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Review

The light revival: Does phototherapy promote wound healing? A review

A.L. Whinfield*, I. Aitkenhead

Department of General Practice and Primary Care, Kings College London School of Medicine, 5 Lambeth Walk, London SE11 6SP, UK

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ABSTRACT

Background: Throughout history, light has been recognised as a potential source of healing. The introduction of lasers made it possible to modify and control light for optimum therapeutic use.
Aim: This paper reviews recent clinical trials that test phototherapy on human models in order to assess the value of phototherapy in routine wound care.
Method: A literature search was undertaken using a variety of sources including online databases.
Results: The results of numerous in vitro and animal investigations suggest that phototherapy may stimulate cell activity and promote tissue repair. Reports of human clinical trials are relatively few. There is inconsistency of selected treatment parameters amongst studies testing the effect of phototherapy on wound healing. Clinical trials using human models do not provide sufficient evidence to establish the usefulness of phototherapy as an effective tool in wound care regimes.
Conclusion: Further well designed research trials are required to determine the true value of phototherapy in routine wound care.

Contents

1. Introduction

Interest in the clinical application of phototherapy (the therapeutic use of light) has increased in recent years [1–3]. The idea that light may be used medicinally is not new, however, as it has been recognised as a potential source of healing throughout history. Ancient Egyptians and Greeks believed the sun could strengthen and heal the body [3,4]. In the middle ages, sunlight was also considered to be an ally in the battle against virulent diseases such as the plague [4].

It was not until the 1960s that attempts to harness the power of light led to the development of the laser, and in 1960 Dr. Maiman published the first account of laser radiation [5]. Since that time, lasers have been developed to modify and control the production of light for optimum therapeutic use, and these devices found rapid application in medicine and surgery.

During the 1960s and 1970s, lasers were regarded as destructive, and those lasers using photothermal and ablative properties are used routinely to cut and destroy tissue. This is known as laser *surgery*. The therapeutic properties of relatively low intensity, athermic laser irradiation were then recognised. This is referred to as laser *therapy*. This application of lasers in medicine was explored by Dr. Mester, a Professor of Surgery in Budapest. His discoveries laid the foundation for further research, much of

* Corresponding author. Tel.: +44 1653 618525/7876 453462 (Mobile).
E-mail address: annewhin@googlemail.com (A.L. Whinfield).

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which was carried out in Hungary and Russia in the mid-1960s [6–8].

LASER is an acronym for Light Amplification by the Stimulated Emission of Radiation.

Early lasers were based on the use of inert gases, such as Helium Neon (HeNe) and argon. In his original laser prototype, Maiman used a ruby crystal as a lasing medium [5]. Lasers with semiconductor diodes were later introduced including Gallium Arsenide (GaAs), and Gallium Aluminium Arsenide (GaAlAs). Today, whilst HeNe devices are still used, the majority of work is done with GaAs and GaAlAs diodes, with wavelengths between 820 and 904 nm (nanometres). Dosages of 1–4 J/cm^2 (joules per square centimetre) were established by early investigators, and these have remained the most frequently used radiant exposures delivered to treatment sites.

There is wide variation amongst users however, of other treatment parameters, such as pulse rate, wavelength, mode of application (contact/non-contact) number and length of treatments. Laser light is coherent (all wavelengths are produced in phase), monochromatic (of single colour or wavelength) and collimated (produces a close parallel beam). Monochromaticity is considered pertinent to the use of light as a therapy as it has been shown that the effects present with narrow band light are absent when broad spectrum light is used [4]. Light emitting diodes (LEDs) were originally developed by the National Aeronautics and Space Administration (NASA) to grow plants in space, but were found to also have therapeutic effects [9]. Whilst lasers emit coherent, narrow line width light, LEDs emit non-coherent light with broader line width. The role coherence may play in effects on wound healing is not yet clear.

An array of different terms evolved to establish the idea of using light for a therapeutic effect, some of these being phototherapy, low level laser therapy (LLLT), low power laser therapy (LPLT), low intensity laser therapy (LILT), cold laser, therapeutic laser, light emitting diode, low reactive level laser, and diode laser [10].

Much confusion has arisen from describing the same treatment in so many different ways. As today's therapeutic light source may also include superluminous diode (SLD), or polarised light (PL), as well as the semiconductor or diode lasers, a common term which recognises all these light sources would seem appropriate. To this end, the use of the terms 'phototherapy' or 'light therapy' has been recommended [10].

Wound healing is a complex series of reactions and interactions which requires the performance of a well-orchestrated process of biological and molecular events [26,27]. Injuries that do not have an underlying pathophysiological defect will proceed through a complex linear progression of biological events, which include inflammation, proliferation and remodelling [26].

Chronic wounds, however, and those with pre-existing pathophysiological abnormalities (such as diabetic ulcers) do not proceed in this way, and there may be marked modulation of the healing process [27]. Ulcers are the most frequent and characteristic type of skin lesion and may be defined as any break in the cutaneous barrier [28]. A wound that is not continuously progressing towards healing may be described as chronic [28]. A chronic ulcer that remains unhealed after 4 weeks is a cause for concern, as it is associated with poor outcomes such as amputation [28,29]. Non-healing ulcers act as a portal of entry for systemic infection. Diabetic foot ulcers, in particular, are associated with substantial costs, and are the single biggest risk factor for non-traumatic foot amputation [30]. This complication of diabetes is a known source of morbidity and mortality [30]. Finding successful treatments for chronic wounds such as diabetic foot ulcers is clearly of great importance.

In practice, ulcer management depends on the clinicians and resources available. It is recommended that primary consideration is given to prevention and correction of systemic problems which exacerbate the condition [31]. Standard treatment regimens include debridement, infection control, offloading, and appropriate dressings [31,32].

Phototherapy is one among a range of alternative treatment options (including biological therapies, hyperbaric oxygen, negative pressure therapy (VAC), and reconstructive treatments) which may enhance wound healing [28].

Although the usefulness of phototherapy in wound healing is still controversial, it has become a popular treatment modality in many clinics [25]. As this therapy has few contraindications and no reported side effects, it could be considered as a potentially useful treatment option if shown to be effective. There appear to be many anecdotal claims that phototherapy stimulates wound healing but the question arises as to whether sufficient scientific evidence exists to justify its routine use in wound care.

2. Aim

The intention of this review is to analyse and evaluate recent investigations which measure the effect of phototherapy on wound healing in humans. These are discussed in the light of results from laboratory and animal experiments. We consider whether these studies provide sufficient evidence to justify the use of phototherapy in chronic wound care.

3. Method

Literature was sought and obtained from library and government sources, online databases, journals, and papers cited in articles from these sources, and a trial carried out within Lambeth PCT. Online database sources include ASSIA, AMED, Bandolier, BIOSIS, Cochrane Library, CINAHL, Embase, and MEDLINE. Primary databases were sourced from 1950 to date.

To determine recent activity a detailed review is presented utilising human studies reported within the last 10 years in which phototherapy is the primary treatment. Case histories, studies with fewer than 6 subjects, and non-English language papers are excluded.

Search terms: diabetes, diabetic, foot, leg, ulcer, wound, low level laser, low-intensity laser, phototherapy, photo-stimulation, diode laser, light emitting diode, soft laser, biostimulation, and light therapy.

4. Results

The literature search yielded many hundreds of publications for phototherapy and wound healing. The majority of experimental studies were carried out in the laboratory, or were performed using animal models.

4.1. Laboratory reports

Early work by researchers in Hungary and Russia found that low level lasers produced a stimulatory effect, a phenomenon which became known as biostimulation [33]. Much of the work by Mester and other researchers focused on the effect of low level laser on those cells involved in wound healing [11–17,33–35]. As the fibroblast cell plays a crucial role in wound healing, many consequent and later studies have focused on fibroblast growth and locomotion [35–42]. Other findings from in vitro studies support the idea that phototherapy enhances the wound healing process and the immune response. Increased cell proliferation, cell activation, cell division, cell maturation, release of interleukins, mast cell degranulation, collagen synthesis, secretion of growth factors, DNA synthesis, ATP production, osteoblast proliferation, and cal-