INTRODUCTION

Aggressive periodontitis (AgP) comprises a group of rare, often severe, rapidly progressive forms of periodontitis often characterized by an early age of clinical manifestation and a distinctive tendency for cases to aggregate in families. Although the amounts of microbial plaque deposits are inconsistent with the severity of periodontal tissue destruction, it is well-indicated that elevated proportions of Aggregatibacter actinomycetemcomitans (Aa) are implicated in the pathogenesis of the disease. The disease is also characterized by abnormalities of phagocyte functions and hyper-responsive macrophage phenotype, including the elevated production of prostaglandin E₂ and interleukin (IL-1β) in response to bacterial endotoxins. Such responses at the cellular level could lead to rapid attachment loss and bone destruction resulting in tooth loss.

The successful treatment of AgP is considered to be dependent on early diagnosis, as well as directing therapy toward the elimination or suppression of the infecting microorganisms and providing an environment conducive to long-term maintenance. This, however, relates to specific efforts to affect the composition and not only the quantity of the subgingival microbiota. Scaling and root planing (SRP) is by far the gold standard treatment in treating any form of periodontitis, including AgP. Several researchers have reported that SRP of AgP lesions could not predictably suppress Aa...
below detection levels, and has been implicated as the reason that AgP does not respond to conventional SRP alone. These pathogens are known to remain in the tissues after therapy to re-infect the pocket. Therefore, the use of local and systemic antibiotics was thought to be necessary to eliminate pathogenic Aa from tissues. However, antibiotics are associated with certain systemic side-effects that limit their use. To circumvent these problems, several new therapeutic modalities have been introduced to abate periodontal infections in AgP, including photodynamic and low-level laser therapy (LLLT).

A number of studies have reported the outcomes of LLLT in the treatment of AgP with conflicting results. A recent clinical study by Annaji et al showed that clinical and immunological outcomes were significantly better for the LLLT group compared to the SRP group at follow up. Similar results were reported by Kamma et al. However, in a recent study, Ertugrul et al concluded that patients with AgP treated with LLLT showed comparable improvement in clinical outcomes between the LLLT and SRP groups at follow up. There appears to be controversy in regard to the role of LLLT in the treatment of AgP, and considering the diversity of these results, a systematic review was warranted. Therefore, the aim of the present study was to systematically review the efficacy of LLLT as an adjunct to SRP vs SRP alone in the treatment of AgP.

2 | MATERIALS AND METHODS

2.1 | Focus question

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines were followed, and a focused question was developed. The addressed PICO (Population, Interventions, Comparisons, and Outcomes) question was: Is LLLT as an adjunct to SRP effective in the treatment of AgP?

2.2 | Selection criteria

The reviewer independently screened and assessed potential articles. Studies that did not fulfill the inclusion criteria were excluded. The inclusion criteria of the present review followed the PICO5 question: (a) Population, diagnosis of AgP; (b) Interventions, experimental group in the included studies allocated to SRP with adjunctive LLLT; (c) Comparisons, compared to SRP alone; (d) Outcomes, with outcome measures of interest were primary and secondary. The primary outcome was clinical attachment level (CAL) gain; the secondary outcomes were bleeding on probing (BOP), plaque index (PI), and probing depth (PD); and (e) Study design, randomized clinical trials (RCT) and non-RCT or retrospective controlled clinical trials published in English only. Animal studies, in vitro studies, opinion articles, letters to the editor, review articles, interviews, updates, abstracts, and unpublished studies were excluded.

2.3 | Search strategy

Electronic databases, including MEDLINE via PubMed, Cochrane Central Register of Controlled Trials and Cochrane Oral Health Group Trials, and EMBASE, were searched until March 2018. The literature search was conducted using the combinations of the following MeSH text words: laser therapy OR laser AND periodontal diseases OR periodontitis OR aggressive periodontitis. Manual searching of the following journals was performed from 1982 to 2018: Photomedicine and laser surgery, Journal of cosmetic and laser therapy, photodiagnosis and photodynamic therapy, Lasers in medical science. Additional relevant articles were searched manually from the reference lists of full texts. Any differences regarding study selection were resolved by the author.

2.4 | Screening methods and data abstraction

Titles and abstracts of studies that fulfilled the inclusion criteria were screened and assessed. Data were extracted from the included studies based on the following parameters: author/country, study design (RCT), patients (sample size, mean and age range in years), inclusion of confounders, periodontal diagnostic criteria, study groups, study outcome, follow ups, and characteristics of laser.

2.5 | Statistical analysis

In the present review, the primary outcome was CAL gain in millimeters, whereas the secondary outcome was reduction in PD. Meta-analyses were conducted separately for each of the primary and secondary outcomes. In addition, heterogeneity among the included studies for each outcome was assessed using the $\chi^2$-test and I² statistic. For analyses, if the test indicated substantial or considerable heterogeneity ($I^2 > 50\%$), a random effects model would be used; otherwise ($I^2 \leq 50\%$), a fixed effects model would be applied. $P < 0.05$ represented significant heterogeneity. Forest plots were computed reporting weighted mean difference (WMD) of outcomes and 95% confidence intervals (CIs). The pooled effect was considered significant if $P < 0.05$. Data unsuitable for quantitative analysis were assessed descriptively. All above statistical analyses were carried out using specialized statistical software (B-8400 v 15.11.04; MedCalc Software, Ostend, Belgium).

3 | RESULTS

3.1 | Study selection

In total, 114 and 42 study titles and abstracts were initially identified in the manual and electronic databases, respectively; 146 articles were excluded, as they were considered irrelevant to the focus question. Ten papers were selected for full-text reading. Of these 10 studies, six were further excluded. After the final stage of selection, four studies were included and processed for data extraction. The study identification flowchart according to PRISMA guidelines and reasons for article exclusion are shown in Figure 1.
3.2 | General characteristics of included studies

One non-RCT\textsuperscript{16} and three RCT\textsuperscript{12,14,15} were included in the present review. The studies were carried out in Italy,\textsuperscript{12} Turkey,\textsuperscript{16} India,\textsuperscript{14} and Greece.\textsuperscript{15} In all of the studies, the number of participants ranged between 13 and 31, with a mean age range of 27.3–41.8 years.\textsuperscript{12,14–16} All of the studies reported the percentage of female participants, which ranged between 53% and 60%.\textsuperscript{12,14–16} The presence of confounders, such as smokers, were included in one study,\textsuperscript{15} and was unclear in one study.\textsuperscript{12} All of the studies used the combined approach LLLT+SRP in the test group and SRP alone in the control group;\textsuperscript{12,14–16} the follow-up period for all of the studies ranged from 4 to 52 weeks (Table 1).\textsuperscript{12,14–16}

3.3 | Laser parameters of the included studies

All the studies used diode lasers.\textsuperscript{12,14–16} The wavelengths of different lasers used in the included studies ranged between 810 and 980 nm. Energy fluence and power output were 94.3 J cm\textsuperscript{-2} and 1000 mW, respectively. The duration of irradiation ranged from 20 to 30 seconds in the included studies. Three studies did not mention power density\textsuperscript{12,14,16} and optic fiber diameter.\textsuperscript{15–16} The total number of low-level laser application was unclear in three clinical studies (Table 2).\textsuperscript{12,14,15}

3.4 | Clinical periodontal parameters of the included studies

All of the studies reported clinical periodontal outcomes. These results are summarized in Table 3. In all of the studies, PD ranged from 2.56 to 5.63 mm at follow up. CAL gain ranged from 3.44 to 9.17 mm at follow up. PI was reported in percentage in two studies, with a range of 18.27%–29.2%, whereas two studies reported mean values that ranged from 0.42 to 1.59 at follow up. BOP was reported to range from 24.3% to 56.97% in three studies.\textsuperscript{12,15,16}

3.5 | Main outcome of the studies

All of the studies reporting clinical periodontal parameters showed that LLLT as an adjunct to SRP was effective in the treatment of AgP
### TABLE 1  General characteristics of the included studies

<table>
<thead>
<tr>
<th>Investigators &amp; country</th>
<th>Study design</th>
<th>Sample size, mean age in years (range)</th>
<th>Female (%)</th>
<th>Confounders</th>
<th>Periodontitis diagnostic criteria</th>
<th>Study groups</th>
<th>Follow up (weeks)</th>
<th>Study outcome</th>
<th>Funding source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matarese et al&lt;sup&gt;12&lt;/sup&gt; Italy</td>
<td>RCT, split mouth</td>
<td>31, 34.9 (30–40)</td>
<td>55</td>
<td>Unclear</td>
<td>≥8 sites with PD ≥5 mm on each quadrant</td>
<td>SRP+LLLT (31) SRP (31)</td>
<td>Up to 52</td>
<td>Clinical and immunological outcomes were significantly better for the test group compared to the control group at follow up</td>
<td>Reported</td>
</tr>
<tr>
<td>Ertugrul et al&lt;sup&gt;16&lt;/sup&gt; Turkey</td>
<td>Non-RCT, split mouth</td>
<td>13, 30.38 (16–30)</td>
<td>54</td>
<td>Excluded</td>
<td>≥1 site with PD and CAL mm at ≥30% of sites</td>
<td>SRP+LLLT (13) SRP (13)</td>
<td>Up to 4</td>
<td>Clinical and immunological outcomes were comparable for both groups at follow up</td>
<td>Reported</td>
</tr>
<tr>
<td>Annaji et al&lt;sup&gt;14&lt;/sup&gt; India</td>
<td>RCT, split mouth</td>
<td>15, females: 27.33, males: 27.83 (18–35)</td>
<td>60</td>
<td>Excluded</td>
<td>≥1 tooth with PD ≥5 mm</td>
<td>SRP+LLLT (15) SRP (15)</td>
<td>Up to 12</td>
<td>Clinical and microbiological outcomes were significantly better for the test group compared to the control group at follow up</td>
<td>Not reported</td>
</tr>
<tr>
<td>Kamma et al&lt;sup&gt;15&lt;/sup&gt; Greece</td>
<td>RCT, split mouth</td>
<td>30, 41.8 (NA)</td>
<td>53</td>
<td>Smokers</td>
<td>CAL &gt;5 mm at 2-3 sites in &gt;14 teeth</td>
<td>SRP+LLLT (10) SRP (10)</td>
<td>Up to 24</td>
<td>Clinical and microbiological outcomes were significantly better for the test group compared to the control group at follow up</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

CAL, clinical attachment loss; LLLT, low-level laser therapy; NA, not available; PD, pocket depth; RCT, randomized clinical trial; SRP, scaling and root planing.

### TABLE 2  Laser and photosensitizer parameters of the included studies

<table>
<thead>
<tr>
<th>Investigators</th>
<th>Type of laser</th>
<th>Wavelength (nm)</th>
<th>Energy fluence (J cm&lt;sup&gt;−2&lt;/sup&gt;)</th>
<th>Power output (mW)</th>
<th>Power density (W cm&lt;sup&gt;−2&lt;/sup&gt;)</th>
<th>Duration of irradiation (s)</th>
<th>Optic fiber diameter (μm)</th>
<th>Frequency of laser application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matarese et al&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Diode laser</td>
<td>810</td>
<td>24.84</td>
<td>1000</td>
<td>NA</td>
<td>20</td>
<td>300</td>
<td>Unclear</td>
</tr>
<tr>
<td>Ertugrul et al&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Diode laser</td>
<td>940 ± 15</td>
<td>13.5</td>
<td>150</td>
<td>NA</td>
<td>20</td>
<td>NA</td>
<td>1</td>
</tr>
<tr>
<td>Annaji et al&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Diode laser</td>
<td>810</td>
<td>NA</td>
<td>100</td>
<td>NA</td>
<td>30</td>
<td>NA</td>
<td>Unclear</td>
</tr>
<tr>
<td>Kamma et al&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Diode laser</td>
<td>980</td>
<td>94.3</td>
<td>200</td>
<td>2830</td>
<td>30</td>
<td>NA</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

NA, not available.
When compared with SRP alone, three studies showed significant improvement in periodontal outcomes among LLLT group compared to SRP alone, whereas only one study showed comparable periodontal outcomes between the adjunctive LLLT and SRP groups at follow up.

Three studies presented data considering the effects of adjunctive LLLT on CAL gain, and four studies for PD reduction. One study used relative CAL gain in the test group; this study was therefore excluded from the meta-analysis. Significant heterogeneity for CAL gain was noticed between the groups at follow up. However, significant difference for PD reduction was observed between the groups at follow up.

### 4 DISCUSSION

The present systematic review was based on the hypothesis that LLLT as an adjunct to SRP is effective in the treatment of AgP
compared to SRP alone. All the included studies demonstrated that LLLT showed significant improvement in the clinical periodontal parameters among AgP patients.12,14–16

Laser therapy involves the intensification of electromagnetic fields excited by an external source of energy, such as light which emits coherent, well-collimated, and monochromatic laser beams.19 All available laser wavelengths are used in dentistry as an adjunct to SRP.20 The benefits of LLLT include instant suppression of causative periopathogenic bacteria, minimum antibiotic resistance, absence of systemic disturbance, and undesirable side effects on healthy periodontal tissue.21 Depending on the tissue interaction each wavelength and the power applied, many laser treatment strategies have been proposed. LLLT has a bio-stimulatory, anti-infective, and anti-ablation effect.22 Higher energy doses can be used for additional support to the periodontal treatment. For example, LLLT using erbium-doped:yttrium-aluminium-garnet laser probes set inside the periodontal pocket can be used to make space for better access for removing the calculus and microbial reduction from deeper areas,23,24 and at the same time, have a bio-stimulatory effect on the surrounding tissues. There are other studies that use high intensity diode laser with laser probe set outside the periodontal pocket to irradiate and ablate the external area of the sulcus, remove the epithelium superficially and aim to retard the epithelium cells during the healing process, allowing connective tissue cells like osteocytes and others to connect to tooth walls and this way reduce the depth of the sulcus.25

The results of the present review should be interpreted with caution due to a number of factors. It is noteworthy that the included studies had a lack of data pertinent to laser parameters. Parameters, such as energy fluence, power output/density, and the number of applications, either varied considerably or were not reported in some studies. The total application of LLLT varied from one application to just one in the studies included, which could have influenced the overall efficacy of LLLT in the studies included. Moreover, there was a significant range in fiber diameter between the studies. It is known that fiber diameter influences the overall power density and energy output during LLLT, and can modify the actual amount of energy released during the process, potentially affecting the antimicrobial efficacy of LLLT.26 Therefore, RCT with standard laser parameters are warranted in order to reach stronger conclusions.

The main limitation of the present systematic review was the small number of included studies. In addition, it is noteworthy that only one author performed screening and data abstraction. The involvement of multiple authors performing independent screening could result in the eligibility of pertinent studies being missed from screening and data extraction by one author alone. Furthermore, a short follow-up period with a small sample size was reported in the included studies. These methodological shortcomings should be considered when analyzing the findings, as the reported data were highly heterogeneous in terms of laser parameters. The present systematic review seems to support the hypothesis that LLLT promotes efficacious outcomes in periodontal parameters compared to SRP.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>SRP + LLLT</th>
<th>SRP</th>
<th>Mean difference IV, random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matarese et al12</td>
<td>3.44 .28</td>
<td>31</td>
<td>-3.15 (-3.9, -2.39)</td>
</tr>
<tr>
<td>Ertugrul et al16</td>
<td>4.11 .38</td>
<td>13</td>
<td>-1.74 (-2.67, -0.81)</td>
</tr>
<tr>
<td>Kamma et al15</td>
<td>4.93 1.62</td>
<td>10</td>
<td>-.15 (-1.05, .74)</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>54</td>
<td>-1.69 (-3.46, .07)</td>
</tr>
</tbody>
</table>

**FIGURE 2** Forest plot presenting weighted mean difference for clinical attachment level gain between the test and control groups. CI, confidence interval; LLLT, low-level laser therapy; SD, standard deviation; SRP, scaling and root planing.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>SRP + LLLT</th>
<th>SRP</th>
<th>Mean difference IV, random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matarese et al12</td>
<td>2.56 .44</td>
<td>31</td>
<td>-1.65 (-2.24, -1.07)</td>
</tr>
<tr>
<td>Ertugrul et al16</td>
<td>4.28 .39</td>
<td>13</td>
<td>-1.35 (-2.23, -0.48)</td>
</tr>
<tr>
<td>Annaji et al14</td>
<td>5.63 .47</td>
<td>15</td>
<td>- .43 (-1.16, .30)</td>
</tr>
<tr>
<td>Kamma et al15</td>
<td>3.87 .91</td>
<td>10</td>
<td>.25 (-1.15, .65)</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>69</td>
<td>.95 (-1.66, .23)</td>
</tr>
</tbody>
</table>

**FIGURE 3** Forest plot presenting weighted mean difference for probing depth reduction between the test and control groups. CI, confidence interval; LLLT, low-level laser therapy; SD, standard deviation; SRP, scaling and root planing.
alone in the treatment of aggressive periodontitis. However, because there is limited evidence present and severe heterogeneity in the laser parameters in the included studies, it is difficult to suggest adjunctive LLLT being superior to SRP alone at this stage. Further RCT are needed to reach a stronger conclusion.

4.1 Conclusion

Whether LLLT as an adjunct to SRP is more effective than SRP alone in the treatment of AgP remains debatable. Further RCT are required with a long follow-up period and standard laser parameters to reach a strong conclusion.

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REFERENCES


