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Effect of Photobiomodulation on Mesenchymal Stem Cells

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Abstract

Objective: The purpose of this study was to review available literature about the effect of photobiomodulation (PBM) on mesenchymal stem cells (MSCs). ***Background data:*** The effects of coherent and noncoherent light sources such as low-level lasers and light-emitting diodes (LEDs) on cells and tissues, known as PBM, form the basis of photomedicine. This treatment technique effects cell function, proliferation, and migration, and plays an important role in tissue regeneration. Stem cells have been found to be helpful elements in tissue regeneration, and the combination of stem cell therapy and laser therapy appears to positively affect treatment results. ***Materials and methods:*** An electronic search in PubMed was conducted of publications from the previous 12 years. English language articles related to the subject were found using selected key words. The full texts of potentially suitable articles were assessed according to inclusion and exclusion criteria. ***Results:*** After evaluation, 30 articles were deemed relevant according to the inclusion criteria. The energy density of the laser was 0.7–9 J/cm^2. The power used for visible light was 30–110 mW and that used for infrared light was 50–800 mW. Nearly all studies showed that low-level laser therapy had a positive effect on cell proliferation. Similar outcomes were found for LED; however, some studies suggest that the laser alone is not effective, and should be used as an adjunct tool. ***Conclusions:*** PBM has positive effects on MSCs. This review concluded that doses of 0.7–4 J/cm^2 and wavelengths of 600–700 nm are appropriate for light therapy. The results were dependent upon different parameters; therefore, optimization of parameters used in light therapy to obtain favorable results is required to provide more accurate comparison.

Introduction

Human organ tissue can be lost from injury, congenital defect, or disease.[1] Impaired tissue should be replaced by normal healing or by autograft, xenograft, or allograft, depending upon the defect size. Healing can be facilitated using guided tissue engineering approaches. These approaches are useful when the defect size is relatively small, because they persuade cells to migrate from surrounding host tissue to prepared scaffolds. This procedure can be influenced by the availability of a proper cell source, distance required for cell migration from surrounding host tissue (depending upon the size of the defect), cell response to migration, blood supply for cell nutrition, and growth factors.

When there is a large defect or impaired cell supply, cell transplantation, which requires progenitor cell sources, is needed, and cell expansion must provide a sufficient number of cells. Autologous cells from the host can be used; however, there are limitations on donor sites and the extended time required for cell expansion. Allogeneic or xenogeneic cells are not limited in quantity or expansion time; however, an immunological response should be expected, because of the differing genetic content and matching human leukocyte antigens (HLAs).[1–3]

Another method is new tissue engineering. Three requisites can be used to regenerate tissue in this manner. First, a scaffolding is required to support cells seeded *in vitro*. The architecture of the scaffold should be effective for cell response and tissue formation.[4] Second is the use of growth factors (GF) delivered through the scaffold as a drug delivery system to encourage cells for engineering tissues. The third approach is the use of cell sources. Primary cells are used for tissue regeneration. This process focuses on three types of stem cells, depending upon on the cell origin and experimental manipulation: embryonic stem cells (ESC), adult stem cells derived from embryos and adult tissue, and induced pluripotent stem cells (iPSC) derived from adult somatic cells by genetic manipulation. ESC and iPSC are pluripotent stem

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cells that can develop into all type cells, whereas adult stem cells are multipotent cells that can differentiate to specific types of cells.[3,5,6]

Stem cells are immature, unspecialized cells with self-renewal features that provide a cell source for tissue regeneration, or to replace damaged, missing, or impaired tissue or organs.[3,5] Differentiation is a critical cellular stage for these cells that allows them to provide specialized cells to form different tissues or organs. GFs are useful in tissue engineering because they increase stem cell differentiation to other cells. Other factors also affect this procedure, such as cell type, extracellular matrices, and soluble factors (GF).[3]

Mesenchymal stem cells (MSCs) are mesenchymal stromal cells regardless of their tissue origin. They were originally found in bone marrow; however, they can be harvested from other adult tissue.[7] Pittenger et al.[8] revealed that these multipotent stem cells can differentiate into osteogenic, chondrogenic, and adipogenic cell lines.[3] MSCs can be isolated from many pre, peri- and postnatal tissues or organs. Prenatal sources consist of first and second trimester fetal blood, liver, and bone marrow and second trimester spleen, lung, metanephros, dermis, pancreas, and thymus. However, the umbilical cord, umbilical cord blood, amniotic fluid are the major perinatal MSC supply. Many postnatal organs can be sources of MSCs, including the skin, adipose tissue, blood vessels, and dental pulp. [3,9,10]

There are several ways to promote proper cell expansion, such as the use of GFs in culture media,[11] and photobiomodulation (PBM). GFs stimulate and guide stem cells to proliferate and differentiate to proper cell numbers and types. Soon after the first laser was introduced, it was used in medical applications.[12] Photomedicine embraces the study and application of light (coherent or noncoherent) with respect to health and disease.[13–15] It has been used in dermatology (UVA therapy), surgery, interventional radiology, optical diagnostics, cardiology, and oncology (photodynamic therapy). Photobiostimulation therapy promotes cell growth, regeneration, and healing of tissue by means of light sources such as light-emitting diodes (LEDs) and low-level lasers (LLL), or those that emit light in the visible red to near infrared (NIR) range and are known as PBM.[16]

Several basic *in vitro* and *in vivo* studies have discussed the effects of PBM. This effect can be either inhibitory or stimulatory for pain control, as an anti-inflammatory, or for metabolic or immunological effects.[17] PBM affects the activity of endogenous enzyme photoaccepters for initiation of cell signaling pathways. It alters cell and tissue metabolism and cell proliferation. Cytochrome C oxidase enzyme has been identified as one of the major endogenous photoacceptors; however, the mechanism of the therapeutic laser remains unclear[16] with regard to its cellular and molecular effects. It appears to improve tissue engineering in keeping with stem cells.

Different coherent or noncoherent light sources are used for PBM. Although the diode laser is most frequently used for laser therapy, the He-Ne, Argon, Nd:YAG, and Er:YAG lasers have different wavelengths, power requirements, energy densities, and types of exposure, and have been successfully used for cell activation.[18] LEDs offer advantages such as low price, acceptable efficacy, high switching rate, and long life.[19,20] PBM has various biostimulatory effects on wound healing,[21–24] extracellular matrix synthesis,[25] and promotion of cellular proliferation and differentiation in tissues such as bone,[26–29] nerves,[30] and skin.[31–36]

Studies in this area are few and contradictory. The present study reviewed the articles to develop an understanding of the effect of PBM on MSCs to help design more accurate studies in the field of PBM.

Materials and Methods

PubMed and Science Direct electronic databases were searched for articles about the effect of PBM on MSCs. The keywords used were laser therapy, low-level laser [MeSH], phototherapy [MeSH], lasers, semiconductor [MeSH], photochemotherapy [MeSH], LED [MeSH], therapeutic lasers [MeSH], and mesenchymal stem cells [MeSH]. The articles retrieved were limited to the English language and were for the period from 1994 to 2015. Data extraction involved cell origin, laser parameters, and final results. Because photobiostimulation therapy and stem cells are a new domain in the human sciences and much change has been discovered to previous findings, it is logical that the majority of related studies would be found in electronic journals mostly published, after 1994.

The articles selected were characterized as *in vitro* or *in vivo* experimental studies and clinical trials that evaluated the effects of irradiation from LLLs and LEDs on MSCs. The initial selection included a review of articles; those that did not reflect the purpose were excluded. All articles that evaluated all lasers types except from other light sources such as Xenon flash lamps were included. Articles that assessed the phototherapy effect on other stem cell types, such as dental follicle stem cells, were excluded. This article only focuses on the photostimulatory effect on the MSCs. The abstracts of other studies were analyzed. At the end of the selection process, after reading the full texts, articles that matched inclusion criteria were reviewed. Figure 1 shows the process of studies selection.

Results

The initial search uncovered 210 articles. After evaluation of the titles and abstracts, 32 articles were duplicated between databases, 18 and 78 articles were excluded because of unassociated light sources and cell types, respectively. Thirty articles were finally included. The data from the studies describe the parameters of the light sources. Diode lasers were the most commonly used laser type in the reviewed studies, which can

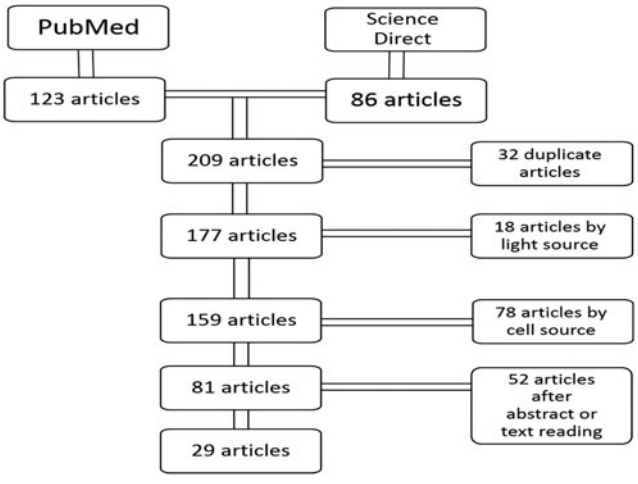

FIG. 1. The process of studies inclusion/exclusion.

be distinguished by specific laser such as GaAs,[37] GaAlAs,[29,38–41] InGaAlP,[42,43] He-Ne,[44,45] and Nd:YAG.[35,46] Laser type was not available in two studies.[47,48] Laser wavelength in both of these was 400–405 nm.

Discussion

Advances in biomedical technology have increased applications for regenerative treatment. PBM of therapeutic light sources such as LEDs or LLLs are some of these technologies. Light energy allows cellular and molecular stimulation of target tissues. The result is regenerative treatment[20,39,49–51] through the effect of chondroblast, neuroblast, and fibroblast proliferation or collagen synthesis and nerve regeneration.

PBM, by visible or NIR light, causes physical or chemical changes in cells. Although some mechanism of laser biostimulation was discovered, it is not exactly known.[47] Different mechanisms have been discussed, such as light absorption by mitochondrial enzymes with localized heating, and photon absorption by electron transport chain enzymes in the mitochondrial respiratory chain by flavins and cytochrome C.[38] Karu et al.[52] suggested that irradiation by LLL intensifies formation of a transmembrane electromechanical proton gradient in mitochondria. One possible mechanism is the absorption of laser energy by intracellular chromospheres, which is converted to metabolic energy. Karu et al. showed that He-Ne energy increased adenosine triphosphate (ATP) levels.

In this review, we found that the visible red light wavelengths were used more than the infrared wavelengths in experimental studies. Some studies compared the red and infrared wavelengths and obtained different results. In most studies, the visible spectrum (600–700 nm) was effective for cellular biostimulation. de Villiers et al.[49] found an increase in cellular viability and proliferation on human adipose-derived MSCs (hADSCs) using a diode laser (Table 1). Mvula et al.[50] reported that proliferation of ADSCs significantly increased after exposure to a diode laser at 636 nm wavelength (5 J/cm^2).

The diode laser was the most predominant light source used. While He-Ne, Er:YAG, and ND:YAG were used as other coherent light sources, LED sources were used as noncoherent light sources (Table 2). Leonida et al.[35] applied Nd:YAG laser to bone marrow MSCs and found that after 7 days of proliferation, the scaffold of the laser-treated group increased significantly over that of the control group. Peng et al.[51] used an LED (620 nm) to irradiate bone marrow MSCs (BMSCs) with and without osteogenic supplements. They found that in the group without osteogenic supplements and under red LED (0, 1, 2, 4 J/cm^2) increased proliferation of cells could be expected. In the group with osteogenic supplements, alkaline phosphatase activity and differentiation increased and proliferation decreased with LED irradiation.

The studies reviewed used laser doses of 0.7–9 J/cm^2. The power used for visible light was 30–110 mW and that used for infrared light was 50–800 mW. One study investigated effect of the Ga-Al-As laser (810 nm) with an energy density of 3 and 6 J/cm^2 for differentiation of BMSCs to neurons and with an energy density of 2 and 4 J/cm^2 for differentiation to osteoblasts.[39] PBM increased proliferation in all doses except for 6 J/cm^2. Cellular differentiation increased at all doses. Soleimani et al.[39] suggested that the effect of low-level laser therapy (LLLT) on proliferation and differentiation is dose dependent.

Other parameters for irradiation, such as the effect of light source and period of irradiation on MSCs, were different in different studies. The minimum time point used was immediately after irradiation and the maximum was 4 weeks after laser treatment. MSCs were often derived from bone marrow, adipose tissue, dental pulp, and periodontal ligaments. In most studies, proliferation and differentiation were assessed, but the evaluation techniques differed. Most studies showed a positive effect for LEDs and lasers on cell proliferation and differentiation.

Farfara et al.[47] evaluated the effect of LLLT on BMSCs in mice with Alzheimer's disease. They concluded that the application of lasers improved maturation of MSCs and increased phagositosis of Aβ protein by elevating the activation state. de Oliveira et al.[38] used a Ga-Al-As laser on human MSCs (hMSCs) and rat MSCs (rMSCs) in a study of nutritional deficiency, to examine the effect of LLLT on adhesion, proliferation, gene expression of vascular endothelial growth factor (VEGF), and type 2 receptor of VEGF (VEGFR2). They reported that low nutritional support significantly decreased proliferation. At lower doses (0 and 7 J/cm^2) proliferation increased and at higher doses (3 and 9 J/cm^2) adhesion increased. They suggested that different specimens and laser doses could cause different results. Kim et al.[45] showed that He-Ne is an effective biostimulator of wound healing using adipose-derived mesenchymal stem cells (ASCs) to stimulate secretion of GF in the wound bed.

The main effect of photobiostimulation therapy in clinical or *in vitro* activity is proliferation. This effect activates the mitochondrial respiratory chain and cell signaling by laser irradiation.[53] Red/NIR LED irradiation leads to heating at the molecular level by ATP production.[54,55] It appears that laser phototherapy inhibits apoptosis, which increases survival of ASCs and produces GFs in the wound bed at the functionally appropriate dose and wavelength.[23,56,57] It is possible for PBM to increase cell response by elevating the mitochondrial membrane potential and ATP and cyclic adenosine monophosphate (cAMP) levels.[56]

Two studies on animal brain tissue found that ATP content increased in response to temperature elevation by red/NIR LED. PBM also increased differentiation of stem cells.[54,55] A few studies investigated cell differentiation caused by laser irradiation. Almost all showed a positive effect for PBM on differentiation; however, some found no significant difference between the irradiated and control groups. One study found that at 647 nm, red light transformed MSCs to osteoblasts[58]; however, Kim et al.[45] found that differentiation of ASCs was not noticeably different between the laser-treated (632 nm) and control groups. Stein et al.[59] found that LLLT (632 nm) promotes proliferation and differentiation of human osteoblast cells. Leonida et al.[35] evaluated the effect of an Nd:YAG laser (1064 nm) on MSCs. After 7 days, significant proliferation was observed in the laser-treated scaffold and, after 14 days, an exponential increase was observed in the laser-irradiated group.

Visible NIR wavelengths were commonly used in the studies. The most effective result was for visible wavelengths (600–700 nm), but some articles reported cell proliferation at 780 nm[60] and 860 nm.[61] Anwer[46] suggested that mitochondrial activity increased at lower wavelengths. There was a large range of wavelengths used that produced a variety of results. It appears that biostimulation is dependent

Table 1. Review of Articles with Coherent Light Beam (Laser) Parameters and Results

	Type of cell	*Laser type*	*Power (mW)*	*Wavelength (nm)*	*Energy density (J/cm^2)*	*Irradiation mode*	*Application regime*	*Result (qualitative)*	*Study*
1	MSCs of mouse with Azheimer's disease (AD)	NA	400	NA	1	NA	6 times at 10 day interval for 2 months	Use of LLLT as a therapeutic application in progressive stages of AD and implying its role in mediating MSC therapy in brain amyloidogenic diseases. In laser-irradiated group increased phagocytosis of Aβ protein	Farfara et al. 2015[47]
2	hMSCs And rMSCs	GaAlAs	30	660	0.75 1.5 3 9	NA	25 sec 50 sec 100 sec 300s	LLLT on human and rat MSCs might upregulate VEGF messenger RNA (mRNA) expression and modulate cell adhesion and proliferation distinctively.	de Oliveira et al. 2015[38]
3	BMSCs and AMSCs of mice	InGaAlP	30	660	0.5 1	Continuous	16 sec 33 sec Irradiation at 0 h, 48 h	Cell proliferation was increased in dose dependent manner. BMSCs responded faster than AMSCs. There was no significant nuclear alteration.	Barboza et al. 2014[42]
4	Canine ASCs	He-Ne	17	632.8	1.083	Continuous	Daily 8 sec from day 0 to 56	LLL accelerated bone formation by ASCs as twice time	Choi et al. 2013[44]
5	Mouse BMSCs	diode laser	890	635	0.326 0.329	continuous	10 sec 26 sec	Cell proliferation was significantly increased by LLL irradiation.	Giannelli et al. 2013[67]
6	BMSCs	Nd:YAG	1.5 W 2.25 W	1064	2.52 3.81	Pulsed	3 cycles 30 sec	Proliferation was significantly increased in scaffolds treated with laser after 7 days. LLLI might lead to a reduction in healing times and risks of failure.	Leonida et al. 2013[35]
7	ADSCs	Nd:YAG	30	532	5, 6.8, 9.2, 28, 45	NA	30, 45, 60, 180, 300 sec	At longer exposures there was significant decrease in proliferation and autofluorescence. Strong correlation was observed between proliferation rates of cells and autofluorescence intensity.	Anwer et al. 2012[46]
8	Canine ASCs	He–Ne	17	632.8	0, 1, 3 *in vitro* 1.2 *in vivo*	NA	20 sec daily for 20 days	LLLT is an effective biostimulator of ASCs in wound healing that enhances the survival of ASCs and stimulates the secretion of growth factors in the wound bed.	Kim et al. 2012[45]

(*continued*)

TABLE 1. (CONTINUED)

	Type of cell	Laser type	Power (mW)	Wavelength (nm)	Energy density (J/cm^2)	Irradiation mode	Application regime	Result (qualitative)	Study
9	Human BMSCs	GaAlAs diode laser	50	810	2, 3, 4, 6	Continuous	12 sec (2 J/cm^2) 18 sec (3 J/cm^2) 24 sec (4 J/cm^2) 36 sec (6 J/cm^2) At day 1, 3, 5	LLLI enhances BMSCs differentiation into neurons and osteoblasts, and at the same time increases BMSCs proliferation (except for 6 J/cm^2). The effect of LLLI on differentiation and proliferation is dose dependent.	Soleimani et al. 2012[39]
10	hMSCs And rMSCs	Diode laser	60	635	0.5	NA	75 sec	Laser-irradiated group showed increase of proliferation of MSCs 2 and 4 days after irradiation.	Wang et al. 2012[68]
11	Rat BMSCs	Diode laser	60	635	0.5	NA	75 sec	Laser-irradiated group showed increased proliferation 2 and 4 days after irradiation	Wu et al. 2012[69]
12	Mouse BMSCs	Diode laser	38	660	1 2 4	NA	100 sec 200 sec 400 sec Once a day	Osteogenic differentiation was increased in a dose-dependent manner.	Wu et al. 2012[70]
13	Bone marrow of exposed tibia and heart of rats after myocardial infarction	GaAlAs	400	804	1	NA	100 sec	Application of LLLT decreased infarct size as compared with control. Irradiation to bone marrow was more effective than to heart to reduce infarct.	Tuby et al. 2011[40]
14	hADSCs	Diode laser	78	636	5	Coherent	6 min and 45 sec	LLLI does not induce differentiation of isolated hADSCs, and increases cellular viability and proliferation.	Villiers et al. 2011[71]
15	EGF on adult $ADSC_S$	Diode laser	110	636	5	NA	NA	Laser irradiation increased the viability and proliferation of human ADSCs cultured with EGF.	Mvula et al. 2010[50]
16	MSCs	NA	NA	405	9, 18, 27, 36	Continuous	180 sec	Irradiation was able to promote extracellular calcification of MSCs.	Kushibiki and Awazu 2009[48]
17	Murine bone marrow	Diode laser	60	660	1.9 3.8	NA	0 h after plating 0–24 h	Biostimulation at lower doses at all time points evaluated and inhibition in cell growth after 48 h at higher doses.	Horvát–Karajz et al. 2009[72]
18	Murine BMSCs	GaAlAs	800	808	4	Continuous	91 sec for 3 times a week	Cellular proliferation and differentiation were similar between control and lased groups. Osteoblastic and osteoclastic markers were found to be similar in control and LLLT conditions.	Bouvet-Gerbettaz et al. 2009[41]

(*continued*)

TABLE 1. (CONTINUED)

	Type of cell	Laser type	Power (mW)	Wavelength (nm)	Energy density (J/cm^2)	Irradiation mode	Application regime	Result (qualitative)	Study
19	Human dental pulp stem cell (hDPSC)	InGaAlP	20 40	660	3 3	Continuous	6 sec 3 sec Under 3.6 mm^2 area	Cell proliferation was significantly increased by laser irradiation under nutritional deficit.	Eduardo et al. 2008[73]
20	Rat BMSCs	InGaAlP	60	635	0 0.5 1 2 5	Continuous	75 150 300 750	LLL irradiation had no cytotoxic effect on MSCs. Cell proliferation was significantly induced optimally by 0.5 J/cm^2 dose. Laser irradiation stimulated VEGF and nerve growth factor (NGF) secretion or myogenic differentiation.	Hou et al. 2008[43]
21	ADSCs	diode laser	50	635	5	NA	15 min	Laser irradiation can positively affect human adipose stem cells by increasing cellular viability, proliferation, and expression of β1-integrin.	Mvula et al. 2008[74]
22	MSCs and CSCs	GaAs	400	804	1, 3	Continuous	20 sec (1 J/cm^2) 60 sec (3 J/cm^2)	LLLI demonstrated a significant increase of MSCs in the laser-treated cultures as compared with the control. LLLI can promote proliferation of MSCs and CSCs *in vitro*	Tuby et al. 2007[37]
23	BMSCs	Diode laser	10	632.8	0.3	Continuous	Single dose	Higher ossification levels were observed in the irradiated samples when compared with the control	Abramovitch-Gottlib et al. 2005[75]
24	BMSCs	GaAlAs	200	810	4	Continues	20 sec every other day for 3 weeks	Higher bone formation was detected in LLL treated group, whereas MSCs or MSCs along LLL groups had no significant differences with control group.	Fekrazad et al. 2015[29]

MSCs, mesenchymal stem cells; LLLT, low-level laser therapy; hMSCs, human MSCs; rMSCs, rat MSCs; VEGF, vascular endothelial growth factor; BMSCs, bone marrow MSCs; AMSCs; LLLI, low-level laser irradiation; ADSCs, adipose-derived MSCs; hADSCs, human ADSCs; CSCs, cancer stem cells.

Table 2. Review of Articles with Noncoherent Light Beam (LED) Parameters and Results

	Type of cell	*Power (mW)*	*Wavelength (nm)*	*Energy density (J/cm^2)*	*Irradiation mode*	*Application regime*	*Result (qualitative)*	*Study*
1	hADSCs	NA	660	30	NA	10 min daily from day 1 to 13	LLLT is an effective biostimulator of cluster hADSCs in wound healing that enhances the survival of hADSCs and stimulates the secretion of growth factors in the wound bed.	Park et al. 2015[76]
2	hADSCs to hindlimb of mice	NA	660	30	NA	10 min daily from day 1 to 20	LLLT is an effective biostimulator of spheroid hASCs in tissue regeneration that enhances the survival of ASCs and stimulates the secretion of growth factors in the ischemic hindlimb.	Park et al. 2014[77]
3	orbital fat stem cells (OFSCs)	NA	530 625	NA	Continuous	Single dose	Stem cells are sensitive to green LED irradiation-induced directional cell migration through activation of ERK signaling pathway via a wavelength- dependent phototransduction.	Ong et al. 2013[78]
4	BMSCs	1	620	1 2 4	NA	15 sec 300 sec 600 sec	Nonconherent red light can promote proliferation but cannot induce osteogenic differentiation of MSCs in normal media, whereas it enhances osteogenic differentiation and decreases proliferation of MSCs in media with osteogenic supplements	Peng et al. 2012[51]
5	Murine bone marrow	5, 15	630	2, 4	NA	Single and every 2 days for 13 days	The group that received multiple radiation had a higher cell proliferation at intervals of 3, 5, 7, 9, 11, and 13 days	Li et al. 2010[79]
6	Murine bone marrow	9.29	647	0.093, 0.279, and 0.836	NA	Single	Cell proliferation was statistically significant when compared with the unirradiated group. LED irradiation increased osteoblastic differentiation	Kim et al. 2009[58]

hADSCs, human adipose-derived mesenchymal stem cells; LLLT, low-level laser therapy; ERK, extracellular signal-regulated kinases; BMSCs, bone marrow mesenchymal stem cells.

upon factors such as output power,[62] energy density,[63,64] and cell type.[65] Hawkins,[33] Mvula,[50] and Anwer[46] found that PBM increased cell viability and proliferation. Most *in vitro* studies indicated that different cell cultures do not respond in the same way to lasers.[66]

The positive effect of PBM on proliferation of MSCs in some studies suggests that lasers alone do not cause significant cell differentiation. One study showed that noncoherent red LED of BMSC specimens with osteogenic supplements increased differentiation, but proliferation increased in the group without osteogenic supplements.[27] One theory is that there is a reciprocal relationship between proliferation and differentiation in MSCs.[66] This theory also suggests that the induction of osteogenic differentiation by red LED occurs during proliferation. It theorizes that light alone cannot activate cell signaling pathway and could be an adjunct tool in osteodifferentiation.[27] It appears that more study is required, especially for *in vivo* and clinical trials.

Conclusions

A review of articles has shown that PBM increases proliferation of MSCs. These results depend upon factors such as energy density, power output, frequency of radiation, type of light source, and type of cell or medium culture. It appears that standardization of parameters in PBM by experimentation is required to obtain the favorable results that allow for more accurate comparisons.

This review found that doses of 0.7–4 J/cm^2 and visible wavelengths from 600 to 700 nm were the most appropriate for PBM to increase cell proliferation. Although contrary results have been mentioned in studies, most agreed that PBM had positive effects of biostimulation of bone tissue and increasing cell proliferation and differentiation and was a helpful tool in regenerative treatments.

Author Disclosure Statement

No competing financial interests exist.

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