The effectiveness of low level laser therapy in the treatment of verrucae pedis

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ABSTRACT
A pilot study was conducted to investigate the effectiveness of low level laser therapy (LLLT) in the treatment of verrucae pedis. 24 participants were randomly allocated to either a treatment or placebo group and lesion size was assessed using digital photography. An energy dose of 54 J/cm² was delivered to the infected tissue of 12 participants using a Gallium Aluminium Arsenide (Ga-Al-As) laser (wavelength 915nm) followed by application of a Multi Scan™ system. A placebo was given to the remaining 12 participants. Participants presented several times per week for an average of ten treatments. No significant difference was seen between treatment and placebo groups (p>.05). Results of this study suggest that LLLT at these parameters is ineffective in the treatment of verrucae pedis. However, the results of this study should be considered in light of the low sample size.

INTRODUCTION
For centuries humankind has been plagued with verrucae. In response, a multitude of remedies to banish the lesions have evolved. One of the earliest descriptions of verrucae was made in 25AD by Celcius. He described the appearance of plantar warts as “myrmecia”, meaning anthill. Of the numerous treatments available, the lack of one truly effective treatment emphasises the perplexing nature of the lesions. Common treatments include cryotherapy, keratolytics and electrosurgery. Although utilising different modes of action, these treatments may have undesirable side effects such as pain, scarring, infection and damage to surrounding, healthy tissue. Ineffectiveness is also of concern as the eradication rates between and within each of the treatments are highly variable. For example, success rates of keratolytics are reported to range from 32% to 99%. Most treatments also fail to target satellite viral particles, this can lead to recurrence of the lesions. The host’s systemic status; the type, size and location of lesions; patient compliance; administration technique; age of subjects and practitioner experience can contribute to a variable outcome. Overall, the treatment of verrucae can be a frustrating experience for both the practitioner and patient, highlighting the need to consider alternative options. It has been suggested that low level laser therapy (LLLT) may be useful in the treatment of verrucae. The proposed mechanism for this is through stimulating an immune response without causing tissue damage. It also has a low side effect profile. Consequently, further investigation of LLLT as a modality capable of eradicating verrucae is warranted. To date, research devoted to the use of low-level laser (LLL) in this area is scarce and inconclusive.

Laser is an acronym for Light Amplification by Stimulated Emission of Radiation. This unique form of light lacks divergence, is coherent and monochromatic. Laser produces a photochemical, rather than a photothermal reaction, as it only increases the temperature of the tissue irradiated by 0.5 to 0.7°C. This reaction is claimed to be beneficial in the treatment of a large variety of disorders. For example, the recommended use of LLLT ranges from ligament and tendon injuries, peripheral nerve regeneration, bone healing, nerve conduction therapy, pain relief, acupconeture, edema reduction, scar tissue reduction, immunosuppression, immunostimulation and acceleration of the wound healing process.

In the minimal research devoted to LLLT in the management of verrucae pedis, Morton compared the effects of LLLT and cell-mediated immunity in the treatment of this condition. Ten subjects assigned to the LLLT group received weekly treatments involving application of the 660nm probe
that delivered a total dose of 18 joules (J) per lesion. The second probe was then applied, emitting a wavelength of 311nm and delivering 1564J per lesion. Lesions in the colloid-mediated group were debrided with a sterile scalpel blade until capillary bleeding occurred. 70% (n=7, N=10) of the lesions in this group resolved compared with 30% (n=3, N=10) of the subjects allocated to the LLLT group. The mean time for lesion resolution was 3.1 and 5.6 weeks respectively. In this study, scalpel debridement was found to be more effective than LLLT in the eradication of verrucae pedis.

In light of insufficient research, evidence of the effectiveness of LLLT in the treatment of verrucae pedis is unavailable. Therefore, the aim of this study was to further investigate the effectiveness of LLLT in the treatment of this disorder.

METHODS

Following approval from the La Trobe University Faculty of Health Sciences Human Ethics Committee, the study was advertised within the university and at surrounding locations. Prior to commencement of the study, respondents were required to satisfy a number of inclusion criteria: their verrucae must have been present for at least six months; no treatment other than the LLLT was undertaken within the last six months; and the participants agreed to refrain from using other treatments during the study. These criteria minimised the possibility of previous treatments interfering with the verrucae and removed the potential for treatments other than the LLLT to alter the verrucae. A number of respondents were excluded from the study on the basis of time constraints, recent treatment of lesions and an incorrect diagnosis by the respondent. Twenty-four participants satisfying the inclusion criteria were recruited (refer to Figure 1).

During the initial consultation, lesions were assessed against specific diagnostic criteria of verrucae. This included: the absence of normal dermatoglyphics; the presence of a firm palpable hyperkeratotic mass; a circumscribed lesion with a definitive border; thrombosed capillaries; and the potential for lateral pressure to elicit a painful response. A consent form was completed, and using a data sheet, the researcher obtained information regarding the participants' health status and verrucae history. Participants were informed that they would be randomly allocated to either a treatment or control group. Using a random digit table, participants were randomly allocated to either the treatment or control group. Twelve participants were allocated to the treatment group and twelve to the control group.

All lesions in both groups were swabbed with a 70% chlorhexidine solution and underwent mechanical debridement in order to remove surrounding and overlying hyperkeratosis and the outer layers of the infected verrucous tissue. While the amount of tissue debrided varied between participants, it enhanced lesion margin identification and aimed to increase the depth of penetration of the laser light into the verrucous tissue. Following debridement, the area was again swabbed in order to remove any surface lipids, sebum and debris that may cause reflection or attenuation when the laser was placed in contact with the tissue.

In most cases, bleeding was avoided but where it occurred, pressure was applied to the area and following laser treatment, Mefix<sup>TM</sup> was applied. In two instances where pressure alone failed to induce haemostasis, ferric chloride (13%) was also applied.

Following debridement, feet were draped and a ruler was placed adjacent to the lesion, providing a scale for measurement. Acetone tracings and digital photographs were taken of each lesion. The soft-wear package, NIH<sup>TM</sup> Image, was then used to determine the surface area of the lesion. Since the primary researcher measured all lesions it was necessary to determine the intra-tester reliability of these measurements prior to data analysis. Thus, repeated measurements of two different lesions were taken at different times and compared. The intraclass (ICC) correlation coefficient type (2,1) was then calculated.

Three of the digital photographs were unclear and could not be used. In these instances, the acetone tracings were used instead of digital photographs. To determine surface area of the lesions, the tracings were also analysed using NIH<sup>TM</sup> Image. In order to determine the accuracy of this method, lesions depicted by clear photographs were measured and then compared with the measurement obtained from the acetone tracings.

Laser Application

All participants were blinded regarding group allocation. Each participant, regardless of group allocation, and the researcher were required to wear protective goggles during treatment. These goggles protected the retina from damage. Participants attended for a minimum of nine treatments, conducted two to three times per week. Those in the treatment group received laser therapy as specified by the Australian Institute of Laser Therapy (AILT<sup>TM</sup>). This consisted of application of the Pulsar Puls<sup>TM</sup> 915nm probe followed by the Multi Scan<sup>TM</sup> probe. Clear film was placed over each probe to prevent cross-contamination. The probe was held perpendicular and in contact with the skin to deliver the required amount of energy. In the presence of large or multiple verrucae, the probe did not completely cover the lesion and consequently, the process was repeated in a systematic manner, until the required energy dose was delivered to tissue. One researcher administered all the treatments: a similar amount of force was applied to the...
probe during each application. The amount of force could not be standardised but was sufficient to maintain contact between the probe and the skin without obstructing blood flow or causing discomfort to the participant.

The Pulsar Plus™ probe was initially applied followed by the Multi Scan™. The Pulsar Plus™ 915nm probe consisted of a class 3B Gallium Aluminium Arsenide laser diode with a modulated average power output of 100mW and peak power of 1W. This was placed in contact with the skin for 60 seconds and delivered 45J/cm². The Multi Scan™ laser delivery system enabled simultaneous application of different wavelengths of light to the specified area. This was placed in contact with the skin for 120 seconds and delivered 6J/cm². A total energy dose of 54 J/cm² was applied to the tissue. In the control group, the switch directing the laser energy to each probe was placed in a position ensuring that no energy was delivered to the verrucae.

RESULTS

Participant demographics
A range of descriptive statistics including means and standard deviations were used to describe subject demographics and t-tests were employed to analyse group differences on these variables.

Initial assessments revealed participants had used a wide variety of treatments prior to the study. Treatments such as commercial preparations, cryotherapy, electrocautery, salicylic acid and systemic medications had been utilised. The most common past treatment was cryotherapy, with 50% (n=8, N=16) of participants reporting previous experience with this modality. While 12.5% had undertaken multiple therapies, another 33% (n=8, N=24) of participants had not had their verrucae treated.

Table 1 comprises the descriptive statistics of participant demographics. The number of verrucae in the treatment group was significantly greater than the control group, t(22)= -2.840, p<0.05. Prior to analysis, the data was screened and an outlier regarding the duration that the verrucae had been present for was identified and removed. This involved a participant allocated to the control group in which the lesions had been present for 180 months. This improved the distribution of the data obtained and verified the assumptions of normality.

Table 1: Demographic data for the treatment and control groups (p>0.05).

<table>
<thead>
<tr>
<th></th>
<th>TREATMENT (n=12)</th>
<th>CONTROL (n=12)</th>
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<tbody>
<tr>
<td>Participant age (years)</td>
<td>Mean = 21, SD = 16</td>
<td>Mean = 34, SD = 18</td>
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<tr>
<td>Number of pedal verrucae</td>
<td>Mean = 4.9, SD = 3.9</td>
<td>Mean = 1.6, SD = 1.1</td>
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<tr>
<td>Duration of verrucae (months)</td>
<td>Mean = 26, SD = 16</td>
<td>Mean = 36, SD = 46</td>
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The mean age of participants in the treatment group was significantly lower than the control group, but this variation was again not statistically significant t(22)= 1.798, p>0.05.

Reliability of measurements
An ICC of 0.98 (2,1) indicated a high intra-tester reliability regarding the repeatability of measurements taken from the digital photographs. Of those measurements taken from acetone tracings, an ICC of 0.71 (2,1) was obtained. Both measurements demonstrated high reliability allowing their use in this study.

Study findings
A two-way mixed ANOVA was used to evaluate the data obtained. The results of this analysis suggest that there was no statistically significant difference between the size of the lesions allocated to the treatment and control groups.

Figure 2 comprises the mean lesion sizes (mm²) of the two groups measured at the initial and final treatments and demonstrates a statistically significant decrease in size of the lesions over the course of the study.

A two-way ANOVA found that both groups had a significantly larger surface area at the initial assessment (mean= 2.36, SE= 0.490) than at the final assessment (mean= 1.40, SE= 0.33). F(1,18)=4.893, p<0.05, 1-2 = 0.214. However, the main effect of treatment was not statistically significant, F(1,18) = 0.58, p>0.05, 1-2 = 0.03. The surface area of the two groups did not differ with respect to each other over the course of the study.

Figure 2: Mean verrucae pedis legion size, initial versus final measurements for the treatment and control group.
The results of this study suggest that LLLT is ineffective in the treatment of verrucae pedis. A number of factors may have influenced study outcomes. One factor is parameter choice: different wavelengths have been found to have varying depths of penetration and can also affect cellular processes in different ways. As laser light within a therapeutic wavelength penetrates to differing depths, it is difficult to explain any real physiological effect it could have on the cells of the immune system. The thickness of the skin on the plantar aspect of the foot is also another factor that could influence study results. Most of the lesions in the study were located plantarly where the epidermis is thicker than other areas of the body. Consequently, more light may be absorbed into this structure, reducing the amount that is able to act on the targeted T and B lymphocytes. Although some in vivo work has suggested a generalised enhancing effect of LLLT on the immune system of oncology patients, a number of factors differed when compared to this study. Lymph nodes were directly treated with LLLT and tumours were irradiated prior to removal. In contrast to this study, the thick epidermis was avoided as laser was applied directly to the targeted structures.

As LLLT is non-invasive, the basement membrane remains intact. This may effectively hide the virus from the T and B cells of the immune system and consequently, even if these cells are activated by LLLT, they would be unable to reach the infected keratinocytes. The type of verrucae present in the study may have influenced the results gained. A large proportion of lesions in this study were described as ‘recalcitrant’ or resistant to treatment. Although the term recalcitrant varies between centres, 67% (n=16, N=24) of participants in this study had received previous treatment for verrucae. However, it is important that the effectiveness of any modality in the treatment of recalcitrant verrucae is determined because they would be unable to reach the infected keratinocytes. If more light may be absorbed into this structure, reducing the amount that is able to act on the targeted structures.

Lastly, the results of this study should be viewed with consideration of the small sample size. A power analysis was not conducted prior to recruitment and consequently the results may be reflective of a lack of statistical power. Future studies in this area may benefit from larger sample sizes that would allow for grouping of different lesions and/or assessment of multiple parameters.

CONCLUSION

New and potentially superior treatment modalities are always of interest. If laser is to gain wide acceptance, the exact mode of action of LLLT must be established. Future studies aimed at refining the parameters required to induce optimal immunostimulation and the effect of an intact basement membrane are imperative. While these fundamental issues remain unresolved, LLLT will continue to struggle to gain acceptance both within the clinical and scientific fields.

REFERENCES