidados en pacientes con Diabetes Mellitus Tipo 2. Enfermería universitaria, 15(1), 17 29. https://dx.doi.org/10.22201/eneo.23958421e.2018.1.62902.
13. Del Pozo, J., & Vieira V. (2016). Láser y cicatrices. Revista de la sociedad española de heridas. Retrieved August 22 2020, from:

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

https://heridasycicatrizacion.es/images/site/archivo/2016/Revista_SEHER_8_SEPTIEMBRE_2016_12_Septiembre.pdf

14. De la Cruz., Del Olmos, DQ., Quiñones, M., Zulueta, Á. (2011). Comportamiento de las úlceras venosas de los miembros inferiores tratadas con láser de baja potencia. Rev Cubana Angiol y Cir Vasc. Retrieved February 02 2021, from: http://bvs.sld.cu/revistas/ang/vol13_1_12/ang03112.htm.
15. Gæde, P., Oellgaard, J., Carstensen, B., Rossing, P., Lund-Andersen, H., Parving, H., Pedersen, O. (2016). Years of life gained by multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: 21 years follow-up on the Steno-2 randomised trial. Diabetología DOI: 59:2298-2307.
16. Gebala-Prajsnar, K., Stanek, A., Pasek, J., Prajsnar, G., Berszakiewicz, A., Sieron, A., & Cholewka, A. (2016). Selected physical medicine interventions in the trearment of diabetic foot syndrome. Acta Angiologica. DOI: 10.5603/aa.2015.0024.
17. Greaves, N. S., Iqbal, S. A., Baguneid, M., & Bayat, A. (2013). The role of skin substitutes in the management of chronic cutaneous wounds. Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society, 21(2), 194–210. https://doi.org/10.1111/wrr.12029
18. González, H., Berenguer, M., Mosquera, A., Quintana, M., Sarabia, R., & Verdú, J. (2018). Diabetic foot Classifications II. The problem remains. Gerokomos. 29(4):197-209
19. Hernández, E., Khomchenko, V., Sola, A., Pikirenia, I.I., Alcolea, J.M., & Trelles, M.A.. (2015). Tratamiento de las úlceras crónicas de las piernas con láser de Er: YAG y tecnología RecoSMA. Cirugía Plástica Ibero-Latinoamericana, 41(3), 271-282. https://dx.doi.org/10.4321/S0376-78922015000300007
20. Huang, J., Chen, J., Xiong, S., Huang, J., & Liu, Z. (2021). The effect of low-level laser therapy on diabetic foot ulcers: A meta-analysis of randomised controlled trials. International Wound Journal, 18(6), 763–776. https://doi.org/10.1111/iwj.13577
21. Instituto Nacional de Salud Pública. (2016). Encuesta Nacional de Salud y Nutrición de Medio Camino. Informe final de resultados. Salud Pública México. Retrieved September 12, 2021, from: https://www.gob.mx/cms/uploads/attachment/file/209093/ENSANUT.pdf
22. Khamseh, M. E., Kazemikho, N., Aghili, R., Forough, B., Lajevardi, M., Hashem Dabaghian, F., Goushegir, A., & Malek, M. (2011).

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

Diabetic distal symmetric polyneuropathy: effect of low-intensity laser therapy. Lasers in medical science, 26(6), 831–835. https://doi.org/10.1007/s10103-011-0977-z

23. Kierszenbaum. (2016). Sistema tegumentario – Histología y biología celular. 4th ed., pp. 353–386.
24. Lázaro, J., Tardáguila, A., y García, J. (2017). Actualización diagnóstica y terapéutica en el pie diabético complicado con osteomielitis. Madrid, España. JEndocrinología, Diabetes y Nutrición (2017) 64(2) 100-108
25. Lavery, L. A., Armstrong, D. G., & Harkless, L. B. (1996). Classification of diabetic foot wounds. The Journal of foot and ankle surgery : official publication of the American College of Foot and Ankle Surgeons, 35(6), 528–531. https://doi.org/10.1016/s1067-2516(96)80125-6
26. López, G. (2009). Diabetes Mellitus: clasificación, fisiopatología y diagnóstico. Medwave. https://doi.org/10.5867/medwave.2009.12.4315
27. Mansilha, A. (2017). Tratamiento y gestión del pie diabético. Angiología, 69(1), 1–3. https://doi.org/10.1016/j.angio.2016.08.012
28. Mansilha, A., & Brandão, D. (2013). Guidelines for treatment of patients with diabetes and infected ulcers. The Journal of cardiovascular surgery, 54(1 Suppl 1), 193–200.
29. Mathur, R. K., Sahu, K., Saraf, S., Patheja, P., Khan, F., & Gupta, P. K. (2017). Low-level laser therapy as an adjunct to conventional therapy in the treatment of diabetic foot ulcers. Lasers in Medical Science, 32(2), 275–282. https://doi.org/10.1007/s10103-016-2109-2.
30. Edmonds, M., Lázaro-Martínez, J. L., Alfayate-García, J. M., Martini, J., Petit, J. M., Rayman, G., Lobmann, R., Uccioli, L., Sauvadet, A., Bohbot, S., Kerihuel, J. C., & Piaggesi, A. (2018). Sucrose octasulfate dressing versus control dressing in patients with neuroischaemic diabetic foot ulcers (Explorer): an international, multicentre, double-blind, randomised, controlled trial. The lancet. Diabetes & endocrinology, 6(3), 186–196. https://doi.org/10.1016/S2213-8587(17)30438-2
31. Narayan K. M. (2016). Type 2 Diabetes: Why We Are Winning the Battle but Losing the War? 2015 Kelly West Award Lecture. Diabetes care, 39(5), 653–663. https://doi.org/10.2337/dc16-0205
32. Nascimento, R., Ferreira, V., Bittencourt, M., et al. (2018). Terapia con láser en la curación de úlceras por presión en pacientes de ICU de baja intensidad, de Núcleo do conhecimiento. Retrieved January 06

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

2021, from: https://www.nucleodoconhecimento.com.br/salud/terapia-con-laser-de-com#4-Metodologia.

33. Organización Panamericana de la Salud/Organización Mundial de la Salud. (1996). Reunión del Consejo Directivo OPS/OMS. Washington, D.C. 39ª edición. Retrieved January 13, 2021, from: https://www3.paho.org/hq/index.php?option=com_content&view=article&id=15326:57th-directing-council&Itemid=40507&lang=es
34. Pan American Health Organization/World Health Organization. (1902-1997). Protecting Americas health. Diabetes cases in the Americas expected to jump from 30 million to 45 million.Washington, DC.: PAHO/WHO. Retrieved March 08 2020, from: https://www3.paho.org/hq/index.php?option=com_content&view=article&id=7460:2012-diabetes-shows-upward-trend-americas&Itemid=4327&lang=en
35. Pereira C., N., Suh, H. P., & Hong, J. P. (JP). (2018). Úlceras del pie diabético: importancia del manejo multidisciplinario y salvataje microquirúrgico de la extremidad. Revista Chilena de Cirugía, 70(6), 535–543. https://doi.org/10.4067/s0718-40262018000600535
36. Pérez, V., Peñaranda, M., & Torres, J.. (2017). Láser de baja potencia en la cicatrización de heridas. Junio 22, 2021, Mediciego.
37. Ramos, D., & Sánchez, L. (2017). Efectos del láser terapéutico en cicatrices hipertróficas o queloides en pacientes con secuelas de quemaduras en extremidades superiores e inferiores que acuden a la fundación Ecuaquem, período octubre 2016 a febrero 2017, de Universidad Católica de Santiago de Guayaquil. Retrieved June 02 2021, from: http://repositorio.ucsg.edu.ec/handle/3317/7625
38. Rojas-Martínez, R., Basto-Abreu, A., Aguilar-Salinas, C. A., Zárate-Rojas, E., Villalpando, S., & Barrientos-Gutiérrez, T. (2018). Prevalencia de diabetes por diagnóstico médico previo en México. Salud Pública de México, 60(3, may-jun), 224. https://doi.org/10.21149/8566
39. Cristina Sandoval Ortíz, M., Herrera Villabona, E., Marina Camargo Lemos, D., & Castellanos, R. (n.d.). Effects of low level laser therapy and high voltage stimulation on diabetic wound healing Efectos del láser de baja potencia y alto voltaje sobre la cicatrización de úlceras diabéticas (Vol. 46, Issue 2).
40. Townsend, CM., Beuchamp, RD., Evers, BM., & Mattox, KL. (2016). Cicatrización de las heridas – Sabiston. Tratado de cirugía – ClinicalKey Student. Elsevier.

 ISSN: 1857-7881 (Print) e - ISSN 1857-7431

41. Wang, L., Hu, L., Grygorczyk, R., Shen, X., & Schwarz, W. (2015). Modulation of Extracellular ATP Content of Mast Cells and DRG Neurons by Irradiation: Studies on Underlying Mechanism of Low-Level-Laser Therapy. Mediators of Inflammation, 2015, 1–9. https://doi.org/10.1155/2015/630361