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Review Article

Exploring Therapeutic Potentials of Photobiomodulation Therapy (PBMT) In Urogenital Disorders: A Comprehensive Review

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Abstract
This comprehensive review aimed to provide an evidence-based overview of the therapeutic potential of photobiomodulation therapy (PBMT) in managing urogenital conditions. A systematic search was conducted in Web of Science, PubMed, Scopus, and Google Scholar using various MeSH terms and keywords, resulting in the identification of 8 preclinical and 14 clinical studies. The findings suggest that PBMT demonstrates promising therapeutic effects in both human studies and animal models by stimulating cellular processes and tissue repair. Although limited by poor penetration with certain devices, PBMT was found to prevent bladder cancer development and improve renal oxidative stress markers in diabetic rats. In humans, PBMT has been shown to improve sperm parameters, manage chronic pelvic diseases, alleviate pain, and enhance pelvic floor muscle strength. These findings indicate that PBMT has broad therapeutic potential for pelvic and urogenital disorders, warranting further research to clarify its mechanisms and long-term efficacy.
Keywords: Photobiomodulation, Low-level light therapy, Urogenital system, Urology, Pelvic floor disorders

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Introduction

Photobiomodulation therapy (PBMT), commonly known as low-level laser therapy (LLLT), is a non-invasive treatment method utilizing low-level lasers or light-emitting diodes to change the cellular activity and facilitate tissue repair in different pathological conditions. In recent decades, PBMT has gained popularity for treating scars, photoaged skin, and fine wrinkles.[1-3] The therapeutic benefits of PBMT are mediated by the absorption of light by cellular chromophores, which results in a variety of physiological and biochemical reactions, such as the regulation of tissue regeneration, microcirculation, and inflammatory processes.[4]

Urogenital disorders, such as chronic pelvic pain, urinary incontinence, and sexual dysfunction, represent a substantial clinical burden due to their chronic nature, negative impact on quality of life, and the limitations of current therapies. Conventional management strategies often involve pharmacological agents, pelvic floor rehabilitation, or surgical interventions, each associated with varying success rates and potential adverse effects. This creates an unmet clinical need for safe, non-invasive, and cost-effective alternatives.

PBMT has emerged as a promising candidate because of its documented benefits in promoting tissue repair, reducing inflammation, and modulating neural pathways, which are all relevant to the pathophysiology of many urogenital disorders.[5-10] The non-invasive nature of this therapy makes it a desirable choice for individuals who might be reluctant to have more invasive procedures done.[11] However, despite a growing number of studies, evidence is fragmented across different populations, device parameters, and conditions, making it difficult for clinicians to adopt standardized protocols. Therefore, a comprehensive synthesis of available preclinical and clinical research is essential to clarify the therapeutic potential, safety profile, and mechanistic basis of PBMT in this context. Therefore, we conducted a comprehensive literature review to evaluate current evidence on the application of PBMT in urogenital disorders, summarize

its proposed mechanisms of action, and identify gaps that future studies need to address.

Literature Search

To find the relevant research, we looked through electronic medical databases including PubMed, Scopus, Web of Science, and Google Scholar from inception to January 2025. The search included a combination of MeSH terms and free-text keywords to ensure comprehensive coverage of the literature, and it was limited to publications in English. The search strategy included terms such as "Urogenital System", "Urinary Tract", "Urinary Incontinence", "Lower Urinary Tract Symptoms", "Genital Diseases", "Pelvic Floor Disorders", "Urinary Bladder Diseases", "Kidney Diseases", "Sexual Dysfunction", Physiological", "Prostate", "Prostatitis", "pelvic inflammatory disease", "chronic prostatitis with chronic pelvic pain syndrome", "CCPS", "Sexual Dysfunction", "Sexual Disorder", "Sexual condition", "urologic*", "genital*", "urogenital", and "genitourinary", combined with terms related to "Low-Level Light Therapy", "photobiomodulation", "photobiomodulation therapy", "PBMT", and "LLLT". Both preclinical and clinical studies investigating the therapeutic effects of PBMT in the context of urogenital disorders were considered.

Eligibility Criteria

We included studies that met the following criteria:

- **Study Design:** Preclinical studies (in vitro and in vivo) and clinical studies (randomized controlled trials, cohort studies, and observational designs)
- **Population/Condition:** Studies investigating PBMT in urogenital conditions, including urinary tract disorders, pelvic floor dysfunction, sexual dysfunction, and chronic pelvic pain syndromes
- **Intervention:** Photobiomodulation therapy (including low-level light therapy and low-level laser therapy) applied as a primary intervention
- **Outcomes:** Reports on at least one clinical, physiological, or mechanistic outcome related to urogenital health
- **Language:** English language publications only

Exclusion Criteria

- Reviews, editorials, letters, and commentaries
- Studies not related to urogenital or pelvic disorders
- Articles without sufficient detail on PBMT parameters or outcomes

The History of PBMT

While the therapeutic use of light has roots in ancient Greece, Rome, and Egypt, modern developments in the field began in the 1960s with key discoveries that laid the groundwork for today's understanding of PBMT.[12, 13, 14] The area was greatly advanced by recent studies conducted by Bjordal,[15, 16] Michael,[17] De Freitas and Hamblin,[18] and Karu.[19] While Hamblin showed that PBM is useful in treating problems like wound healing and neurological diseases,[17, 18] Karu investigated how particular light wavelengths and intensities could improve cellular processes.[19] Bjordal enhanced the comprehension of the function of PBM in pain management and tissue healing, providing substantial evidence via his systematic reviews and meta-analyses that refined the applications of light therapy in clinical environments.[15, 16]

Mechanism of Action

The absorption of light photons by cellular chromophores initiates a cascade of biological reactions leading to physiological changes at the molecular level. The primary mechanisms through which PBMT exerts its effects are as follows:

1. **Stimulation of ATP Production**: One of the main ways that PBM improves mitochondrial function is by activating cytochrome C oxidase (CCO), a vital enzyme in the electron transport chain of the mitochondria that lowers oxygen during oxidative phosphorylation, a crucial step in the synthesis of ATP. CCO is a key photon absorber in the red to near-infrared light spectrum used in PBM therapy. By absorbing these photons, the redox status of the enzyme is changed, which increases the synthesis of ATP in the mitochondria. This light absorption also generates reactive oxygen species (ROS) and nitric oxide (NO), key signaling molecules involved in numerous metabolic processes. The subsequent increase in ATP availability triggers kinases that aid in the release of calcium and the synthesis of cyclic adenosine monophosphate (cAMP). These molecules function as second messengers, triggering a cascade of intracellular events that affect metabolic pathways within the nucleus. This modulation can result in beneficial adaptations, enhancing neuronal physiology and overall cerebral function.[20, 21]
2. **Increased Cellular Oxygenation:** PBM increases the bioavailability of NO by activating endothelial NO synthase (eNOS) in cells. This results in enhanced blood flow and vasodilation, which can aid in cellular regeneration and repair.[22, 23] Akt kinase phosphorylates serine 1177 to bring about this activation, which raises NO generation.[22, 23]

In addition, it has been shown that PBM induces the photo-dissociation of NO from heme proteins. At low concentrations, NO functions as a reversible inhibitor of CCO and competes with oxygen by attaching to heme a3. The activity of the electron transport chain is modulated by this contact, which also initiates retrograde signaling pathways. The function of oxygen can be redirected to the generation of ROS, which can activate ROS- or NO-mediated retrograde signaling through pathways involving forkhead box Os (FOXOs), NF-κB, activator protein-1 (AP-1), and Myc. These processes contribute to the control of tissue oxygen gradients and the induction of cytoprotective effects.[22, 23]

3. **Modulation of Inflammatory Response:** As mentioned earlier, PBM modulates the homeostasis of reactive oxygen species (ROS) and inflammatory responses.[24, 25] For instance, the release of cytokines and growth factors from platelets plays a crucial role in wound healing, which starts as soon as tissue damage occurs. This inflammation is necessary for repair. Transforming Growth Factor-beta (TGF-β) is a critical cytokine that promotes the recruitment and activation of inflammatory cells, as well as the deposition of extracellular matrix (ECM). It is of significance that TGF-β enables the lesion to transition from the inflammatory phase to the proliferation phase. In this phase, TGF-β drives fibroblasts to develop into myofibroblasts, which are necessary for collagen synthesis and wound contraction, ultimately leading to the formation of scars or wound remodeling. Dysregulation of this system, particularly when rooted in chronic inflammation due to insufficient TGF-β response, may result in non-healing chronic wounds. PBM has the potential to optimize the healing of acute and chronic lesions by enhancing TGF-β activity, thereby modulating these inflammatory responses.[24, 25]
4. **Stem Cell Stimulation:** PBM has been shown to stimulate stem cell differentiation and proliferation, which can facilitate tissue remodeling and wound healing.[26-28] Molecular signaling pathways coordinate this process. One of these mechanisms is the Tyrosine-Protein Kinase Receptor (TPKR) signaling pathway, which triggers the MAPK/ERK pathway. This cascade leads to heightened expression of proliferation-associated factors, including eIF4E and CyclinD1. The PI3K/Akt route is another crucial mechanism where PBM activates Akt and its downstream targets by boosting PI3K phosphorylation, hence promoting cell growth, proliferation, and migration, frequently via the phosphorylation of eIF4E. Furthermore, PBMT affects the expression of proteins such as Bcl-2 and Bax, resulting in an elevation of Bcl-2 and a reduction of Bax, which can promote stem cell survival and proliferation.[26-28]
5. **Enhancement of Neurotransmitter Release:** PBM can promote the release of neurotransmitters that are involved in mood regulation and pain modulation, including endorphins and serotonin. The release of this neurotransmitter can also facilitate pain alleviation and enhance mood and overall well-being.[29, 30]

A primary mechanism entails a reduction in the expression of metabotropic glutamate receptor type 1 (mGluR1) in the dorsal root ganglion (DRG), which regulates excitatory neurotransmission by diminishing the sensitization of DRG neurons and decreasing glutamate release. By decreasing glutamate, a crucial excitatory neurotransmitter, nociceptive signaling is reduced, and the pain threshold is raised. Additionally, by increasing prostatic acid phosphatase (PAP), an enzyme associated with pain regulation, the PBM indirectly reduces pain signals by lowering adenosine monophosphate (AMP) levels. Additionally, PBMT causes reversible tubulin aggregation, a cytoskeletal component that modifies cellular dynamics and may improve the efficiency of neurotransmission.[29] Another important mechanism is the activation of intrinsically photosensitive retinal ganglion cells (ipRGCs), which react to light and affect how pain is modulated by going after central pain processing regions such as the rostral ventromedial medulla (RVM). The expression of Proenkephalin-A mRNA in the spinal cord is increased by green light exposure, which leads to higher amounts of enkephalins that activate descending pain-inhibitory pathways and produce analgesia. At the peripheral level, the application of red light through the skin targets mitochondrial chromophores and thereby increases intracellular calcium levels and ATP production, as mentioned earlier. Within neurons, this metabolic cascade promotes a regenerative environment and eases the release of neurotransmitters.[30]

6. **Regulation of Gene Expression:** PBM influences gene expression by activating specific pathways related to cell survival, proliferation, and repair. This regulation of gene expression can result in long-term impacts on the health of tissues and cellular function.[31,32] The activation of transcription factors is one way that PBM influences gene expression. Target genes may be upregulated or downregulated because of these transcription factors being activated by the light energy that cells absorb. As mentioned earlier, PBMT increases TGF-β expression, which is crucial for wound healing, by triggering the phosphorylation of Smad proteins (Smad2 and Smad3). These proteins subsequently associate with Smad4 to regulate gene transcription in the nucleus. This activation leads to the upregulation of genes essential for tissue repair, including those encoding collagen types COL1A1 and COL3A1. Improved fibroblast proliferation, myofibroblast differentiation, increased ECM synthesis, and angiogenesis, which are necessary for efficient wound closure and tissue regeneration, are the overall results of these gene expression alterations. Furthermore, PBM can boost cellular energy generation and shield cells from oxidative stress by increasing the expression of genes linked to mitochondrial biogenesis and antioxidant enzymes.[25,33]

All things considered, diverse cellular actions of PBM support its therapeutic advantages in fostering tissue repair, lowering inflammation, boosting cellular function, and improving blood flow.

Preclinical Investigations of PBMT in Urological Conditions

Through our comprehensive search, we found several experimental studies that investigated the potential

therapeutic effects of PBMT on tissue samples and animal models. The characteristics of this study are summarized in Tables 1 and 2.

The study conducted by Zipper and Pryor focused on using a specific PBMT device (SoLá Therapy, UroShape, LLC) for delivering near-infrared (NIR) laser beams with a transvaginal applicator through the vaginal mucosa of an adult Suffolk/Dorset Ewe.[34] The irradiance levels were measured in the bladder, inside the muscle, and on the surface of the levator ani muscle. This laser system provided a surface irradiance of 738 mW/cm^2 and 74 mW/cm^2 at 5 and 0.5 W, respectively. Neither the bladder nor the levator ani muscle received therapeutic energy from the 0.5 W power setting (Table 1).[34]

By applying blue laser irradiation (450 nm) with varying energy densities to the human bladder cancer cell lines T24 and EJ, as well as the uroepithelial cell line SV-HUC-1 in human tissue samples, Xia et al sought to understand the impact of PBM on the progression of bladder cancer and the related mechanisms.[35] In T24 and EJ cell lines, blue laser irradiation suppressed migration, invasion, and the epithelial-mesenchymal transition (EMT) process, which in turn decreased bladder cancer proliferation in a density-dependent manner. They also found that a significant reduction in cell viability was observed following blue laser irradiation at > 4 J/cm^2 in cell lines and that the blue laser decreased the viability of SV-HUC-1 cells when the density exceeded 16 J/cm^2. This suppression may have been achieved by suppressing the MAPK/MEK/ERK pathway (Table 1).[35]

In the study conducted by Asghari et al, 20 streptozotocin-induced diabetic rats were randomly distributed into two groups: control (G1) and PBM (G2).[36] Radiation was applied three times: immediately after skin suturing and 1 and 2 hours after starting reperfusion for 6 minutes. The results revealed that the blood levels of BUN, creatinine, and malondialdehyde were considerably greater in the control group compared to the PBM group. The control group produced a lower level of glutathione in the renal tissue than PBM. The levels of catalase and superoxide dismutase were shown to have significantly recovered in the PBM group compared to the control group. In comparison with the PBM group, the renal tissue of the control group had considerably greater amounts of NO and myeloperoxidase activity. Moreover, the histological damage in the control specimens was noticeably higher than that in the PBM specimens (Table 1).[36]

The effects of caffeine and PBM on acute kidney injury (AKI) in 7-day-old rat pups that received a hypoxic ischemic encephalopathy (HIE) intervention were examined in a more recent research by Groves et al.[37] PBM was given for 5 days after HIE, while caffeine was given for 3 days. Weighing and urine testing were performed before HIE, every day after the intervention and during the sacrifice to measure biomarkers. According to their findings, KIM-1 was considerably raised for 7 days post-HIE and was lowered by both treatments. Urinary neutrophil gelatinase-associated lipocalin (NGAL) and albumin levels were raised by HIE on days 1-3, although they eventually returned to normal. PBM or caffeine greatly decreased this elevation. When administered separately, neither therapy lessened the kidney damage observed under an electron microscope. Neither HIE nor the therapies had any effect on osteopontin. Treatments ameliorated HIE-induced decreases in the enzymatic activity of mitochondrial complexes III, but not in combination. Caffeine and PBM both enhanced weight gain (Table 1).[37]

Several studies have investigated the effects of PBM on sperm analysis measures.[38-41] Initially, Dadras et al assessed the impact of PBM on testicular tissues and fresh sperm analysis factors in mice that were given streptozotocin (STZ) to induce type 1 diabetes mellitus (T1DM).[38] The mice were randomized into three groups: first laser group (890 nm, 80 Hz, 0.03 J/cm^2), second laser group (0.2 J/cm^2), and control group. Comparing the two PBM groups to the control group, a substantial increase in the length of the seminiferous tubules, the Leydig cell count, and the Sertoli cell count was seen. In addition, a substantial increase was reported in the Sertoli cell count and length in the seminiferous tubules in the second PBM group compared to the first PBM group. PBM with 0.2 J/cm2 and 0.03 J/cm2 energy densities significantly increased the fresh sperm analysis factors and stereological parameters in STZ-induced T1DM mice as compared to the control group (Table 1).[38]

Safian et al examined the effects of the red and NIR ranges of PBM alone and in combination on fresh human sperm.[41] They randomly split 30 normal human semen samples into three distinct PBM protocols (red, NIR, and red + NIR lasers). Three protocols were modified at three different energy densities (0.6, 1.2, and 2.4 J/cm2). After 60 minutes, the progressive sperm motility was significantly increased by the NIR and red + NIR lasers at 2.4 J/cm2 energy density in comparison to the control group. The vitality of the samples treated with the red laser at 0.6 J/cm2 was significantly lower than that of the control group. The NIR laser had no discernible effect on sperm viability in the control or experimental groups. At 2.4 J/cm2 density, 120 minutes after exposure, the groups treated with red + NIR and red laser had a significantly greater DNA Fragmentation Index (DFI) than the control groups. Therefore, in terms of sperm motility, viability, and DFI statistics, the NIR laser at 0.6 J/cm2 energy density was better than the red and red + NIR PBM methods (Table 1).[41]

Hasani et al evaluated the effects of PBM on spermatogenesis using a transient scrotal oligospermia-induced hyperthermia animal model.[40] Their findings demonstrated that PBM could considerably enhance sperm parameters and stereological parameters, such as spermatogonia, primary spermatocytes, round spermatids, and Leydig cells, in addition to raising serum testosterone and glutathione disulfide activity,

Table 1. General Characteristics of Experimental Studies

Study	Origin	Study design	Condition	Study group(s)				Intervention	Safety profile	Results
Groves (2023) [37]	USA	Experimental study	HIE-induced AKI rat model	PBMT Caffeine	7 days 7 days	- -	4-6 4-6	PBMT and caffeine	-	Both PBMT and caffeine treatments reduced kidney injury seen on electron microscopy, but not when combined.
Xia (2021) [35]	China	Experimental study	The human uroepithelial cell line SV-HUC-1 and human bladder cancer cell lines T24 and EJ	-	-	-	-	Blue laser irradiation (450 nm) at various energy densities	-	LLLT can be used in the diagnosis and treatment of bladder cancer.
Zipper (2022) [34]	USA	Experimental study	Pelvic pain and spasm in an adult Suffolk/ Dorset Ewe	-	-	-	-	NIR ranges of PBM	-	Therapeutic effects were reported by applying PBM irradiance to the levator ani muscle and bladder at a power setting of 5 W. A power setting of 0.5 W failed to deliver therapeutic energy.
Asghari (2016) [36]	Iran	Experimental study	Ischemia/reperfusion-induced renal damage in diabetic rats	PBMT group Control group	10–12 weeks	-	10 10	PBMT	-	In diabetic rats, PBM reduced renal damage caused by renal ischemia/reperfusion injury.
Dadras (2018) [38]	Iran	Experimental study	Stereological parameters and sperm analysis factors in type 1 diabetes mellitus mice	First laser group (0.03 J/cm²) Second laser group (0.2 J/cm²) Control	-	All M	5 5 5	PBMT using NIR at two different energy densities (0.03 and 0.2 J/cm²)	-	In comparison to the control group, the stereological parameters and fresh sperm analysis factors were dramatically enhanced by PBM with 0.2 J/cm² and 0.03 J/cm² energy densities.
Safian (2020) [41]	Iran	Experimental study	Sperm motility and viability in a fresh human sperm sample	Red group NIR group Red + NIR group Control group	-	All M	30 samples	PBM with 3 different protocols (red, NIR, and red + NIR lasers)	-	The advantage of NIR laser over the red and red + NIR PBM procedures was supported by data on sperm motility, viability, and DNA Fragmentation Index at 0.6 J/cm2 energy density.
Hasani (2020) [40]	Iran	Experimental study	Spermatogenesis in the transient scrotal hyperthermia-induced oligospermia mouse model	Scrotal hyperthermia group Scrotal hyperthermia receiving laser 35 days after the induction of scrotal hyperthermia. Scrotal hyperthermia receiving laser immediately after induction of scrotal hyperthermia. Control	-	All M	6 6 6 6	PBM immediately after or 35 days after the induction of scrotal hyperthermia	-	PBM might be considered a different approach to enhance spermatogenesis in animals with induced scrotal hyperthermia.
Espey (2022) [39]	Germany	In vitro study	Sperm DNA fragmentation level and acrosomal integrity in human samples	Asthenozoospermic group Normozoospermic group	40.04 ± 6.875 36.16 ± 9.286	All M	42 22	PBM with 4, 6, and 10 J/cm² energy	-	By preserving DNA and acrosome integrity, PBM enhances sperm motility. It is a potentially useful new method for assisted reproductive treatment.

Abbreviations: AKI: Acute kidney injury; F: Female; HIE: Hypoxic-ischemic encephalopathy; LLLT: Low-level laser therapy; M: Male; NIR: Near-infrared; PBM: Photobiomodulation; PBMT: Photobiomodulation therapy

Table 2. General Characteristics of Human Studies.

Study	Origin	Study design	Condition	Study group(s)				Intervention	Safety profile	Results
				Arm	Age	Gender (F/M)	Number			
Leibaschoff (2019) [51]		Two-arm placebo-controlled	Vulvovaginal atrophy	Active PBMT group + Kegel exercise The control group that received only Kegel exercises	45 to 69	All F	8 8	10-minutes, two times per week for four weeks (total of eight sessions) using a TV-PBMT device	No side effect was reported by patients.	Treatment for vulvovaginal atrophy symptoms in postmenopausal women with PBMT showed positive subjective and objective improvement. The treatment is feasible because of its ease of use, cost, and lack of side effects.
Zipper (2021) [48]	USA	Prospective, single-center, before and after, observational pilot study	CCP	Study group	62.8	All F	13	TV-PBMT for 2 days and then semiweekly until nine treatments	No adverse events were reported or identified.	For up to six months, TV-PBMT significantly and sustainably reduced pain in women with CCP.
Kohli (2021) [8]	USA	Prospective, before and after, observational study	CCP	Study group	44.3 ± 15.1	All F	128	TV-PBMT in 9 sessions	No serious adverse events were reported. An increase in bladder symptoms was observed, 13.2% (n = 19) had temporary noninfectious vaginal discharge, and 1.4% (n = 2) were diagnosed with a urinary tract infection around the time of treatment.	Based on the results, 64.5% of women reported improvements in their overall discomfort, vulvar pain, pain during bowel movement, sexual activity, exercise, and urine as compared to baseline.
De Marchi (2023) [45]	Brazil	Prospective, three-arm, parallel, double-blinded, placebo-RCT	Stress urinary incontinence	Placebo of PBMT/sMF plus Pilates method PBMT/sMF active plus method Pilates (PPActG) only PBMT/sMF active (PG)	45 ± 9.56 44.81 ± 10.77 51.19 ± 8.85	All F	11 11 11	Placebo PBMT/sMF Plus method Pilates, PBMT/sMF active plus method Pilates, and only PBMT/sMF active	None	The signs and symptoms of women with SUI were found to improve with PBMT/sMF alone, Pilates, and the combination of the two treatments.
Cassano (2019) [53]	USA	Secondary analysis of a double-blind clinical trial	Major depressive disorder	NIR transcranial PBM Sham therapy	47.3 ± 11.1 50.7 ± 13.3	5/4 6/5	9 11	Transcranial PBMT with NIR or red light	-	Treatment effects on sexual dysfunction may be linked to repeated NIR transcranial PBM sessions.
García (2020) [52]	Spain	Prospective non-placebo-controlled study	Vaginal dryness	Study group	44.8 ± 7.4	All F	20	PBMT and magnetic fields	No pain, complications s or side effects were reported during treatment.	The use of PBMT for the treatment of vaginal dryness provided excellent results, with the improvement of most symptoms of this condition.
Schardong (2021) [42]	Brazil	RCT	CKF	PBMT group Control group	58.1 ± 16.9 53.0 ± 17	7/7 5/9	14 14	PBMT Before the second weekly dialysis session	No adverse effects were observed	Patients with CKF respond better to PBMT when it is used as a monotherapy for 8 weeks in the lower leg.

Table 2. Continued.

Study	Origin	Study design	Condition	Study group(s)				Intervention	Safety profile	Results
				Arm	Age	Gender (F/M)	Number			
Hwang (2022) [44]	Korea	Prospective, double-blind, placebo-controlled, multicenter RCT	Overactive bladder	Intervention group	60.0 ± 9.7	All F	78	skin-adhesive, self-administrative LLLT	The incidence rates of device-related treatment-emergent adverse events were similar between the LLLT and sham groups (25.9% vs. 25.6%). The device-related TEAEs were maculopapular rash, burning sensation, pigmentation, urticaria, and pruritus. However, there were no serious adverse events, such as intolerable abdominal pain or device-related skin reactions. The device was tolerated by all patients	LLLT may be a safe and effective therapeutic technique for an overactive bladder.
				Sham group	59.1 ± 10.2		82			
Butrick (2022) [50]	USA	Before-and-after observational cohort	Interstitial Cystitis/ Bladder Pain Syndrome (IC/BPS)	Study group	48.2 ± 15.1	All F	125	TV-PBMT	No serious adverse events were reported.	Two-thirds of patients who chose to receive TV-PBM treatment in real-world clinical settings reported a significant reduction in dysuria and pelvic discomfort.
Frederice (2022) [47]	Brazil	Double-blind RCT	Pelvic floor myofascial pain	Vaginal stretching + PBMT	40 ± 15.0	All F	51	Vaginal stretching + TV-PBMT	-	Vaginal stretching alone and in combination with PBMT has short-term efficacy in reducing painful intercourse.
				Vaginal stretching + sham PBMT	45 ± 13.9		52			
Hanfy (2007) [46]	USA	RCT	Pelvic inflammatory disease	LLLT group	NR	All F	20	The patients were assigned into two equal groups, group (A) received laser for three months and group (B) received interferential current for three months.	-	LLLT and interferential current were both effective in the treatment of pelvic inflammatory disease; however, LLLT was a more effective modality as an alternative, conservative therapy compared to pharmacotherapy due to its minimal adverse events.
				Interferential current	NR		20			
Ajewole (2022) [49]	USA	Before-after prospective cohort	Chronic pelvic pain associated with endometriosis	Study group	NR	All F	48	8 TV-PBM treatments administered 1-2 times a week for 8 weeks	-	In nearly 60% of patients, TV-PBM significantly reduced the severity of pelvic pain.
Longo (2022) [43]	Italy	Before-after prospective cohort	Peyronie's disease	Study group	35-65	All M	41	PBMT	-	The majority of patients reported positive outcomes after one cycle of treatment. Follow-up findings were also positive after 2 years.

Abbreviations: CKF: Chronic kidney failure; F: Female; LLLT: Low-level laser therapy; M: Male; NIR: Near-infrared; PBM: Photobiomodulation; PBMT: Photobiomodulation therapy; RCT: Randomized controlled trial; sMF: Static magnetic field; TV-PBMT: Transvaginal photobiomodulation therapy

when compared to the scrotal hyperthermia-induced mice. Additionally, the research demonstrated that, in contrast to the animals given scrotal hyperthermia, the groups treated with PBM showed a statistically significant reduction in ROS generation, seminiferous tubule diameter, and the expression of the IL1-α, IL6, and TNF-α genes. Nonetheless, there was no discernible variation in the testis weight or Sertoli cells across the study groups (Table 1).[40]

In the most recent work, Espey et al used a pulsed laser probe (655 nm, 25 mW/cm^2) to apply PBM to native fresh liquefied semen samples of 42 asthenozoospermic patients and 22 normozoospermic controls. The samples were exposed to PBM radiation at energy levels of 0 (control), 4, 6, and 10 J/cm^2, and parameters were measured 0, 30, 60, 90, and 120 minutes after radiation. The results showed that exposure to laser energy doses of 4 and 6 J/cm2 improved sperm motility and velocity in asthenozoospermic patients. Additionally, PBM had no appreciable effect on the level of DNA fragmentation and the expression of CD46, which is a biomarker for acrosome integrity (Table 1).[39]

Clinical Studies and Observations of PBMT in Urological Settings

First, the study conducted by Schardong et al assessed the long-term impact of PBMT on the functional capacity and upper limb muscular strength of patients with chronic kidney failure (CKF).[42] The main goal was to assess the long-term impact and the effects of PBMT on patients' strength, muscle thickness and echogenicity, pain perception, weariness, and quality of life (QoL) after 24 sessions of PBMT on the lower limb during hemodialysis. Only hemodialysis sessions were provided to the control group with physical therapy interventions. Consequently, there was an improvement in lower limb muscle strength and an increase in functional capacity (measured using the six-minute walk test) of the intervention group when compared to the controls. Regarding the remaining outcomes assessed, there was no discernible variation between the groups (Table 2).[42] This was the only randomized controlled trial (RCT) we could find that addressed the application of PBMT for a condition related to the upper urinary tract system.

In one study, Longo and Longo reported the application of PBMT for treating chronic Peyronie's disease.[43] They included 41 patients who showed inflammatory signs for more than 12 months who underwent PBMT at laser wavelengths of 808, 1064, and 10600 nm based on the clinical characteristics of their lesions. One month after the end of the treatment protocol, an echographic test was conducted again to assess the outcome. Most patients had positive results after one treatment cycle, and two years later, follow-up showed continuous improvement (Table 2).[43]

In the RCT conducted by Hwang et al, patients suffering from overactive bladder (OAB) were instructed to apply a self-adhesive LLLT device or a sham device at home three times daily for 12 weeks.[44] The results suggested that LLLT can effectively improve urinary incontinence compared to the sham-controlled group, with similar incidence of device-related adverse events between the two groups (Table 2).[44]

In a three-arm parallel RCT, De Marchi et al investigated the effects of PBMT and a static magnetic field (sMF) on patients with stress urinary incontinence (SUI).[45] In their study, a total of 33 SUI patients were selected and randomly divided into three groups: PBMT/sMF + method Pilates as a placebo, PBMT/sMF active plus method Pilates as an active treatment, and only PBMT/sMF active. On the first and last days of the intervention, muscle strength was assessed, and the ICIQ-SF was filled out. Additionally, the Pad test was used at the baseline, one month, two months, and three months of intervention. When comparing the pre- and post-intervention results for all groups, they saw improvements in strength, tone, and quality of life along with a decrease in urine loss (Table 2).[45]

Hanfy et al reported the results of comparing the therapeutic effects of LLLT and interferential current in 40 patients with chronic pelvic inflammatory disease (PID).[46] The interventions consisted of one 30-minute session every other day for three months. Results demonstrated a very significant decrease in the degree of pain and a highly statistically significant improvement of pain alleviation in the LLLT group compared to the interferential current group (Table 2).[46]

The impact of PBMT with vaginal stretching (VS) on sexual function was investigated in a second RCT by Frederice et al. The study included 103 women with pelvic floor myofascial pain who were randomized into two groups. One group underwent 10 sessions of VS with PBMT (4 Joules of near-infrared light-808 nm at 3 points), while the other group underwent VS with sham PBMT.[47] Their research revealed that compared to the VS with the sham PBMT group, significantly fewer women experienced painful sex in the VS with PBMT group. Perturbation was significantly reduced, according to the Visual Analog Scale (VAS). In both the VS with PBMT group and the VS with sham PBMT group, the number of patients having sexual dysfunction significantly decreased after therapy. Only the VS with sham PBMT group had a statistically significant increase in Female Sexual Function Index (FSFI) desire and total score after treatment (Table 2).[47]

We found three observational studies addressing the application of transvaginal PBMT (TV-PBMT) for chronic pelvic pain (CPP).[8, 48, 49] A regimen of nine treatments was given to 128 CPP-afflicted women over three to four weeks in the cohort study by Kohli et al.[8] Overall, 64.5% of women showed improvement in discomfort, pain associated with bowel movement, sexual activity, exercise, urine, sitting, and vulvar pain. No major adverse events were noted (Table 2).[8] In the 6-month follow-up, Zipper et al showed that TV-PBMT significantly and sustainably

reduced pain in 10 CPP patients (Table 2).[48] Moreover, another observational study by Butrick and Lamvu reported pain management quality (including overall pelvic pain, pain with urination, pain with exercise, pain with intercourse) of TV-PBMT in 140 patients with Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS).[50] After 8 sessions, meaningful improvement (≥2 points) was reported by 63.9% and improvement of ≥1 NRS point was recorded by 73.5% (Table 2).[50]

Eight TV-PBM treatments (1-2 times a week for eight weeks) were administered to women with endometriosis and pelvic discomfort that had persisted for more than 6 months as part of the observational cohort study by Ajewole et al.[49] Their results showed that following TV-PBMT, nearly 60% of endometriosis-affected women reported significantly less severe pelvic pain. Every pain measure showed improvement; the biggest reductions were observed in total pelvic pain, dyspareunia, and dysuria (Table 2).[49]

Using PBMT for the management of vulvovaginal atrophy (VVA) symptoms was a research interest across the literature.[51, 52] In one RCT, the histological and clinical outcomes associated with PBMT application in postmenopausal women were investigated by Leibaschoff and de la Torre.[51] The study participants exhibited notable improvements in their vaginal health, such as notable thickening of the epithelium at the lamina propria, neocollogenesis, and increased angiogenesis and glycogen. The mean VAS and FSFI scores significantly improved one month after treatment and remained positive at three months. After a month, however, there was very little improvement in the FSFI score in the placebo-control group. No adverse events were reported in this RCT (Table 2).[51]

Furthermore, TV-PBMT was applied for treating vaginal dryness associated with VVA in a pilot study by García et al.[52] The treatment protocol consisted of one session of 5 minutes of PBMT per week for 12 weeks. According to their findings, there were no significant side effects, and the majority of the symptoms of vaginal dryness improved when PBMT was used as a treatment for the condition (Table 2).[52]

So far, PBMT has primarily been used for the management of pelvic disorders and sexual function by targeting the genitourinary organs. However, a shift in this traditional approach was observed in a study conducted by Cassano et al.[53] The researchers explored the use of transcranial PBMT for the treatment of sexual dysfunction associated with major depressive disorder.[53] NIR transcranial PBMT or sham therapy was administered twice a week to 20 people for 8 weeks. The Systematic Assessment for Treatment-Emergent Effects-Specific Inquiry was used to measure orgasm, arousal, and sexual desire. Between the entire sample and the sham group, as well as between the completers and the sham group, the improvement in sexual function was considerably higher in participants receiving transcranial PBMT in NIR-mode (Table 2).[53]

Table 3 summarizes the PBMT protocols used in human and experimental studies on urogenital disorders. There is substantial variation in wavelengths (450–10,600 nm), power outputs, energy doses, and treatment schedules. Most human studies employed NIR light via intravaginal or transvaginal devices, with treatment durations ranging from 3 to 12 weeks and frequencies ranging from 1 to 3 sessions per week. Energy densities varied widely, from 0.03 J/cm² to over 1000 J/cm². Experimental studies also showed protocol diversity, but commonly used red or NIR wavelengths. Overall, the table reflects a lack of standardization in PBMT parameters across studies.

Safety and Considerations in PBMT

Across the literature, no serious adverse events have been reported with PBMT. This favorable safety profile is attributed to the use of light within the wavelength range of 650–1200 nm. This spectrum is ideal for cellular chromophores to absorb.[54] Although PBMT shows promise as a treatment for urogenital and pelvic floor problems, it is important to take safety precautions and possible contraindications into account. To maximize therapeutic efficacy while lowering the possibility of side effects, it is essential to use the right light parameters, such as wavelength, energy density, and treatment duration. Furthermore, the distinct features of the pelvic floor and urogenital area, such as their proximity to reproductive organs and possible influence on sexual function, should be given particular attention. Additionally, to guarantee the safe and efficient use of PBMT in this patient population, patient selection, thorough evaluation, and customized treatment planning are crucial.

Future Directions and Research Implications

Future directions and implications for urogenital and pelvic floor disorders need consideration as the field of PBMT develops further. In order to evaluate the potential for disease modification and the durability of treatment effects, long-term follow-up studies are required. Additionally, combining PBMT with behavioral therapy, pelvic floor exercises, or other modalities may provide synergistic benefits for complex pelvic floor and urogenital disorders.

Clinical Implications

Although the evidence base for PBMT in urogenital disorders remains preliminary, some important clinical takeaways can be drawn:

- Adjunctive Role rather than Stand-alone Therapy: Current data suggest that PBMT may serve best as an adjunct to established treatments such as pelvic floor exercises or behavioral interventions, especially in chronic pelvic pain, urinary incontinence, and sexual dysfunction.
- **Patient Selection:** PBMT appears particularly promising for conditions characterized by chronic inflammation, neuromuscular dysfunction,

Table 3. The Protocol of Photobiomodulation Therapy

Study	Device	Wavelength	Pulse frequency	Power	Energy	Duration of sessions	Frequency of sessions	Duration of treatment
			Human Studies					
Leibaschoff (2019) [51]	Intravaginal Class II multi-modality medical device (vSculpt, Joylux, Seattle, WA, USA)	662 +/-20 nm and 855 +/-30 nm	75 to 110 Hz	NR	22 J/cm2	10 min	2/week	4 weeks
Zipper (2021) [48]	SoLa´ Pelvic Therapy (Uroshape, LLC) transvaginal PBM system (TV-PBMS)	NIR	NR	5–8 W	3000 - 3500 J	NR	First 2 days and then semiweekly for a total of 9 treatment sessions	-
Kohli (2021) [8]	SoL´a Pelvic Therapy device	810 and 980 nm	NR	15 W	NR	NR	Total of 9 sessions	3–4 weeks
De Marchi (2023) [45]	Portable model MR5-ACTIVET PRO Laser Shower, Multi Radiance Medical ® (Solon, OH, USA)	905 (±1)	250 Hz	2.84 mW/cm^2	0.085 J/cm^2	NR	2/week	12 weeks
Cassano (2019) [53]	Omnilux New U, light-emitting diode, manufactured by Photomedex Inc.	NIR: 823 nm	NR	36.2 mW/cm^2	65.2 J/cm^2	30 min	2/weeks	8 weeks
García (2020) [52]	Miltagynea® (Milta Technologie, Mudaison, France) intravaginal probe	850 nm	10 kHz	120 W	NR	5 min	1/week	12 weeks
Schardong (2021) [42]	Probe cluster, containing five LLL diodes (Thor® Photomedicine, DD2, London/UK)	810 nm	NR	34.5 W/cm^2	1034.5 J/cm^2	NR	3/week	8 weeks
Hwang (2022) [44]	Skin-adhesive LLLT device called the Color DNA-WSF, a class II device consisting of a power supply unit and two microprocessor-controlled light-emitting diodes	610±10 nm	NR	1.8 mW/ cm^2 ±20%	NR	20 min	3/day	12 weeks
Butrick (2022) [50]	Transvaginal photobiomodulation (TV-PBM) laser system called SoLa Pelvic Therapy (SPT) (Uroshape, LLC)	810 and 980 nm	NR	15 W	NR	NR	2/week	3-5 weeks
Frederice (2022) [47]	Low-level laser device (Model Therapy EC, DMC, Sao Carlos, Brazil, produced in 2018)	Red (660nm) to NIR (808nm)	NR	100 mW	43 J/cm^2	40 s each at the same 3 points	2/week	6 weeks
Hanfy (2007) [46]	Laser LTU 904 H with Gallium arsenide laser diodes	635-670 nm	5 Hz	Max: 5 W	NR	30 min	3/week	12 weeks
Ajewole (2022) [49]	NR	NR	NR	NR	NR	NR	1-2/week	8 weeks
Longo (2022) [43]	NR	808, 1064, and 10,600 nm	NR	NR	NR	NR	NR	NR

Table 3. Continued.

Study	Device	Wavelength	Pulse frequency	Power	Energy	Duration of sessions	Frequency of sessions	Duration of treatment
			Experimental Studies					
Groves (2023) [37]	A custom-built clinical light therapy device (Multi Radiance Medical)	670 nm red light	NR	NR	30 J/cm²	Initial dose: 10 min Subsequent doses: 5 min	2/day	5 days
Xia (2021) [35]	Blue diode laser system (Ligenesis, China)	450 nm	NR	100 mW/cm²	2 to 24 J/cm²	20 s to 240 s	-	-
Zipper (2022) [34]	SoLá Therapy, UroShape, LL	NIR	NR	74 to 738 mW/cm²	-	15 min	-	-
Asghari (2016) [36]	InGaAlP laser irradiation (Teralaser; DMC® São Carlos, SP, Brazil)	685 nm	NR	15 mW	3.2 J/cm²	6 min	-	-
Dadras (2018) [38]	An infrared laser (MUSTANG 2000, LO7 pen, Technica Co., Moscow, Russia)	890 nm	80 Hz	1.08 mW/cm²	0.03 J/cm² and 0.2 J/cm²	NR	3/week	3 weeks
Safian (2020) [41]	Laser probes (NILTVIR202 Noura Instruments, Tehran, Iran)	Red (630 nm), NIR (810 nm), or Red+NIR (630+810 nm)	NR	0.0261 W/cm²	0.6, 1.2, 2.4 J/cm²	-	-	-
Hasani (2020) [40]	NR	890 nm	80 Hz	NR	0.03 J/cm²	30 s	-	-
Espey (2022) [39]	Laser-probe (Reimers & Jansen, Berlin, Germany)	655 nm	584 Hz	25 mW/cm²	0, 4, 6, 10 J	-	-	-

Abbreviations: cm²: Square centimeter H: Hertz; J: Joule; min: Minute; mW: Milliwatt; NIR: Near-infrared; nm: Nanometers; NR: Not reported; s: Second; W: Watt

or pain syndromes (e.g., chronic pelvic pain, overactive bladder, and vulvovaginal atrophy). In contrast, conditions involving severe fibrosis or neurodegeneration (e.g., advanced interstitial cystitis or chronic kidney failure) may show less consistent responses.

- **Safety Profile:** The absence of serious adverse events across clinical studies indicates that PBMT can be considered a low-risk option when delivered with appropriate wavelength (650–1200 nm), energy density, and duration parameters.
- **Individualized Protocols:** There is no universal PBMT regimen for urogenital disorders. Clinicians should carefully consider device specifications, depth of the target tissue, and treatment frequency when applying PBMT, preferably following parameters used in published trials until formal guidelines are established.
- **Integration into Multimodal Programs:** Combining PBMT with pelvic floor physical therapy or lifestyle interventions may optimize outcomes, especially in complex cases where monotherapy has shown limited benefit.

Until robust clinical guidelines are developed, PBMT should be used on a case-by-case basis in consultation with specialists, ensuring informed consent regarding its experimental nature.

Conclusion

Overall, research into the use of PBMT as a treatment for pelvic floor and urogenital problems shows promise. Through the utilization of biological effects of light energy on tissue regeneration and cellular function, PBMT has the potential to treat a variety of ailments. Through our comprehensive investigation of the current literature, we found that in human studies, conditions including Peyronie's disease, OAB, SUI, CPP, PID, VVA, and sexual dysfunction were addressed, while in the animal and in vitro studies, AKI, bladder cancer, and sperm analysis studies were the research focus.

A general pattern of positive effects of PBMT without significant adverse events was observed in both preclinical and clinical studies. It is too soon to recommend incorporating PBMT into standard management procedures, even though comprehensive multidisciplinary approaches for urogenital and pelvic floor disorders may present new opportunities for enhancing overall quality of life and improving patient outcomes. Furthermore, even though there is increasing evidence that PBMT is effective in treating urogenital and pelvic floor disorders, further research is necessary to improve our understanding. This includes well-designed clinical trials, mechanistic studies, and safety evaluations.

Ethics statement

This study was conducted according to the Declaration of Helsinki. This study was supported by the Student Research Committee of Tabriz University of Medical Sciences, Tabriz, Iran (ID: 72831).

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Conflict of interests declaration

The authors declare no potential conflict of interests.

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Consent for publication

Not applicable, as this study is a comprehensive review and does not involve human participants.

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