

Antinociceptive action of Light Emitting Diode in an experimental model with hyperalgesia by capsaicin

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OBJECTIVE: To assess the antinociceptive effect of a light emitting diode (LED) in the acute phase of pain induced by capsaicin.

METHOD: Twelve Wistar rats were used, divided into a control and an experimental group. The pain process was induced in both groups by applying 50 microliters of a 2% capsaicin solution in the plantar region of the right hind limb. In the experimental group, a single application of LED 627 nm (70 mw, 7 Joules/cm² dose) was also applied. Nociception was assessed 30 minutes and 24 hours after LED application using a digital analgesymeter (Von Frey).

RESULTS: Twenty four hours after irradiation, an increase in the nociceptive threshold was observed in the LED group in comparison to the 30 min level, as well as in the inter-group comparison.

CONCLUSIONS: The use of LED can be considered as a non-invasive analgesic method as it increases of the nociceptive threshold 24 hours after pain is induced.

KEYWORDS: Light Emitting Diode; nociception; pain measurement.

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INTRODUCTION

Pain can be described as a disagreeable sensory or emotional experience associated with real or potential tissue damage. This concept, which was established by the International Association for the Study of Pain (IASP), is currently used for animals submitted to nociceptive or painful stimuli.^{1,2}

The pain process may be associated with environmental stimuli, which sensitize receptors in the skin, organs, blood vessels and skeletal muscle fibers. The modulation of these receptors is performed by chemical or mechanical stimuli. Chemical stimuli include algogenic substances liberated by the injured cells secondary to inflammatory, traumatic and/or ischemic processes. The receptors generate nociceptive impulses that are transferred through peripheral nervous fibers to the laminae of the spinal cord, where they are processed and follow afferent pathways from the thalamus to the cerebral cortex and limbic system.³

It has been suggested that Light Emitting Diodes (LEDs) may be effective in the treatment of various types of pain.⁴ LEDs are semiconductor devices that exhibit great efficiency in the conversion of electrical energy into optical energy, while generating very little thermal energy^{5,6}. When directly

and electrically polarized, they emit a monochromatic and non-consistent light. The emitted visible or ultra-violet light defines the band in which they operate.⁷ Furthermore, LEDs require less energy to emit the desired wavelengths.⁸

The main differences between the light emitted by LEDs and lasers include the absence of coherent radiation, the divergence of the beam and the emission of a wide range of the spectrum (almost 20 nm).⁹ Furthermore, there is also an absence of a resonant cavity in the light emitted by LEDs.¹⁰

LED therapy can generate effects similar to those caused by low-level laser therapy,^{8,11,12} thereby permitting a significant reduction in the cost of treatment when compared to laser therapy. Coherence is not one of the most important physical characteristics of the effects of phototherapy with low-level lasers. This property is lost in the first layers of the biological tissue.¹³

However, the analgesic effect of LEDs has not yet been widely investigated experimentally or clinically.⁴ Due to the scarcity of studies on the analgesic properties of LEDs, the aim of the present study was to assess the acute antinociceptive effect of LED emission.

MATERIALS AND METHODS

Sample

Twelve male *Rattus Norvegicus*, of the Wistar pedigree, were used. They weighed between 200 and 220 grams and

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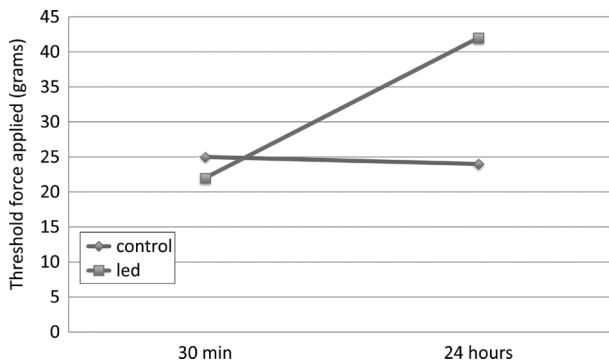


Figure 1 - Analysis of applied pressure to rat paw, between groups 30 min and 24 hours after capsaicin, in controls and LED treated animals.

were provided by the vivarium of the *Universidade Estadual do Centro-Oeste* (UNICENTRO). The animals were housed in acrylic cages in groups of three, with free access to food and water (*ad libitum*) in a light/dark cycle of 12/12 hours. The light cycle started at 7am and finished at 7pm. The temperature in the storage area was a constant 23 ± 1 °C.

Experimental Groups

The 12 animals were randomly allocated to two groups: control (GC), in which hyperalgesia was induced, and the experimental group (LED), in which hyperalgesia was induced and LED 627 nm was applied. Each group contained six animals.

Induction of hyperalgesia

The animals received a single dose of 50µl of capsaicin (Sigma Aldrich) diluted at 2% in dimethyl sulfoxide (DMSO). The dose was applied in the plantar region of the right hind limb.

Application of LED

After the application of capsaicin, a 30-minute period was allowed to pass for the pain process to develop. The animals were then submitted to LED application. The specifications of the LED apparatus used were as follows: 627 nm wavelength; output power of 70 mW and bundle area of approximately 1 cm². The energy density used was 7 J/cm², applied to a single point in the area where the capsaicin had been administered. The equipment was previously calibrated and certified using an Ipm1 laser meter.

Nociceptive Assessment

The nociceptive effect of the LEDs was assessed using the increasing pressure test on the rats' paws and a digital analgesymeter (Von Frey Digital), which consisted of a pressure transducer and a digital counter of force, expressed in grams. The contact between the pressure transducer and the paw of the animal was performed using an adapted disposable tip made of polypropylene (0.5 mm diameter). The animals were placed in wooden boxes, the floor of which was made of non-malleable wire, through which linearly increasing pressure was applied to the sole of the animals' paws until they produced the characteristic flinch response.

The intensity of nociception was quantified by varying the pressure. Once capsaicin and LED had been administered to the experimental group, all of the animals were reassessed after 30 minutes and again 24 hours later.

Statistical Analysis

GraphPad Prism 6.0 software was used for the statistical analysis. The normality and homogeneity of the data were tested first in order to select the most appropriate statistical test. The data were analyzed using the Kruskal-Wallis test, with the significance level set at $p < 0.05$.

RESULTS

In the inter-group assessment performed 30 minutes after the application of capsaicin, no differences in nociception were found between the groups ($p = 0.110$). No analgesic effect of the LEDs was observed at this point in time.

Twenty-four hours after the induction of the pain process, the LED group exhibited an increased threshold in relation to the day before, as well as a greater threshold when compared to the control group ($p < 0.001$).

The control group did not exhibit any differences in the nociceptive threshold in the tests performed 30 minutes and 24 hours after the induction of the pain process ($p = 0.217$).

However, the experimental group exhibited an increased nociceptive threshold 24 hours after the application of LEDs ($p < 0.001$).

DISCUSSION

The results of the present study show that the LED group exhibited an increased pain threshold. This indicates resolution of the pain process and an analgesic influence of the LEDs, because the pressure tolerated 24 hours after their application was greater than that tolerated in the initial assessment. However, the analgesic effects of LEDs are still being compared to the effects of lasers. There are two ways to explain these effects: effects on nerve conduction and on the liberation of endorphins.

In the present study, the analysis of the analgesic effect of LEDs was studied using the same principle as low-level lasers, with a non-coherent light for physiological effects similar to those produced by a coherent light. LEDs have the same properties as lasers. However, they differ in terms of the coherence of radiation, since LEDs produce incoherent light. Their biological effects are similar because they are both absorbed by tissue chromophores.¹⁴

The neuronal system is the basic vehicle of pain. It is believed that irradiation by LEDs affects nervous conduction through biomodulation. Irradiation in clinical densities has an immediate localized effect on the characteristics of the underlying nerve conduction. To be more specific, treatment with LED reduces the speed of nervous conduction and increases the latency of the negative peak, leading to a reduced number of impulses per unit of time and possibly inducing pain relief.⁹ Previous studies have demonstrated that low-level laser therapy decreases the number of peripheral impulses, which is one of the main analgesic mechanisms, thereby contributing to sensitivity and the consequent reduction in pain levels.^{15,16}

A comparison of the effects of a red laser (660 nm) and an infrared laser (830 nm), applied before an injection of formalin (2%) in the plantar section of rats paws, revealed

that only the red laser achieved better results than the control group. Analgesia was observed five minutes after the application of the laser.¹⁷ A random double-blind study assessed the immediate effect of irradiation from a Helium-Neon (HeNe) laser on the distal latency of the peripheral sensory nerve in healthy humans and demonstrated that the HeNe laser increased the distal latency of the sensory nerves. This could be explained by the analgesic effects of the irradiation of the laser. These results suggest that interfering with sensory nervous transmission could be a mechanism to attain the analgesic effects of the irradiation of the HeNe laser; conduction in the sensory nerve continued after irradiation with the laser, although at a slower pace.¹⁸

The present study differed from these two studies^{17,18} in that significant results were only obtained 24 hours after the induction of the pain process. LEDs were shown to be an effective, although not immediate, acute analgesic in the period after their application.

The use of low-level LEDs in cases of dentin hypersensitivity produced a 40% reduction of pain in the first applications, with significant differences in the 4th application. These results suggest that LED's are responsible for stimulating the release of β -endorphins and that the effect obtained by LED therapy is similar to that obtained with lasers.¹⁹ Laser therapy promotes an increase in the synthesis and liberation of endorphins, as well as a decrease in the release of nociceptive receptors, such as bradykinin and serotonin, which causes their analgesic effects.²⁰

Due to the scarcity of studies referring to the antinociceptive properties of LEDs, it was difficult to compare the results of the present study to others. For this reason, the results were compared to laser results by analogy. In the present study, the mean response to noxious stimuli increased 24 hours after LED application, when compared to the response after 30 minutes. In other words, the analgesic effect was more significant in the 24-hour period, which corroborates the analgesic effects cited in previous studies.

CONCLUSION

Considering the experimental conditions described, the use of LEDs can be considered as a non-invasive analgesic method since they increase the sensitivity of the nociceptive threshold 24 hours after pain is induced.

RESUMO

OBJETIVO: Avaliar o efeito antinociceptivo de um diodo emissor de luz (LED) na fase aguda da dor induzida por capsaicina.

MÉTODO: Foram utilizados doze ratos Wistar, divididos em grupos controle e experimental. O processo da dor foi induzida em ambos os grupos, aplicando 50 microlitros de uma solução a 2% de capsaicina na região plantar da pata traseira direita. No grupo experimental, uma única aplicação de LED 627 nm (70 mw, 7 Joule/cm²) também foi realizada. A nocicepção foi avaliada 30 minutos e 24 horas após a aplicação de LED através de um analgesímetro digital.

RESULTADOS: Vinte e quatro horas após a irradiação, observou-se um aumento do limiar nociceptivo no grupo de LED, em comparação com o valor observado 30 min após a aplicação bem como na comparação entre os grupos.

CONCLUSÕES: A utilização de LED pode ser considerado como um método analgésico não-invasivo, uma vez que aumenta o limiar nociceptivo de 24 horas após a indução da dor.

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