

RESEARCH ARTICLE

## The difference in scaling root-planing results between addition of photodynamic therapy and application of metronidazole gel of 25% in chronic periodontitis treatment

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### ABSTRACT

Scaling Root-Planing (SRP) is a mechanical treatment for removing hard and soft deposits as well as bacteria that adhere to the tooth surface. The additional use of Photodynamic Therapy (PDT) can lead to damage of pathogen bacteria cell. Metronidazole is a common antibiotic with broad spectrum that goes against periodontal pathogen. This study aimed to compare the treatment outcomes between combined treatment SRP+PDT and SRP+metronidazole gel 25% in treating chronic periodontitis from the clinical parameters of Pocket Depth (PD), Relative Attachment Level (RAL), Papillary Bleeding Index (PBI) and the number of bacterial colonies. The study samples were taken from 30 periodontal pocket points, which were divided into two treatment groups. The first group was treated with SRP, then had an application of chlorophyll into the pockets and was lighted by 405 nm light, while the second group was treated with SRP, and was applied by metronidazole gel 25% into the pocket. The procedures were started by taking bacteria in the pocket using paper point in two treatment groups, then measuring PD, RAL and PBI as the baseline. After the treatments, PD and RAL results were calculated within observation time of the baseline, the 3<sup>rd</sup>, the 6<sup>th</sup> and the 9<sup>th</sup> weeks, while PBI and the number of bacterial colony were calculated at the baseline and the 3<sup>rd</sup> week. Distribution of data was analyzed by Shapiro Wilk test and the data reduction used non parametric test of Mann Whitney. The result showed a decreasing level in PD, RAL, PBI and the number of bacterial colony in both groups, but significant difference was seen in PD, and RAL of the baseline of the 9<sup>th</sup> week. Thus, the study concludes that the combination of SRP+PDT has the same effectiveness when compared to the combination of SRP+metronidazole gel of 25% in chronic periodontitis treatment, and the result is even greater in reducing the level of PD and RAL as seen from the baseline of 9<sup>th</sup> week measurement.

**Keywords:** chronic periodontitis; metronidazole gel of 25%; photodynamic therapy; scaling root-planing

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### INTRODUCTION

Periodontal disease is a common oral diseases, which according to a professional dentist organization, in 2009, is caused by bacteria. This bacteria dogma causes clinical management and researches to show a greater interest in terms of vaccine, microbial diagnosis, dental plaque, immunology, antimicrobial and the use of antibiotics.<sup>1</sup> There is no doubt, antibiotic has been used for therapeutic purposes since it was first introduced in the mid 20<sup>th</sup> century by Alexander Fleming and Paul Ehrlich.<sup>2</sup> Since penicillin was invented in 1920, more antibiotics have been produced but large increase in demands as well as

its use has led to the emergence of strain resistance.<sup>3</sup> Based on an average calculation, starting from the invention of the first antibiotic up to the current one, it takes about 8 to 9 years to find a new antibiotic. Therefore, subsequent antibiotic modification is used to overcome both new pathogen resistance and the reemergence globally.<sup>4</sup>

Periodontal disease as in chronic periodontitis is one of dental health problems with high prevalence rate and widespread distribution in the world.<sup>5</sup> Chronic periodontitis is an inflammatory infectious disease which is caused by dental plaque bacteria. It results in progressive tissue damage that supports the teeth, i.e. cementum,

periodontal ligament, gingiva and alveolar bone.<sup>1</sup> Periodontitis can involve progressive alveolar bone loss surrounding the teeth and causes tooth loss. It occurs due to the presence of microorganisms that adhere and grow on the tooth surface as well as supported by an overly aggressive immune response against the microorganisms.<sup>6,7</sup>

Chronic periodontitis treatment is generally carried out chemically with drugs and mechanically with Scaling Root-Planing (SRP). It removes hard and soft deposits as well as bacteria adhering on tooth surface and subgingiva, thereby it eliminates bacteria.<sup>8</sup> New attachment from junctional epithelium and connective tissue on the tooth surface are major components of the success of periodontal regeneration therapy.<sup>9</sup> In periodontal disease case, additional antimicrobial control which is pointed directly to periodontal pathogen can serve as a way to improve the treatment's effect. The use of local drug delivery systems, such as tetracycline fibers, metronidazole gel, minocycline ointment, minocycline microspheres, chlorhexidine chip and doxycycline hyclate possesses good result without exposing patient to systemic complication. This is because over time, it is found that certain patients continue to experience periodontal damage despite having completed the ideal treatment.<sup>10</sup> Metronidazole gel of 25% is one of common broad spectrum antibiotics, which actively goes against most periodontal pathogens. This antibiotic is widely used in chronic and aggressive periodontitis with the same dosage as those in soft tissue infection treatment. Cytotoxic metabolite in metronidazole gel of 25% is found to interact directly with bacterial DNA and other possible macromolecules resulting in cell death.<sup>11</sup>

Following the golden era of antibiotics coupled with technological development, many people are increasingly aware of bacterial resistance against drugs, so that they take another alternative step by avoiding the use of antibiotics.<sup>12</sup> It emerged that the use of Photodynamic Therapy (PDT) in treatment for patients with chronic periodontitis, aggressive periodontitis and periimplantitis results in a greater increase in clinical attachment as well as reduction of bleeding on probing and pocket depth.<sup>13</sup> This is

based on the principle that photosensitizer binds the cell target which is activated by light from appropriate wavelength to produce singlet oxygen and other highly toxic reactive agents to certain cells and bacteria.<sup>14</sup>

PDT works with photosensitizer by way of absorbing bacterial species then irradiating with specific wavelength to excite singlet state. The reaction that occurs can be substrated to form reactive oxygen species. It produces cytotoxic product, or the second one, and the photosensitizer is excited directly with oxygen to form free radical that is also cytotoxic against the bacteria.<sup>15</sup> Chlorophyll absorbs maximum light at 405 nm wavelength and produces inactivation of bacterial cell.<sup>16</sup> This research was conducted to examine the effect of PDT and metronidazole gel of 25% toward healing after SRP on chronic periodontitis with the assessed parameters, such as Pocket Depth (PD), Relative Attachment Level (RAL), Papillary Bleeding Index (PBI) and the number of bacterial colonies.

## MATERIALS AND METHODS

This is a quasi experimental research with ethical clearance No.0063/KKEP/FKG-UGM/EC/2019 received from ethics and advocacy unit of the Faculty of Dentistry, Universitas Gadjah Mada. Observation time of PD and RAL was measured on the baseline, 3, 6 and 9 weeks, while PBI and then number of bacterial colonies were measured on the baseline and 3 weeks after the treatment. The research subjects involved patients who came to Periodonsia specialist clinic at RSGM UGM Prof. Soedomo with the inclusion criteria of age 21-55 years old, chronic periodontitis with 4-6 mm pocket depth and those willing to approve informed consent. The exclusion criteria were the smokers, pregnant and breastfeeding patients, those with systemic disease and bleeding disorder, patients who were on long term antibiotic treatment, restoration of extensive subgingiva/crown/partial denture, and implant.

Samples were taken from 30 periodontal pocket points and divided into 2 groups. Group I

was treated with SRP and PDT with chlorophyll photosensitizer and group II was treated with SRP and metronidazole gel of 25%. The total sample from each group was determined by the following formula:<sup>17</sup>

$$n1 = n2 = \left[ \frac{(Z\alpha + Z\beta) \times S}{(x1 - x2)} \right]$$

$$n1 = n2 = \left[ \frac{(1.96 + 0.84) \times 0.48}{(0.5)} \right]$$

$$n1 = n2 = \left[ \frac{1.62}{0.5} \right]$$

$$n1 = n2 = 7.22$$

Note:  $n1 = n2 =$  total sample for each group

$$Z\alpha = (\alpha = 0.05) \rightarrow Z\alpha = 1.96$$

$$Z\beta = (\beta = 0.1) \rightarrow Z\beta = 0.84$$

S = standard deviation of value difference between groups = 0.48

$x1 - x2$  = minimum average difference that is considered as significant = 0.5

The main research materials were chlorophyll (K-link liquid chlorophyll), metronidazole gel of 25% (Ti-es, Indonesia), and gingival sulcus fluid, while supporting materials were paper point, brain heart infusion agar, 3,5 L anaeroGen, and PBS fluid. The main research devices were periodontal probe of PBUNC 15 type with the length of each limit of 1 mm and 405 nm light, while supporting devices were ultrasonic scaler, microtube, petri dish, vortex vibrator, micropipette, vacuum container, and incubator.

Numerical scale in variable description was presented in mean and standard deviation, while categorical data as in PBI was with median (min-max). Data distribution was tested using Saphiro-Wilk test since the number of sample was less than 50 samples (30 samples). Reduction of PD, RAL, PBI and the number of bacterial colonies in the groups used non parametric test of *Mann Whitney*. The research data were analyzed using statistical program of SPSS version 22.0 for Windows.

## RESULTS

Pocket Depth (PD) was measured at the baseline, 3<sup>rd</sup> week, 6<sup>th</sup> week, and 9 week, then reduction measurements were taken and the results were obtained as shown in the Table below:

Table 1 shows reduction level or highest PD reduction that is on group of SRP plus photodynamic therapy from the baseline to 9<sup>th</sup> week with mean and standard deviation of  $2.00 \pm 0.65$ . The lowest reduction was seen on group of SRP+metronidazole from 3<sup>rd</sup> to 6<sup>th</sup> week along with the result of  $0.00 \pm 0.85$ . The Shapiro-Wilk normality test for PD reduction showed significance level of  $p < 0.05$ , which means that the data were not normally distributed, so that the reduction of PD between PDT and metronidazole gel of 25% was tested using Mann Whitney test. The table 2 shows that there is no difference in PD reduction on the baseline to 3<sup>rd</sup> week, baseline to 6<sup>th</sup> week, 3<sup>rd</sup> to 6<sup>th</sup> week, 3<sup>rd</sup> to 9<sup>th</sup> week and 6<sup>th</sup> to 9<sup>th</sup> week except on the baseline to 9<sup>th</sup> week with  $p = 0.029$  ( $p < 0.05$ ).

Relative Attachment Level (RAL) was measured at baseline, 3<sup>rd</sup> weeks, 6<sup>th</sup> weeks and 9 weeks, while reduction measurements were taken and the results were obtained and shown in the Table 3. Table 3 illustrates the highest RAL reduction in SRP+PDT group that is on the baseline to 9<sup>th</sup> week with mean and standard deviation of  $2.00 \pm 0.65$ , while the lowest RAL of  $0.00 \pm 0.85$  is seen on 3<sup>rd</sup> to 6<sup>th</sup> week in SRP+metronidazole group. The Shapiro-Wilk normality test for RAL reduction showed significance level of  $p < 0.05$ , which means that the data were not normally distributed, so that the reduction of RAL between PDT and metronidazole gel of 25% was tested by Mann Whitney test.

The Table 4 shows that there is no significant difference in RAL reduction on the baseline to 3<sup>rd</sup> week, baseline to 6<sup>th</sup> week, 3<sup>rd</sup> to 6<sup>th</sup> week, 3<sup>rd</sup> to 9<sup>th</sup> week and 6<sup>th</sup> to 9<sup>th</sup> week between PDT and metronidazole ( $p > 0.05$ ) except on the baseline to 9<sup>th</sup> week ( $p < 0.05$ ).

Table 5 presents PBI between observation time of the baseline and 3<sup>rd</sup> week both in group I and II. The highest PBI is seen on the baseline in

**Table 1.** Mean and standard deviation of Pocket Depth (PD) (mm) reduction between SRP+PDT and SRP+metronidazole

Time	n	Mean ± SD	
		SRP + PDT	SRP + Metronidazole
Baseline – 3 <sup>rd</sup> week	15	1.67 ± 0.82	1.20 ± 0.77
Baseline – 6 <sup>th</sup> week	15	1.53 ± 0.64	1.20 ± 0.68
Baseline – 9 <sup>th</sup> week	15	2.00 ± 0.65	1.47 ± 0.64
3 <sup>rd</sup> -6 <sup>th</sup> week	15	0.13 ± 0.74	0.00 ± 0.85
3 <sup>rd</sup> -9 <sup>th</sup> week	15	0.33 ± 0.82	0.27 ± 0.59
6 <sup>th</sup> -9 <sup>th</sup> week	15	0.47 ± 0.52	0.27 ± 0.70

**Table 2.** Mann Whitney test of Pocket Depth (PD) reduction between SRP+PDT and SRP+metronidazole

Time	n	Significance Level (p)
Baseline – 3 <sup>rd</sup> week	15	0.142
Baseline – 6 <sup>th</sup> week	15	0.120
Baseline – 9 <sup>th</sup> week	15	0.029*
3 <sup>rd</sup> -6 <sup>th</sup> week	15	0.659
3 <sup>rd</sup> -9 <sup>th</sup> week	15	0.836
6 <sup>th</sup> -9 <sup>th</sup> week	15	0.471

Note: (\*) : significant

**Table 3.** Mean and standard deviation of Relative Attachment Level (RAL) (mm) reduction between SRP+PDT and SRP+metronidazole

Time	n	Mean ± SD	
		SRP + PDT	SRP + Metronidazole
Baseline – 3 <sup>rd</sup> week	15	1.67 ± 0.82	1.20 ± 0.77
Baseline – 6 <sup>th</sup> week	15	1.53 ± 0.64	1.20 ± 0.68
Baseline – 9 <sup>th</sup> week	15	2.00 ± 0.65	1.47 ± 0.64
3 <sup>rd</sup> -6 <sup>th</sup> week	15	0.13 ± 0.74	0.00 ± 0.85
3 <sup>rd</sup> -9 <sup>th</sup> week	15	0.33 ± 0.82	0.27 ± 0.59
6 <sup>th</sup> -9 <sup>th</sup> week	15	0.47 ± 0.52	0.27 ± 0.70

**Table 4.** Mann Whitney test of Relative Attachment Level (RAL) reduction between SRP+PDT and SRP+Metronidazole

Time	n	Significance Level (p)
Baseline – 3 <sup>rd</sup> week	15	0.142
Baseline – 6 <sup>th</sup> week	15	0.120
Baseline – 9 <sup>th</sup> week	15	0.029*
3 <sup>rd</sup> -6 <sup>th</sup> week	15	0.659
3 <sup>rd</sup> -9 <sup>th</sup> week	15	0.836
6 <sup>th</sup> -9 <sup>th</sup> week	15	0.471

Note: (\*) : significant

**Table 5.** Median of Papillary Bleeding Index (PBI) according to observation time in both groups

Time	n	Median (Min-Max)	
		SRP + PDT	SRP + Metronidazole
Baseline	15	4 (0-4)	3 (0-4)
3 <sup>rd</sup> week	15	0 (0-2)	0 (0-2)

**Table 6.** Mann Whitney test of Papillary Bleeding Index (PBI) between SRP+PDT and SRP+metronidazole therapy

Time	n	Significance Level (p)
Baseline	15	0.683
3 <sup>rd</sup> week	15	0.677

**Table 7.** Mean and standard deviation in the number of bacterial colonies reduction of Gingival Crevicular Fluid (GCF) between SRP+PDT and SRP+metronidazole

Time	n	Mean ± SD	
		SRP + PDT	SRP + Metronidazole
Baseline – 3 <sup>rd</sup> week	15	758.40 ± 2002.02	297.27 ± 408.49

**Table 8.** Mann Whitney test in the number of bacterial colonies of Gingival Crevicular Fluid (GCF) reduction between SRP+PDT and SRP+metronidazole

Time	n	Significance Level (p)
Baseline – 3 <sup>rd</sup> week	15	0.419

SRP+PDT group with 4 median score. Meanwhile, on the 3<sup>rd</sup> week, median of PBI in both groups turned into 0 score with the range of 0-2. It was clear that PBI difference was seen on the baseline and 3<sup>rd</sup> week. PBI reduction between SRP+PDT and SRP+metronidazole was analyzed using Mann Whitney test since the PBI data were ordinal data with the results presented in the following Table 6.

Papillary Bleeding Index (PBI) between PDT and metronidazole does not show significant difference at either the baseline and 3<sup>rd</sup> week ( $p > 0.05$ ). The observation of then number of bacterial colonies decreased from  $844.13 \pm 2003.90$  to  $85.73 \pm 84.11$  after SRP+PDT treatment, while in SRP+metronidazole, there was a decrease from  $359.40 \pm 409.58$  to  $67.13 \pm 86.77$ .

The decreasing number of bacterial colonies in SRP+PDT was higher than SRP+metronidazole

group. Reduction data on the number of bacterial colonies in both groups were not normally distributed as shown by value of  $p < 0.05$  then continued by Mann Whitney test. From Mann Whitney test's result, it is known that there is no significant difference for colonies reduction between SRP+PDT and SRP+metronidazole groups with  $p = 0.419$  ( $p > 0.05$ ).

## DISCUSSION

Initial descriptive data of PD in both groups is quite large so that reduction of the PD on the baseline to 9<sup>th</sup> week has a significant difference. The mechanism of PD and RAL reduction in this research is that SRP at the baseline can eliminate periodontal pathogen mechanically by removing hard and soft tissues as well as bacteria adhering on tooth surface and subgingiva, thereby eliminating bacteria.<sup>8</sup> It is continued by addition of

PDT along with chlorophyll as photosensitizer by firstly having chlorophyll to absorb maximum light at a 405 nm wavelength to produce inactivation of bacteria cell inside the sulcus.<sup>16</sup> Metronidazole becomes an antimicrobial agent to be used for active periodontitis therapy, which contains gram-negative anaerobic bacteria and spirochete. It happens by causing RNA dysfunction and destruction of bacteria structure.<sup>18</sup>

A decrease in the pocket at each observation time of RAL indicates formation of new attachment to dental root. After the treatment of SRP+PDT as well as SRP+metronidazole, wound healing process progresses over time from hemostatic, inflammation, proliferation and remodelling. Hemostatic phase occurs immediately after injury then followed by inflammation phase. It occurs during the first day to the first 2 days after injury. 2 to 3 days after the two initial processes, a proliferation phase occurred with a formation of new tissue to replace the damaged tissue. Proliferation phase starts from the fifth day to the 3<sup>rd</sup> week of formation of granulation tissue containing inflammatory cell, fibroblast and blood vessel.<sup>19</sup> New attachment of junctional epithelium to tooth surface and connective tissue to the tooth surface causes a decrease in RAL.<sup>9</sup>

A decrease of PBI value indicates a healing process. This is in line with wound healing process in remodelling phase which starts from the 3<sup>rd</sup> week after injury and lasts for approximately 12 months. This phase completes the formation of strong new tissue and starts the decline of blood capillaries.<sup>20</sup> The process of wound healing is likely to be one of causes of the PBI decrease on the 3<sup>rd</sup> week.

In this research, variation in the range number of bacteria colonies that is high at baseline is likely caused by different oral hygiene of each research subject when collecting initial data of the number of colonies. There are subgingiva plaques which adhere to paper point and affect baseline value of the number of colonies. Other possibilities are the difference of paper point depth which is inserted into the pocket, and time difference when taking the GCF and location of paper point placement that is uncontrolled, whether it touches the teeth

or not. It can cause variation in the amount of colonies with a very large range.

## CONCLUSION

The combination of SRP+PDT has the same effectiveness when compared to the combination of SRP+metronidazole gel of 25% on chronic periodontitis treatment, and it is even greater in reducing PD and RAL as seen from the baseline of the 9<sup>th</sup> week measurement.

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