



# The Role of Laser and Microwave in Treatment of Endocrine Disorders: A Systematic Review

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## Abstract

**Introduction:** The treatment of endocrine problems like thyroid disease, diabetes mellitus (DM), and polycystic ovary syndrome (PCOS) faces significant challenges so that medical professionals worldwide try to find a new therapeutic approach. However, along with common treatments which include medications, hormone replacement therapy, and surgery; there is a growing interest in alternative therapies like laser therapy, which offers a non-invasive and unique technique for treating endocrine disorders alone or in combination with traditional methods. The main goal of this review was to do a systematic review on the role of the laser and Microwave in the treatment endocrine disorders.

**Methods:** In the present systematic review, the most important databases, including PubMed, Scopus and Google Scholar, were searched for the studies examining the effect of lasers on the treatment of endocrine problems by using appropriate keywords and specific strategies from 1995 to 2023. All the studies that were not about lasers and endocrine were excluded.

**Results:** Based on 51 reviewed studies, lasers and radiofrequency ablation such as RFA are effective in the treatment of thyroid diseases, hyperparathyroidism, pancreatic disorders, and sexual dysfunctions. Laser-induced interstitial thermal therapy (LITT) and microwave ablation (MWA) are genuine minimally invasive methods for the treatment of benign nodules, adenomas, and tumor ablation including pancreatic carcinomas and adrenal tumors. Intravenous laser blood irradiation (ILBI) which uses red, UV, and blue light could be effective in treating various metabolic disorders, such as DM.

**Conclusion:** Laser as a cutting-edge and minimally invasive approach could treat various endocrine disorders. It has a great potential to treat and regulate hormonal imbalances, decrease inflammation, and relieve symptoms of various ailments, such as endocrine disorders.

**Keywords:** Laser; Endocrine disorders; Minimally invasive therapy; Systematic review.

## Introduction

Endocrine disorders such as thyroid dysfunction, diabetes mellitus (DM), and polycystic ovary syndrome (PCOS) have posed significant challenges to healthcare providers worldwide. Conventional treatment methods frequently contain the utilization of medications, hormone replacement therapy, or surgical interventions. Traditional treatments for many endocrine problems are successful, but sometimes they are not effective and there is an interest in investigating alternative therapies

to improve or replace them.<sup>1</sup> Laser therapy as a non-invasive and unique technique is being considered due to its potential efficacy in the treatment of various problems. Laser therapy can treat endocrine disorders alone or in combination with traditional treatments.<sup>2</sup> Low-level laser therapy (LLLT) which is in the wavelength range of 600-1100 nm is used in obstetrics, gynecology, andrology, and urology, and it is considered a beneficial physical therapy for male infertility.<sup>3</sup> The local application of LLLT modulates follicular dynamics by regulating apoptosis

and vascular stability in ovaries, together with improving oocytes, as well as boosting sperm quality and motility.<sup>3-6</sup> The interstitial laser therapy of ovaries is suggested as an alternative method for the treatment of reproductive disorders such as PCOS.<sup>7-9</sup> Image-guided thermal ablation (TA), such as laser and radiofrequency ablation (LA and RFA), has become an alternative treatment for symptomatic thyroid nodules and parathyroid adenomas. Several studies presented the efficacy of LA and RFA in treating benign gland disorders.<sup>10-22</sup> Laser-induced interstitial thermal therapy (LITT) and microwave ablation (MWA) that use heat to kill tumors are being used to treat cancers in pancreas, liver, and adrenal glands. These treatments are minimally invasive and use special devices called catheters to deliver heat directly to the tumors.<sup>23-28</sup>

LLLT improves the hormonal and immunological arrangements, cellular respiration, and metabolic modulation, and promotes stem cell differentiation.<sup>29-31</sup> The mechanics of LLLT on biological objects are unknown, and its clinical and biological effects vary by wavelength, strength, and irradiation type. The basic ways it works are by helping biostimulative, palliative, vasodilative, antiseptic, anti-hypoxic, antispasmodic, and anti-inflammatory operations.<sup>32-34</sup> LITT via thermal effect cause the necrosis of tumor related to liver, prostate, lung, and breast cancer. Thermal necrosis at 55 °C kills cancer cells.<sup>35-37</sup> Intravenous laser blood irradiation (ILBI) employing red, UV, and blue light treats various disorders by altering the metabolome and cells and boosting ATP synthesis. It decreases plasma glucose, cholesterol, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL) and boosts arginine and nitric oxide synthesis. In diabetic patients, laser blood irradiation alters plasma metabolite levels. In diabetic patients, laser blood irradiation lowers glucose and raises L-arginine concentration.<sup>15,21,31</sup> Despite the growing evidence that these methods work, there are still obstacles preventing them from being used in endocrine clinical practice. This review aimed to investigate the effectiveness and advantages of laser and microwave in the treatment of endocrine disorders.

### Search Strategy

The PubMed, Google Scholar and Scopus databases were reviewed to identify any study published in the English language, reporting the effect of lasers on the treatment of endocrine disorders in human. Databases were searched by using the keywords “laser”, “Microwave”, “endocrine”, “therapy”, “disorder”, “treatment”, “endocrine problem”, “endocrine disorder”, “laser type”, “low level laser”, “endocrine dysfunction”, “endocrine disease”, and their combinations. All papers, with keywords presented in their titles or abstracts, were used in the initial list, and other unrelated articles were eliminated. Studies were

excluded if they were written in languages other than English, if they were very old, or if they were duplicated studies. In addition, papers with titles or abstracts that did not fit the purpose of this review were excluded from the study. Inclusion criteria included studies in English and on laser and endocrine glands (Figure 1).

## Results

### Parathyroid Disorder

80%–85% of primary hyperparathyroidism (pHPT) is caused by an adenoma in parathyroid.<sup>38</sup> Patients with a parathyroid adenoma respond well to ethanol and RFA.<sup>39</sup> Ultrasound-guided MWA proved to be a safe and efficient treatment. RFA is a popular alternative to parathyroidectomy because of its safety, lack of transcervical incisional scar, and lack of general anesthesia.<sup>40</sup> Secondary hyperparathyroidism is a common and dangerous consequence of chronic renal failure in dialysis patients.<sup>41</sup> Secondary hyperparathyroidism patients benefit from radiofrequency, laser, and MWA.<sup>42</sup>

### Thyroid Disorders

Most individuals with Hashimoto’s thyroiditis (HT) need long-term levothyroxine medication. It has been reported that LLLT recovers thyroid function, lowers TPO antibody, and boosts thyroid ultrasonography echogenicity in hypothyroidism patients.<sup>43</sup> LLLT may improve thyroid function and reduce inflammation in thyroiditis and autoimmune thyroid diseases.<sup>44</sup> It stimulates tissue regeneration and anti-inflammatory mechanisms and increases T3 and T4 levels.<sup>45</sup> TA, LA, RFA, and MWA have been employed to ablate solid or complicated benign thyroid nodules as well as small malignant thyroid lesions like papillary thyroid microcarcinomas and metastatic lymph nodes in high-risk surgical patients. These procedures are also utilized for palliative purposes.<sup>46, 47</sup> LA substantially shrinks solid nodules and relieves local symptoms without affecting thyroid function.<sup>11</sup>

### Pancreatic Disorders

Research shows that laser irradiation may recover pancreatic tissues, including Langerhans  $\beta$ -cells, even at advanced stages.<sup>48</sup> ILIB modifies hormones, metabolic state, and immunity. It reduces plasma cholesterol, LDL, VLDL, glucose. The systematic effects of ILBI may treat complex diseases like DM by lowering plasma insulin-glucagon, glucose-6-phosphate, dehydroascorbic acid, R-3-hydroxybutyric acid, L-histidine, and L-alanine.<sup>31,49</sup> Low-intensity laser blood irradiation (LLBI) regenerates pancreatic function, and it significantly improves blood metabolites in type 2 DM patients.<sup>48,49</sup> One research showed that 630-nm laser therapy improved insulin secretion in isolated pancreatic islets in rats before transplantation.<sup>50</sup> Another study found that extravascular ILBI combined with hypoglycemic medications (metformin and

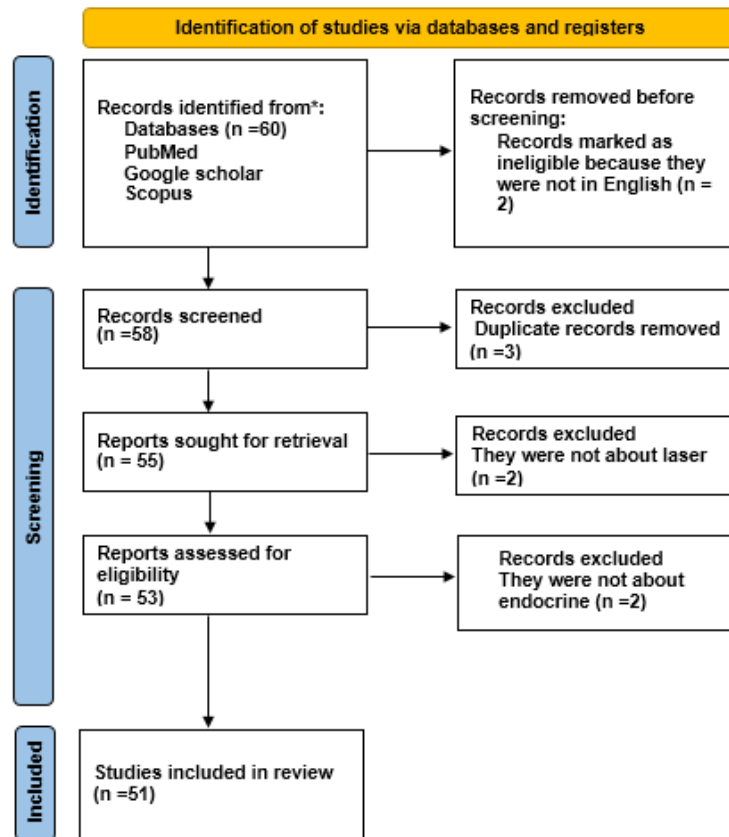


Figure 1. Flow diagram of study selection in this review

sulphonyl urea) in type 2 DM patients could lower fasting blood sugar and HbA1c levels. Their study suggested intravascular laser irradiation as a novel diabetes treatment.<sup>51-53</sup> One investigation proved that PBM might lower insulin levels by 75%, allowing type 1 and type 2 DM patients to stop taking medication for six months.<sup>54,55</sup> Acute pancreatitis causes 30% mortality mostly due to systemic inflammation and multiple organ failure. Severe pancreatitis is described with low albumin and high toxicity index, resulting in pancreatic encephalopathy. Some suggest phospholipase A2 hyperactivation, low oxygen saturation, and lipid peroxidation as the mechanism. LLBI possesses antioxidant characteristics, which alleviate the severity of endogenous intoxication and symptoms of encephalopathy and cure acute destructive pancreatitis.<sup>56,57</sup> Minimally invasive laser treatments including LLBI reduce mortality in sterile pancreatic necrosis from 20.4% to 4.9%. The low-intensity laser and mexidol antioxidant can cure acute pancreatitis.<sup>58</sup> Pancreatic cancer (PC), the fifth most common cause of cancer deaths in the West, requires major surgery to cure; nevertheless, most patients are inoperable upon diagnosis because late symptoms imply metastatic or locally progressed PC. Thus, the treatment of choice would be ablative therapy. Due to a high mortality rate of PC, preclinical studies have used local ablative procedures like RFA to ablate or palliate nonsurgical candidates. LITT for pancreatic neoplasia requires thermal response measurement in irradiated

pancreas.<sup>59,60</sup> Pancreaticobiliary malignancies can be treated by using photodynamic therapy (PDT).<sup>61,62</sup>

### Adrenal Disorders

Nonfunctioning adenomas are the most common adrenal tumors, often misdiagnosed and untreated. These can be malignant or functional, such as cortisol-secreting adenomas, pheochromocytoma, and aldosteronomas. Benign nonfunctioning adenomas can be difficult to distinguish from malignant or functional adrenal tumors, which can be treated. Treatment options include LITT, percutaneous radiofrequency, cryoablation, microwave, and chemical ablation. Percutaneous ablation is popular due to medical imaging enhancing the detection of incidental adrenal tumors and requiring less invasive treatments for patients with multiple comorbidities.<sup>63-68</sup>

Adrenal cortical carcinoma (ACC) is a rare aggressive tumor, with 1-2 incidences per million in the US and with limited treatment options, and it is mostly metastatic at diagnosis.<sup>69</sup> Surgery is the mainstay, and for those who cannot undergo surgery, minimally invasive procedures like percutaneous LA or RFA are being explored as alternatives.<sup>70</sup> Local RFA can treat small primary or metastatic ACC. Nevertheless, the scarcity of ACC has resulted in little familiarity with these methods.<sup>71</sup>

### Ovarian Diseases

Laser therapy has been proven to improve ovarian

function and menstrual regularity in patients with PCOS. New ovarian interstitial laser treatment may help PCOS patients manage anovulation. Recurrent ultrasound-guided transvaginal ovarian interstitial laser treatment for anovulatory PCOS patients has led to an ovulation rate of over 80% and a pregnancy rate of 30% after six months.<sup>72</sup> LLLT improves follicular development in comparison with clomiphene treatment. It has also been reported that LLLT increases VEGF levels in a human granulosa cell line.<sup>73-77</sup> Endometrioma, or deep ovarian endometriosis, is linked to infertility, decreased anti-Mullerian hormone (AMH) levels, and poor ovarian stimulation. Surgical treatment is recommended for larger or advanced endometriomas, but endometrioma surgery may harm ovarian microhistological and microanatomical function. Laser vaporization is a method which may protect ovarian function.<sup>78-81</sup>

### **Testis Diseases**

The treatment of infertility may include LLLT, and it is suggested that local red and infrared lighting should be supplemented with ILBI.<sup>82</sup> Research suggests that low-intensity laser illumination can enhance animal sperm motility, ATP production, cell life expectancy, and fertilization. Studies have shown that laser therapy can boost testosterone production in testicular cells and improve spermatozoa survival, quality, and speed.<sup>83</sup> Studies have shown that LLLT can improve sperm motility and live sperm cell percentage, and it has been found to be more effective than needle acupuncture.<sup>84-86</sup> Research has also demonstrated that LLLT radiation on the vaginal area can enhance sperm motility in individuals with certain sperm conditions.<sup>87,88</sup>

### **Pituitary**

Diode laser-assisted sphenoidotomy is a safe, minimally invasive pituitary gland procedure. It improves surgical field quality and saves operation time. The diode laser has been used in endonasal surgery because of its hemostatic, vaporization, and photocoagulation properties.<sup>89</sup> Endoscopic transsphenoidal technique, first reported by Griffith in 1987 as a revision of Hirsch's original approach, is a modern neurosurgery milestone for treating pituitary and cellular lesions.<sup>90,91</sup>

### **Hypothalamic**

Stereotactic laser ablation due to its early successes is being used for brain metastases, recurrent and original gliomas,<sup>92,93</sup> periventricular nodular heterotopia,<sup>94</sup> hypothalamic hamartomas (HHs),<sup>95,96</sup> and radiation necrosis.<sup>97</sup> Stereotactic laser ablation reduces postoperative morbidity and cognitive impairment in hypothalamic and deep intraventricular lesions, while radiosurgery has a seizures-free rate of less than 40% and open and endoscopic resection has 50%-65%. Evidence

revealed that stereotactic laser ablation may enhance seizure control and reduce complications compared to current therapy.<sup>98-100</sup> The studies about using the laser for the treatment of endocrine disorder are summarized in Table 1.

### **Discussion**

Today lasers have enjoyed successful application to a wide variety of conditions, especially in the medical field. The present review evaluated 51 studies on the use of lasers in the treatment of endocrine dysfunction. Endocrine diseases have a high prevalence, and medical doctors are looking for a new treatment approach.<sup>1</sup> Medical lasers are used to improve cell and tissue function, relieve pain, reduce inflammation, promote wound healing, and prevent tissue damage. They can be used to treat various ailments, such as nerve system ailments, chronic neck discomfort, and diseases like rheumatoid arthritis and osteoarthritis.<sup>32</sup> Laser therapy is a non-invasive treatment option that can be used alongside conventional methods, providing a safe and cost-effective alternative. It is developed by interdisciplinary teams and can be used to treat endocrine disorders like thyroiditis, pancreatitis, and joint pain associated with diseases like PCOS and endometriosis.<sup>101-103</sup> There are many types of lasers in the medical field, but some of them have more applications.<sup>33</sup> Low-level lasers influence biological systems non-thermally.<sup>104</sup> LLLT is a red light near-infrared wave with a wavelength of 600-1000 nm and a power output of 5-500 mW, which is used in the treatment of endocrine disorder. Unlike surgical lasers, which use 300 nm, low-power lasers can penetrate skin without burning or damaging it. Recently developed low-power lasers can relieve pain and speed up healing in various clinical issues.<sup>105</sup> LLLT decreases inflammation and pain while inducing tissue regeneration, without producing thermal effects.<sup>106</sup> It has been found to reduce inflammation by altering the pro-inflammatory factor.<sup>1</sup> LLLT has been explored as a potential treatment for endocrine disorders, especially in the hormone deficiency condition. It also increases hormone production.<sup>107,108</sup> Chronic inflammation is a common characteristic in endocrine illnesses, affecting tissue impairment and hormone dysregulation. LLLT has been shown to exhibit anti-inflammatory properties and facilitate the process of tissue repair.<sup>43,108</sup> According to this review and other studies, laser therapy has the potential to treat endocrine diseases, but there is a further need for investigation in this field. Long-term prospective studies are required to understand the lasting impacts of laser therapy on endocrine disorders.<sup>109</sup> There are some limitations to this review that must be mentioned. It is necessary to investigate more studies. In addition to a number of studies, more endocrine glands should be checked. Therefore, more research of higher quality and with better methodological design is necessary.

**Table 1.** Summary of the Studies Reporting Outcomes for Treatment Strategies Employing a Laser in Endocrine Disorders

Disorder	N	Type of Laser Used	Study Design	Outcome	Ref.
Parathyroid HPT/ parathyroid adenoma	6	LA: 1.064 $\mu$ m 200 nm 15 W	Cohort; pHPT patients underwent flat-tip LA in 2-3 US-guided sessions. PTH, ca levels check for 54 $\pm$ 34-month	LA reduced PTH and calcium levels in patients, but they still required surgery. Also, a definitive cure for HPT was not offered.	17
	10	RFA: 17G needles 40 W-80 W	Cohort; inoperable pHPT ones with Hyper-Ca underwent US-guided percutaneous RFA.	RFA is a safe and effective alternate method for the treatment of parathyroid adenoma.	22
	27	RFA: 10-70 W, EA	Cohort; 19 patients had undergone US-guided RFA, and EA was performed in 8 patients.	RFA reduced PHPT nodule size and volume at 6 and 12 months. EA reduced SNPC cyst size and volume.	18
	104	MWA: (16 G needles or 17 G needles), RFA: 7 mm, 30 W, 35 W	Cohort; 77 patients underwent MWA and 27 underwent RFA, then were tested for pHPT.	Both RFA and MWA are safe and effective techniques for the treatment of patients with pHPT.	19
	12	LA: 3 W power for 400-600, 3600-9000 J of energy	Cohort; before and after study. PTH, Ca levels tested every 6 months for 2 years.	LA lowered the volume of PTH, Ca at 1, 12, and 24 months. RFA treated Hyper-Ca by reducing PTH.	21
Thyroid Autoimmune thyroiditis	43	LLLT: 830 nm with 50 mW power	Clinical trial; case and control. 23 patients received LLLT and 20 received placebo.	LLLT improved thyroid function, reduced TPO Ab autoimmunity, and increased thyroid echogenicity against the control group.	42
	200	LTA: 1064-nm wave length with 3 W power	Clinical trial; 101 cases and 99 controls. Volume and local symptom changes were evaluated 1, 6, 12, 24, and 36 months after LAT.	LTA 50% reduced nodules in 67.3% of cases compared to the control.	11
	406	RFA: 18 needle G LA: 1064 nm diode laser	Cohort; 14 % of patients received RFA and 18 % received LA. For 5 years following benign thyroid nodule, regrowth, prognostic variables evaluated.	LA was 63% effective, whereas RFA was 85% in reducing benign thyroid nodule volume.	20
	62	PLA: PLA was performed with a 1.064 $\mu$ m laser wave length with 3 W.	Clinical trial; 21 PLA groups, 21 LT4 groups and 20 follow-up groups. PLA received a US-guided 1.064 $\mu$ m laser, LT4 received medication, and the follow-up group received no treatment.	A single PLA induced significant volume reduction and improvement of local symptoms. PLA was more effective than LT4.	10
	1531	LAT: 3W, 1200 and 1800 J energy per fiber	Clinical trial; before and after study. The sizes of nodule were tested.	Nodule volume reduced by 72% $\pm$ 11% (48%-96%) at 12 months, with slight adverse effects.	12
	171	Percutaneous LA: 300- $\mu$ m needle G, 510 J energy per mL (424-680)	Cohort; 10-year follow-up study of LA for benign thyroid nodules in 171 patients.	At 1 year, the median nodule volume cut by 68%, and a 59% volume reduction ratio after 10 years. Laser ablation provides long-term benefits and the treatment is well tolerated.	15
	30	Percutaneous LA: 1,064-nm wave laser with 3 W power	Cohort; US evaluation was performed weekly and at 1, 3, 6, and 12 months, and annually for 5 years.	In 1 month, symptoms improved, volume nodules fell 50% at 3 months, and response lasted 5 years.	16
	60	RFA: 55 W LA: 1064 nm with 3 W power	Clinical trial: 30 patients received LA and 30 patients received RFA, and they were assessed for solid nodules, with 6-month evaluation, over 5 years.	Nodule volume reduced 64.3% in RFA and 53.2% in LA at six months.	13

Table 1. Continued.

Disorder	N	Type of Laser Used	Study Design	Outcome	Ref.
DM	60	Helium-Neon (630 nm), LED Red (630-750 nm), Infrared (850-960 nm)	Follow-up study; 60 patients received Helium-Neon, LED Red or Infrared. Patients were evaluated for insulin response.	Helium-Neon LED Red and Infrared may help diabetics live a normal diet and life without insulin injections and hypoglycemic medicines.	46
	16	PDT	Clinical trial: 8 type 2 DM received PDT and 8 received just standard treatment for 90 days. HbA1C levels were assessed before and 90 days after therapy.	PDT could lower glycemic levels in chronic periodontitis patients with improved HbA1c levels after 3 months.	53
	60	LLL: 650 (nm)	Clinical trial; 30 patients with type 2 diabetes received LLL therapy and 30 patients just received medication. The HbA1c, FBS, GTT, and C-peptide responses to 36 ELBI sessions.	There was a significant decrease in HbA1c, fasting plasma glucose, and oral glucose tolerance in the laser group compared with the control group.	50
	9	ILBI: blue light laser 1.5 mW, 405-nm	Clinical trial; this is before and after study. ILBI's effects on type 2 DM was evaluated with blood metabolites before and after.	L-arginine rose, BS, Glu-6-phos, L-histidine, and L-alanine reduced after exposure.	47
	24	ILIB: 1.5 mW, 405-nm, 630 nm	Clinical trial; this is a before and after study. Before and after ILIB, the serum BS level in type 2 DM patients was measured.	There was a 14.445 mg/dL BS reduction after ILIB.	30
Pancreatic disorders	27	Intravenous ILBI: 2 mW, 405-nm	Clinical trial: 3 rounds of daily 10-session laser therapy for 6 months via irradiation of the liver, pancreas, spleen+ intravenous blood laser.	Patients showed a big decrease in their mean blood sugar, lipid reduction, and a significant drop in retinopathies and angiopathies.	55
Acute pancreatitis	118	Low-intensity laser (600-1100 nm)	Clinical trial: 73 cases and 45 control laser therapy were used to treat pancreatitis.	Minimally invasive LLLT reduced pancreas necrosis mortality from 20.4% to 4.9%.	56
	54	Diode laser: 0.63 μM	Clinical trial: 28 cases and 26 controls. The cases received mexidol and Diode laser, and conventional treatment was given to the controls.	Symptoms in cases were eliminated after 3 days of receiving mexidol and Diode laser, with pain reduction and improved clinical and laboratory findings.	57
Pancreatic encephalopathy	60	Low-intensity laser radiation (635 nm, power 2 mW)	Clinical trial; 30 cases received standard therapy and laser therapy and 30 patients received just standard therapy as the control.	Albumin, peptides, o2 saturation, toxicity, lipoperoxidation, endogenous intoxication, & encephalopathy improved in the case group.	54
Pancreatic neoplasia	15	imILT: 1064 nm wave length, 25 W power	Cohort: imILT was performed in advanced pancreatic cancer patients.	After imILT, all patients were treated, but three late pancreatic fistulas were seen.	61
	11	CPL: a 200- to 272-μm	Cohort; CPL for cholangio pancreatoscopes was performed. Success was defined as ability to traverse the stricture with the cholangiopancreatoscope after CPL.	Technical success was 94.1% instant and 88.2% short-term.	62

Table 1. Continued.

Disorder	N	Type of Laser Used	Study Design	Outcome	Ref.	
Adrenal	Adrenal tumors	22	Percutaneous RFA: 200 W, MWA: 60 W, 45 W.	Cohort; patients were ablated in 23 sessions. Successful treatment was defined as a lack of both enhancement on contrast enhanced CT and/or up-take on FDG PET-CT and for functioning tumors.	Laser Adrenal tumor ablation cured 81% of local metastases for 14 months.	60
		6	RFA performed by using a coaxial LeVein needle probe with an active diameter of 3 or 4 cm at 40–80 W	Clinical trial; before/after study. A reduction in tumor size was considered a success.	RFA is effective for local control of adrenal metastases, without major complications and with a low morbidity rate related to the procedure.	63
		12	Laser auto fluorescent spectroscopy wave length 632.8 nm.	Clinical trial; IOLA use to measure autofluorescence intensity, by touching tumor, adrenal tissues with optical catheter.	IOLA can be an effective method for detecting adenomas, pheochromocytoma, aldosteroma, and malignant lymphoma.	64
		5	MWA: 1–100 W power, at 2450 MHz	Clinical trial; this is a before/after study. Technical success was defined as loss of tumour enhancement on contrast-enhanced imaging.	All adrenal metastases were completely ablated after scheduled MW ablation sessions.	65
	Adrenocortical carcinoma	9	MWA: 50-70 W	Cohort; adrenal carcinomas received CT-guided MWA. For 2.1–6.1 cm tumors, in 7.7 min.	Percutaneous CT-guided MWA water-cooling was effective in the treatment all patients after 11.3 months.	24
		4	Percutaneous laser ablation(PLA): (Nd: YAG) 1064 nm, 300 mm	Clinical trial; this is a before/after study. Four Cushing's syndrome and ACC hepatic metastases patients received US-guided PLA.	PLA abated adrenal metastases, reduced tumors and symptoms, and lowered volume after 4 months.	70
	Functional neoplasms	8	RFA: 200-W power, 480-kHz	Clinical trial; image-guided RFA was evaluated over 27 months on 15 primary/metastatic adrenocortical carcinoma (ACC).	Percutaneous, image-guided RFA is a safe and well tolerated procedure for the treatment of unresectable primary or metastatic adrenocortical carcinoma.	28
	Adrenal metastases	13	RFA: 200-W power, 480-kHz	Cohort; patients with adrenal neoplasms underwent RF ablation during a 7-year period.	All patients' demonstrated normal adrenal biochemical and symptoms improved.	27
	9	LITT: (Nd: YAG): 1064 nm	Clinical trial study; this is a before/after study. LITTs were performed, and follow-up studies were performed at 24 h and 3 months and, thereafter, at 6-month intervals (median 14 months).	LITT is a safe, minimally invasive and promising procedure for treating adrenal metastases. Complete ablation was achieved in seven lesions.	26	
Ovary	Ovarian dysfunction/OHS	26	Laser (Nd: YAG): 15 to 20 W, 8 to 10 W	Clinical trial; the laser beams were focused on the wall of the cysts that were larger than 5 mm. The duration of the laser output was approximately 1 to 2 seconds. After treatment as outcomes pregnancy were seen in 26 PCOS patients.	Laser vaporization improved pregnancy outcomes in 19 of 26 PCOS patients.	71
		400	PBM: 808 nm, Red LED: 660 nm.	Clinical trial; the GigaLaser was placed 1 – 2 cm above the bare skin. Each treatment lasted 23 minutes, and the total dose was 20,000 Joules.	PBM induced in 260 pregnancies in 400 women,	74
	Genitourinary syndrome of menopause	30	CO2 laser: 30 W, 26 W, 800 mm.	Clinical trial; it included 14 cases and 16 controls. For six months vaginal health index was checked out.	Fractional CO2 laser reduced vulvovaginal atrophy but not GSM-related dyspareunia.	75
	PCOS	19	YAG laser: 3 to 5 W, 9 to 10 W	Clinical trial; before and after study. In clomiphene citrate-resistant PCOS, transvaginal US-guided laser was assessed for ovulation.	Ovarian interstitial laser surgery could help mature normal follicles in vivo, resulting in 84% spontaneous ovulation. 16 of 19 cases ovulated regularly during the 6-month postoperative period.	76
	Ovarian endometrioma	25	Laser acupuncture 600-1000 nm	Clinical trial; 13 cases and 12 controls of PCOS patients. Laser acupuncture was tested on PCOS women's hormone levels and insulin resistance at baseline and 12 weeks.	Despite similar baseline features, laser acupuncture lowered BMI, blood hormonal, & insulin resistance in PCOS women.	77
		60	CO2 laser 13 W	Clinical trial; 30 cases and 30 controls. CO2 laser vaporization was tested for endometrioma postoperative ovarian reserve.	AFC increased significantly in the case group at 1- and 3-months post-treatment, especially in women under 35 years, but serum AMH did not show reduction.	80
		90	Laser vaporization CO2 laser: 30 W/cm2	Clinical trial; ovarian cystectomy or laser vaporization were used for endometriomas treatment. Patients were compared for a 5-year recurrence.	Laser ablation had greater rates of ovarian endometrioma recurrences than laparoscopic cystectomy.	81

Table 1. Continued.

	Disorder	N	Type of Laser Used	Study Design	Outcome	Ref.
Testis	Testicular dysfunction: male infertility	1	Laser Acupuncture 810 nm, 400 mW power	Clinical trial; before /after study. Laser acupuncture was assessed for semen quality twice a week in 15 sessions to treat male infertility.	After 15 sessions, spermograms exhibited 23% motility, 25% morphology, and sperm count and volume alterations.	5
		20	LLLT: (904 nm, 12 W)	Clinical trial; before/after study. LLLT was used for the treatment of male infertility.	15 of 20 individuals increased libido and improved sperm quality (more motility, fewer abnormalities).	87
	Epididymitis/orchitis	117	LLR: 632.8 nm, 28 mW power	Clinical trial; the general effects of LLR on the exocrine and endocrine functions of the accessory sex glands were examined.	LLR may affect exudative response, macrophage migration, fibroblast activity, LH, FSH, ACTH, prolactin, testosterone, cortisol, and aldosterone.	88
Pituitary	Pituitary adenoma	41	Diode laser: 940 nm	Clinical trial; before/after study. The diode laser was used for transsphenoidal surgery.	The diode laser-assisted sphenoidotomy is a reliable and safe approach of pituitary gland surgery with minimal invasiveness.	91
Hypothalamus	Hypothalamic lesions	5	MRI-guided laser ablation: Visualize laser (titanium inner stylet)	Clinical trial; before/after study. Laser ablation was used for hamartomas with utilizing frameless interventional MRI.	Two patients had no seizures after treating five.	99
		12	Laser ablation	Cohort; LA was done on hypothalamic and deep intraventricular lesions.	67% of patients had a clinically significant reduction in seizure frequency.	100

N, Number of patients; ACC, adrenal cortical carcinoma; ACTH, adrenocorticotropic hormone; AFC, antral follicle count; AMH, anti-Mullerian hormone; Auto Abs, auto antibodies; ART, assisted reproductive technology; BMI, body mass index; BP, blood pressure; bRFA, bipolar radiofrequency ablation; BS, blood sugar; Ca, calcium; CT-guided, computed tomography-guided; CO<sub>2</sub> laser, Fractional carbon dioxide laser; CPL, Cholangiopancreatography guided laser ablation; DM, diabetes mellitus; EA, ethanol ablation; ELBT, extravascular laser blood irradiation; EUS, endoscopic ultrasound; FBS, fasting blood sugar; FSH, follicle-stimulating hormone; Glu, glucose; Glu-6-phos, glucose-6-phosphate; GSM-related, genitourinary syndrome of menopause-related; GTT, glucose tolerance test; Hyper-Ca, hypercalcemia; HbA1C, glycated hemoglobin A1c; HH, hypothalamic hamartoma; HMG, human menopausal gonadotropin; IGTA, image-guided thermal ablation; ILBI, intravenous laser blood irradiation; imILT, immunostimulant interstitial laser therapy; IOLA, intraoperative laser auto fluorescent spectroscopy; LA, laser ablation; LAPC, locally advanced pancreatic cancer; LED, light-emitting diode light therapy; LEDCT, light-emitting diode chromotherapy; LITT, laser-induced interstitial thermal therapy; LBI, laser blood irradiation; LH, luteinizing hormone; LLLT, low-level laser therapy; LLLI, low-level laser irradiation; LLR, low-energy laser radiation; LTA, laser thermal ablation; LT4, long-term levothyroxine; MLIEI, multiple lower-intensity energy illuminations; MRI-guided, magnetic resonance imaging-guided; MWA, microwave ablation; Nd-YAG, neodymium yttrium aluminum-garnet laser; OHS, ovarian hyperstimulation syndrome; PBM, Photobiomodulation; PCOS, polycystic ovary syndrome; PDT, photodynamic therapy; PLA, percutaneous laser ablation; PTH, parathyroid hormone; pHPT, primary hyperparathyroidism; RASS, Richmond Agitation-Sedation Scale; RFA, radiofrequency ablation; SEGA, subependymal giant cell astrocytoma; SNPC, symptomatic nonfunctioning parathyroid cysts; SLAH, stereotactic laser ablation amygdalohippocampectomy; T3, triiodothyronine; T4, tetraiodothyronine; TPOAb, thyroid peroxidase antibodies; UV, ultraviolet; US-guided, ultrasonography-guided; VAS, vascular autonomic signal.

## Conclusion

In summary, on the basis of the studies in this review, laser therapy is effective in the treatment of endocrine disorder, is safe, and has no adverse effects. The laser has the potential for the treatment of endocrine disorder. It modulates hormonal imbalances, reducing inflammation and alleviating symptoms dealing with a variety of illnesses, including endocrine dysfunction.

## Authors' Contribution

**Conceptualization:** Alireza Ahmadzadeh.

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**Methodology:** Alireza Ahmadzadeh.

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**Supervision:** Alireza Ahmadzadeh.

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## Competing Interests

There are no competing interests.

## Ethical Approval

This research has received the code of ethics IR.SBMU.LASER.REC.1402.038 from Shahid Beheshti University of Medical Sciences.

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