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Therapeutic Effects of Low-Level Laser on Male Infertility: A Systematic Review

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Abstract

Introduction: The objective of this study was to assess the effectiveness and safety of photobiomodulation (PBM) in the treatment of male infertility.

Methods: We searched Google Scholar, PubMed, and the reference sections of relevant papers published from January 1, 2000 to September 23, 2022. We retrieved all publications related to the impact of PBM on male infertility. After reviewing the titles, abstracts, and full texts, we included fifteen papers in the research. The studies involved 477 semen samples (in vitro studies) and 70 male participants (randomized clinical trials).

Results: All 14 in vitro studies that evaluated effectiveness reported that PBM was successful in increasing the proportion of progressive sperms in semen samples. Various methods were used to evaluate the safety. One study with a sample size of 58 concluded that PBM was not a safe treatment, whereas the other ten studies confirmed its safety. Only one clinical trial evaluated the effect of laser acupuncture on male infertility and found improvements in sperm progressive motility without any serious adverse effects.

Conclusion: All 15 studies evaluating effectiveness reported that the low-level laser was effective for increasing the proportion of progressive sperm in semen samples and that it was safe to use. However, due to the heterogeneity of population characteristics, source characteristics, duration of exposure, sample size, and instruments for measuring safety and efficacy, we cannot conclude that the positive results obtained from the reviewed studies are solely attributable to the low-level laser on the sperm samples.

Keywords: Biostimulation; Laser acupuncture; Low-level light therapy; Male infertility; Photobiomodulation.

Introduction

Infertility is defined as the inability to conceive after one year of unprotected regular sexual intercourse, with an incidence of 12% to 18% in the United States, which is often attributed to female infertility.[1] However, male factors should also be considered in the management of infertility, as they account for about half of all cases.[2,3] Sperm quality is a major male factor in infertility that can be assessed by semen analysis.[4] Sperms of infertile men are either low in concentration or number (less than 15 million/mL and a total of 39 million per ejaculate), abnormal in morphology (less than 4% normal morphology), non-viable (less than 58% alive), or reduced in motility (less than 32% progressive motility).[4] Motility may not seem to be important for natural pregnancy, but it becomes a critical issue when a high proportion of sperms are immotile in a single ejaculation, especially when performing in vitro assisted reproductive technology procedures such as intrauterine insemination or in vitro fertilization.[5,6] Motility can be used as a selection criterion for sperm samples because it increases the chance of pregnancy.[6] Typically, hypoxic or stressed cells are immotile or less motile.[7] Sperms need intracellular calcium (Ca^{2+}) and adenosine triphosphate (ATP), which are provided by mitochondria, to move their flagella.[8,9] It is now known that the respiratory chain of immobile cells is inhibited when cytochrome c oxidase binds to mitochondrial produced nitric oxide, thereby decreasing intracellular ATP and Ca^{2+}levels.[10-12] Scientists have explored various treatment options, including injecting chemical compounds into sperm samples.[13] However, each has its own limitations and drawbacks. Researchers have recently suggested the use of photons to treat spermatic immobility, but the safety and efficacy of this treatment need further investigations.[14,15] Photobiomodulation (PBM), also known as low-level

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light therapy (LLLT), is a novel treatment that uses light-emitting diodes (LEDs) to apply electromagnetic waves in the visible light and near-infrared (NIR) ranges to the sample's surface.[16] It is safer and more cost-effective than previous alternatives. Numerous in vitro studies evaluating the efficacy and safety of this treatment option at various wavelengths and durations have indicated that this technique can increase sperm motility by stimulating mitochondrial activity and dissociating nitric oxide from its binding sites.[17] More ATP is produced and more Ca^{2+} flows as a result of the resumption of respiratory chains.[18] However, the effects of PBM depend heavily on wavelength, number of exposures, and duration of exposure. There is currently no standard intervention guideline for using this method, although research has been conducted to investigate various aspects of efficacy, safety, related exposure and wavelength factors. There are also some studies in the field of clinical use of biostimulation laser therapy for male infertility. Various laser types and body points for radiation have been used. Considering the aforementioned evidence, the aim of the present study was to conduct a systematic literature review to determine the efficacy of PBM in enhancing sperm motility and related factors.

Methods

We conducted this systematic review of the therapeutic effects of low-level laser therapy on male infertility according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines and the review protocol. We performed a literature search based on the participants (in vitro semen samples or infertile men), interventions (PBM therapy), comparisons (between case samples and controls or between case samples before and after irradiation), and outcomes (improved sperm quality or conception rate). We excluded meta-analyses, reviews, and case reports. The studies had to be available in English. We searched Google Scholar, PubMed, and the reference sections of related articles published from January 1, 2000 to September 23, 2022. We used the following keywords, their combinations, and related synonyms based on Medical Subject Headings (MeSH) to find the relevant literature: Low-Level Light Therapy, Phototherapy, Photobiomodulation, laser biostimulation, Color therapy, Male Infertility, Subfertility, Sperm, Semen, Testis, Oligoasthenoteratozoospermia, and Spermatozoa. Two reviewers screened the titles and abstracts of all retrieved records on semen samples, assessed them for duplication, and then independently examined the full texts of all potentially relevant studies to select the final studies (E.AR, SM.SP). We assessed the quality of all potentially relevant studies using NHLBI-NIH tools for study quality assessment.[19] We used the "Quality Assessment Tool for Controlled Intervention Studies" for controlled trial studies, and for those trials that did not have a control group, we used the "Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group". We excluded studies with a quality score lower than 5. We resolved discrepancies by consensus. We excluded one study due to lack of stating its population and sample size. We excluded two articles because they were only in Russian. Two researchers (E.AR, SM.SP) independently extracted the following information: study characteristics (authors, publication year, study design, sample size), population characteristics (groups), interventions (source, wavelength, duration), and outcomes (results of safety and efficacy assessments).

Results

We identified 1018 articles through PubMed and Google Scholar, and by hand search. After screening the titles, abstracts, and full texts, we included 15 studies in our study (Figure 1). Table 1 shows the characteristics of the 15 included studies in this systematic review. The sample sizes of the reviewed articles ranged from 3 to 100 male participants. In total, 477 semen samples (in vitro studies) and 70 male subjects (randomized clinical trial) participated in the studies. 14 studies were in vitro controlled trials, and only one study was a double-blind randomized clinical trial. To measure outcomes, 10 studies evaluated both safety and efficacy, four studies only evaluated efficacy, and one study only evaluated safety. Nine studies assessed motility by CASA (Compute-Assisted Sperm Analysis). All 14 studies that assessed efficacy reported that PBM was effective in increasing the rate of progressive (PR) sperms in semen samples, but mostly at moderate time intervals and moderate imposed energy. In four out of seven studies that evaluated motility at different time intervals (including 30 minutes), the highest increase in motility was observed after the 30-minute time point. Table 2 summarizes the efficacy results of the included studies. Safety was assessed by various tests. The most common tests were DFI (DNA Fragmentation Index) used by eight studies, SMI (Sperm Membrane Integrity) used by three studies, and oxidation levels using LPL (Lipid Peroxidation Level), ROS (Reactive Oxygen Species), and SOD (Super Oxide Dismutase) activity, used by four studies. Out of 11 studies that conducted safety tests, only one study with a sample size of 58 concluded that PBM was not a safe method, while the other 10 confirmed its safety. Table 3 summarizes the safety results of the included studies.

Discussion

Almost all studies reported that PBM is a safe and effective method for increasing the motility rate of sperm samples. Various types of lasers, including red light, NIR laser, He-Ne laser, and GaAlAs laser, were used in the studies. In one of the studies, laser acupuncture was used to deliver light energy through multiple skin points. The results

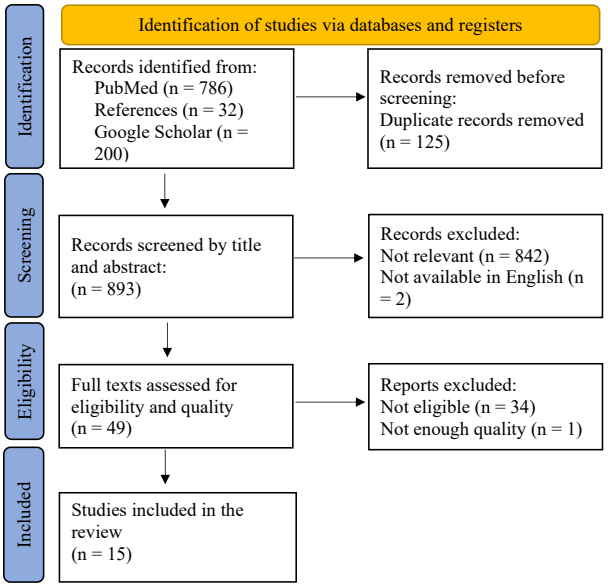

Figure 1. Flowchart of Study Selection

Table 1. Characteristics of the 15 Included Studies in This Systematic Review

Reference	Year	Design	Population (WHO-Based Type of Samples)	Groups		Sample Analysis Criteria	Sperm Measuring Tool	Safety Assessment	
				Intervention	Control			Criteria	Assessment Tool
Salama and E-Sawy [20]	2015	IVCT	27 SS (18 AZ+9 NZ)	27 washed+11 non-washed aliquots	27 washed+11 non-washed aliquots	WHO v5	CASA	SMI SHCC	HOS ANBS
Espey et al[21]	2022	IVCT	64 SS (42 AZ+22 NZ)	3 AES	1 AES	WHO v5	CASA	DFI Acrosomal integrity	LMqPCR CD46 expression
Salman Yazdi et al[22]	2014	IVCT	22 SS (22 AZ+0 NZ)	3 AES	1 AES	WHO v4	CASA	DFI SMI	SCD HOS
Safian et al[23]	2020	IVCT	30 SS (0 AZ+30 NZ)	3 groups of 10 SS (+3 AES)	1 AES as control	WHO v5	ND	Viability DFI	ENS SCD
Allameh et al[15]	2021	DBRCT	70 men (ND)	35 men (3 SS each)	35 men (3 SS each)	ND	ND	ND	ND
Safian et al[24]	2022	IVCT	24 SS (0 AZ+24 NZ)	2 AES	1 AES	ND	ND	Quality	DFI LPL PRM 1 and 2 ADD1
Frangez et al[25]	2015	IVCT	30 SS (30 AZ+0 NZ)	4 AES	1 AES	WHO v5	CASA	ND	ND
Safian et al[26]	2021	IVCT	22 SS (0 AZ+22 NZ)	1 AES	1 AES	WHO v5	CASA	Morphology Viability MMP ROS LPL (MDA)	Diff-Quik ENS JC-1 dye DCFDA TBA
Zupin et al[27]	2020	IVCT	9 SS (ND)	2 AES	1 AES	WHO v5	ND	Morphology Elemental distribution	LE-XRF
Gabel et al[28]	2018	IVCT	3 SS (ND)	3 AES	2 AES	ND	SQA IIB analyzer	DFI	SCSA
Saeed et al[29]	2014	IVCT	100 SS (NS)	1 AES	1 AES	WHO v4	CASA	ND	ND
Firestone et al[30]	2012	IVCT	33 SS (12 AZ+10 NZ+11 AO)	1 AES	1 AES	WHO v4	CASA	DFI	Flow cytometry

Table 1. Continued.

Reference	Year	Design	Population (WHO-Based Type of Samples)	Groups		Sample Analysis Criteria	Sperm Measuring Tool	Safety Assessment	
				Intervention	Control			Criteria	Assessment Tool
Shahar et al[31]	2011	IVCT	30 SS (ND)	1 AES	1 AES	ND	CASA	ROS	DFCDA, SOD, Sodium azide
								ICC	FCI
								DFI	SCD
Fekrazad et al[32]	2014	IVCT	25 SS (ND)	2 AES	1 AES	WHO v4	CASA	ND	ND
Highland et a1[33]	2018	IVCT	58 SS (ND)	2 AES of 28 infertile SS	2 AES of 30 fertile SS	WHO v4	ND	SMI	HOS
								STI	PDNAB
								Apoptosis	DSM
								LPL	MDA
								SOD	SPM
								DFI	SCD

Abbreviations: ND, no data; IVCT, in vitro controlled trial; DBRCT; double blind randomized controlled trial; SS, semen sample; AZ, asthenozoospermic; NZ, normozoospermic; AO, asthenospermic and oligospermic; AES, aliquots from each sample; CASA, computer-assisted sperm analysis; SMI, sperm membrane integrity; HOS, hypo osmotic swelling test; SHCC, sperm head chromatin condensation; ANBS, aniline blue staining; DFI, DNA Fragmentation Index; LMqPCR, ligand-mediated quantitative polymerase chain reaction; SCD, sperm chromatin dispersion; ENS, eosin nigrosin staining; LPL, lipid peroxidation level; PRM, gene expression levels of protamine; ADD1, adducin 1 alpha; MMP, mitochondrial membrane potential; ROS, reactive oxygen species; DCFDA, 2′7′ dichlorofluorescein diacetate; MDA, malondialdehyde; TBA, thiobarbituric acid; LE-XRF, low energy X-ray fluorescence; SCSA, sperm chromatin structure assay; SOD, super oxide dismutase; ICC, intracellular concentration of free Ca^{2+}; FCI, fluorescent calcium indicator; STI, sperm toroid integrity; DSM, dual staining method; SPM, spectrophotometry.

Table 2. Efficacy Results of the Included Studies

Reference	Intervention	Main Results of efficacy
Salama and El-Sawy[20]	Red LED (636.6 nm, 1.3 W, at 5 cm) at intervals of 2, 5, and 10 min (0.496, 1.241, 2.482 J/cm² imposed energy).	# A significant increase in PR sperms and a significant decrease in IM sperms at every time point. # Motility peaked after 5 min, although this peak was not significantly higher than the one happening after 2 min. Then, the PR motility dropped significantly after arriving at the 10-min point. # Motility in washed samples was significantly higher than that in the non-washed samples. # A slight non-significant increase in sperm CK activity after 5 min of treatment was detected.
Espey et al[21]	Pulsed laser probe (655 nm, 50 mW/cm², 200 sec. impulse duration) at intervals of 0, 30, 60, 90, and 120 min (4, 6, 10 J/cm² imposed energy).	# Doses of 4 and 6 J/cm² exhibited the strongest effect on motility and velocity. # The rate of PR raised toward the 32% threshold marker after treatment with 6 J/cm². # In the time-independent comparison, the VSL increased in the AZ group after treatment with 4 J/cm². # LIN & STR were negatively affected in NZ samples by 10 J/cm². # LIN, STR & WOB increased in the AZ group by 6 J/cm² in the overall group comparison.
Salman Yazdi et al[22]	GaAlAs laser (830 nm, 100 mW, 0.67 cm² aperture size) at intervals of 0, 30, 45, and 60 min (0, 4, 6, and 10 J/cm² imposed energy).	# Strongest significant increases in motility were observed in doses of 4 J/cm² at 60 min, and 6 J/cm² at 45 min. # The PR motility significantly increased at each time interval and each dose compared to controls. # The 10 J/cm² group showed the least effect on motility.
Safian et al[23]	Group A: Red laser (630 nm); Group B: NIR laser (810 nm); Group C: Red + NIR laser. All at 18 cm at intervals of 15, 30, and 60 min. (0.6, 1.2, and 2.4 J/cm² exposed energy).	# PR sperms in the groups exposed to the three energy densities of the Red + NIR lasers showed a significant increase only after 60 min in all energy densities. # PR sperms significantly increased in most of the groups exposed to the three energy densities of the NIR laser except the 1.2 J/cm² after 30 min. # The best increase in motility resulted from the shortest radiation time (23 s) of the NIR laser at an energy density of 0.6 J/cm². # This study confirmed the superiority of the NIR laser at 0.6 J/cm² compared with the Red and Red + NIR protocols.
Allameh et al[15]	Light energy was transferred by laser fibers to several specific points performed by technicians of acupuncture using a Laser (810 nm, 300 mW, 18 J/min energy, at 90 degrees) on the skin at intervals of 5 to 10 seconds twice a week for consecutive 5 weeks. In the control group, sham laser acupuncture was performed. Three semen samples were taken from all patients; the first before the intervention, the second immediately after the intervention, and the third three months after the intervention.	# Sperm volume and morphology did not differ significantly in both control and intervention groups (all three samples). # Sperm motility and concentration were significantly higher only in the 3rd sample (3 months after the intervention).

Table 2. Continued.

Reference	Intervention	Main Results of efficacy
Safian et al[24]	The control group underwent conventional sperm cryopreservation, group 2 underwent pre-freezing exposure (810 nm, diode laser, and 0.6 J/cm^2), and group 3 underwent post-freezing and thawing PBM exposure.	# Group 2 exhibited the highest increased motility outcomes compared to groups 1 and 3.
Frangez et al[25]	Group 1: 850 nm, 2.16 mW/cm^2; Group 2: a mix of 625, 660, 850 nm, 3.92 mW/cm^2; Group 3: 470 nm, 5.06 mW/cm^2; Group 4: a mix of 470, 625, 660 nm, 8.23 mW/cm^2. All groups were exposed for 3 min., and their motility was evaluated 30 min. later.	# After treatment, the increase in the ratio of PR sperms was statistically significant in all investigated groups. # The improvement of sperm motility was the largest in group 3 semen samples, although not statistically different from the other treated groups. # This study indicates that LLLT using LED significantly improves sperm motility regardless of the wavelength.
Safian et al[26]	Samples received a single dose of NIR exposure from a laser diode (810 nm, 0.6 J/cm^2, at 18 cm) before cryopreservation. Samples were analyzed 30, 60, and 90 min. after thawing.	# Results showed a significant motility increase in the NIR laser-preconditioning groups compared to the control.
Zupin et al[27]	Group L1: Class IV diode laser (800 nm, 0.1 W/cm^2, 5 J/cm^2); Group L2: Class IV diode laser (800 nm, 0.1 W/cm^2, 15 J/cm^2). Samples were analyzed at 0 and 60 min post-irradiation.	# The total motility increases or stays constant in all irradiated samples compared to that of the untreated ones. # Considering the progressive motility in a couple of cases, it can be seen that the L1 setting induces a decrease while L2 causes an increase, compared to that of the control samples.
Gabel et al[28]	The 104 LED cluster (56 x 660 nm, 10 mW and 48 x 850 nm, 30 mW, total power 2W at 5 cm with 39.5 mW/cm^2) was projected for periods of 25, 50, and 75 seconds to the 1st frozen sample and 50, 100, 200, and 400 seconds to the fresh sample. The GaAlAs single divergent laser beam (200 mW, 810 nm, at 5 cm with 90 mW/cm^2) was projected for periods of 10, 20, and 40 seconds to the 2nd frozen samples and 15, 20, and 30 seconds to the fresh sample.	# 30 min post-irradiation, a maximal effect on motility was achieved. # The 104 LED cluster caused just over a four-fold increase in motility with 75 s. exposure, whilst the laser produced an optimal effect of just below a four-fold increase at 20 s exposure. # The best effect on motility 30 min after exposure came from a treatment time of 50 s of LED while the longevity of the effect from higher doses diminished more rapidly. # The best overall longevity of sperm motility came from the shortest irradiation time (15 s). # The benefit from higher doses was shorter-lived.
Saeed et al[29]	Irradiated using a continuous He-Ne laser model (IFHN05) for 30 min.	# The results showed that 30-min laser irradiation increases the percentage of PR sperms significantly.
Firestone et al[30]	Irradiated with a laser system (905 nm, 50 mW/cm^2, 1.5 J/cm^2) for 30 seconds. Motility was assessed after 30 and 120 min.	# Results showed a statistically significant increase in motility in the treated samples 30 min after exposure. This difference was not observed 120 min after exposure. # Most significantly, those samples that were classified as both AZ+AO exhibited the greatest increase in motility (83.5%) as a result of the treatment.
Shahar et al[31]	Irradiated for 3 min. with 40 mW/cm^2 visible light (400–800 nm) with maximum energy at 600 nm.	# Exposure caused a significant increase in PR sperms. However, no effect was seen on total motility. # This significant effect of light on PR sperms was seen within 10 min of incubation and it continued for at least 3 h. # A significant increase in VSL and LIN of the samples was observed 30 min after the treatment.
Fekrazad et al[32]	Red and Infrared lasers with 635 and 830 nm wavelengths were used.	# The mean total motility, PR motility, and VLC significantly increased in both Red and Infrared groups. The size of this effect was higher in the Infrared group, but the difference between the Red and Infrared groups was not significant.
Highland et al[33]	Exposed to a NIR source using a Philips Infrared bulb (750-1100 nm, 230 V, 50 Hz, 150 W) for a short duration of 15 min.	In this study, the efficacy of PBM in motility was not assessed and only safety tests were done.

Abbreviations: PR, progressive motile sperms; IM, immotile sperms; CK, creatine kinase; AZ, asthenozoospermic; NZ, normozoospermic; AO, asthenospermic and oligospermic; NIR, near infrared; VSL, straight-line velocity; LIN, linearity of the curvilinear path; STR, straightness of the average path; WOB, wobble parameter for oscillation; PBM, photobiomodulation.

showed that laser acupuncture was effective in improving sperm motility and concentration in infertile patients with oligospermia and had no significant adverse effects. We can infer from the findings of the studies that PBM efficacy is optimal when applied for a moderate duration and dose of irradiation, and when either of these factors (time or energy dose) is increased, its efficacy decreases or lasts for a shorter time. In four out of seven studies that evaluated motility at different time intervals, the highest increase in motility was observed after the 30-minute time point, but 2 studies reported that the best results could be achieved after 60 minutes or 45 minutes with a higher irradiation dose, and one study reported that the increase in motility was not significant after 30 minutes at 1.2 J/cm^2 (Table 2). A possible reason for such discrepancies in the efficacy results of PBM in increasing motility after different time intervals among various studies is the lack of a common standard. Different radiation sources (in terms of wavelength, output power, distance, and other characteristics of the source), various sample sizes and population characteristics (some studies had only NZ (normozoospermic) or AZ (asthenozoospermic) samples or a combination of both), and imposed energies are the potential factors that need standardization. Out of 11 studies that conducted safety tests, only one study concluded that PBM was not a safe method, while the other 10 confirmed its safety. However, it should be noted that since there are some major differences in terms of

Table 3. Safety Results of the Included Studies

Reference	Results
Salama and El-Sawy[20]	# CK activity increased insignificantly after 5-minute LED treatment. # Both SMI and SHCC remained stable after the treatment for 10 min.
Espey et al[21]	# No significant changes in the DFI were detected after therapy. # The pattern of CD46 expression confirmed the maintenance of acrosomal integrity after therapy.
Salman Yazdi et al[22]	# The results of SCD and HOS tests in the 10 J/cm^2 group were not significantly different compared to the control group.
Safian et al[23]	# Both the Red and Red + NIR lasers at 0.6, 1.2 and 2.4 J/cm^2 significantly decreased viability and increased DFI. However, this difference was not significant between NIR and control groups.
Allameh et al[15]	In this study, the safety of PBM in motility was not assessed and only motility tests were done.
Safian et al[24]	# DFI and LPL were significantly reduced in group 2 compared to group 1. # Early apoptosis and necrotic cells decreased significantly in group 2 compared to either group. # The expression levels of PRM1, PRM2, and ADD1 were not significantly different among the study groups. # PBM therapy prior to cryopreservation has a significant protective role against cryo-damage.
Frangez et al[25]	In this study, the safety of PBM in motility was not assessed and only motility tests were done.
Safian et al[26]	# No significant differences were observed in the morphological features. # PBM treatment before cryopreservation significantly increased the concentration of viable spermatozoa. # PBM before cryopreservation significantly increased the number of high MMP sperms and decreased the number of low MMP sperms post-thawing. # The PBM-preconditioning significantly decreased the intracellular ROS level and LPL.
Zupin et al[27]	# An increase in the Na^+content was detected after PBM, suggesting that this change could be vital in the enhancement of sperm movement.
Gabel et al[28]	# SCSA assay revealed no increase in DFI from the very high doses of both laser and LED therapy.
Saeed et al[29]	In this study, the safety of PBM in motility was not assessed and only motility tests were done.
Firestone et al[30]	# DFI was not significantly different.
Shahar et al[31]	# ROS was produced after 1–3 min of light irradiation, while there was a significant reduction in ROS in the presence of SOD or azide. # Mitochondrial respiration is the main source of ROS produced by light therapy in sperms. # HAM in DCF loaded cells was enhanced by light. # Azide caused complete inhibition of the light effect on HAM. # Light therapy did not affect DFI. # Intracellular Ca^{2+}concentration increased significantly after PBM.
Fekrazad et al[32]	In this study, the safety of PBM in motility was not assessed and only motility tests were done.
Highland et al[33]	# The sperm viability significantly decreased in both groups after exposure to NIR which was higher in group 2 compared to group 1. # A significant decrease in the number of swollen spermatozoa was observed after NIR exposure in both groups as compared to pre-treated samples. # Percent of apoptotic cells increased more significantly after NIR exposure in both groups as compared to pre-treated groups. This increase was significantly higher in group 2 compared to group 1 post-treatment. # Toroid disruption increased insignificantly after NIR exposure in group 1, but group 2 showed a highly significant increase. # The number of sperms with normal chromatin dispersion decreased significantly in groups 1 and 2 after NIR exposure as compared to the pre-treated samples. # SOD activity diminished significantly after NIR exposure in both groups. # LPL increased significantly after NIR exposure in groups 1 and 2.

Abbreviations: SMI, sperm membrane integrity; HOS, hypo osmotic swelling test; SHCC, sperm head chromatin condensation; ANBS, aniline blue staining; DFI, DNA Fragmentation Index; LPL, lipid peroxidation level; PRM, gene expression levels of protamine; ADD1, adducin 1 alpha; MMP, mitochondrial membrane potential; ROS, reactive oxygen species; SCSA, sperm chromatin structure assay; SOD, super oxide dismutase.

population characteristics (some studies had only NZ or AZ samples or a combination of both), sample size (from 3 to 100 samples and from 1 to 5 aliquots from each sample), and the type of methods used to conduct safety tests, it is very difficult to draw a strong conclusion on the safety of PBM on semen samples in male subjects (Table 3).

Conclusion

Because of the heterogeneity in the population characteristics, source characteristics, duration of exposure, sample size, and instruments for safety and efficacy measurement, we cannot attribute the positive results obtained from the reviewed studies solely to the effect of PBM on the semen samples.

Author's Contribution

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Competing Interests

The authors declare no competing interests.

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Not applicable.

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