A randomized controlled trial of manual versus powered tooth brushing during haematopoietic stem cell transplantation

Carin M.J. Potting1 | Stephanie J.M. van Leeuwen1,2 | Marie-Helene Kurstjens3 | Ewald M. Bronkhorst2 | Renske Z. Thomas2 | Nicole M.A. Blijlevens1 | Marie-Charlotte D.N.J.M. Huysmans2

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a treatment used mainly for blood malignancies, such as leukaemia, lymphomas and multiple myeloma. The procedure usually involves high-intensity chemotherapy as the conditioning therapy, just before the stem cells are returned to the patient. As a result of this myeloablative conditioning regimen, virtually every HSCT recipient suffers

Received: 21 February 2021 | Revised: 8 April 2021 | Accepted: 28 April 2021
DOI: 10.1111/odi.13899

1Department of Haematology, Radboudumc, Radboud Institute for Health Sciences, Nijmegen, The Netherlands
2Department of Dentistry, Radboudumc, Radboud Institute for Health Sciences, Nijmegen, The Netherlands
3Department of Oral Hygiene, HAN university of applied sciences, Nijmegen, The Netherlands

Correspondence
Marie-Charlotte Huysmans, Department of Dentistry, Philips van Leijdenlaan 25, Internal postal code 309, Nijmegen 6525 TX, The Netherlands.
Email: marie-charlotte.huysmans@radboudumc.nl

Abstract

Aim: To compare manual and powered tooth brushing (MT and PT) with respect to patient compliance to brushing frequency advice, plaque removal and severity of oral mucositis (OM) in patients undergoing hematopoietic stem cell transplantation (HSCT) after high-dose chemotherapy.

Materials & methods: A randomized controlled trial was conducted. Forty-six patients scheduled to receive myeloablative conditioning regimen before autologous HSCT were included and randomly assigned to control (MT, n = 23) or test (PT, n = 23) groups. Starting at day 1 (day of hospital admission for HSCT), brushing frequency (patient recorded diary), plaque scores (Plaque Control Index) and oral mucositis (Oral Mucositis Nursing Index) were recorded daily. Data for days 1 to 17 were analysed using regression analysis and general linear models.

Results: Few patients maintained 4 times per day brushing, but most brushed at least 2 times per day throughout the study. In PT, overall plaque scores were lower by 6.98% (p = .006) as compared to MT. No differences were seen in OM scores between the groups (p = .968). A small but significant positive correlation was found between plaque scores and OM severity: $R^2=0.15$ ($p < .01$).

Conclusions: Powered tooth brushing resulted in lower plaque scores, but was not associated with reduced OM severity. Individual plaque scores were positively related to OM severity.

KEYWORDS
hematopoietic stem cell transplantation, oral care, oral mucositis, plaque, tooth brushing
from oral mucositis (Curra et al., 2018; Vera-Llonch et al., 2007). Oral mucositis presents as a generalized inflammation of the oral mucosal tissues. In its most severe form, it involves widespread ulceration and is very painful, requiring opioid analgesics and impairing nutritional intake and quality of life (Harris (2006); McGuire et al., 1993).

In the international literature and guidelines, the most commonly recommended intervention for managing oral mucositis is basic oral care (Djuric et al., 2005; McGuire et al., 2013; Potting et al., 2008; Raber-Durlacher et al., 2004), which in a healthy population is normally understood to consist of tooth brushing two or sometimes three times per day. However, the MASCC guideline 2014 (Multinational Association for Supportive Care in Cancer) specified brushing four times per day with a soft toothbrush and with regular replacement of the toothbrush (Lalla et al., 2014). In a pilot study at our Haematology ward, we observed that patient compliance with the oral care protocol was moderate, and that especially the number of times teeth were brushed was lower or quickly dropped during hospitalization (not published). This may be related to fact that the general condition of the patients deteriorates during this period, because of neutropenia and oral mucositis, possibly making tooth brushing uncomfortable, but may also simply reflect the return to habitual behaviour.

Increasing number of people use a powered toothbrush. As this requires less effort, it may be easier to continue powered brushing during a period of illness than manual brushing. Systematic literature review has shown that powered tooth brushing results in less plaque and gingivitis in healthy patients, compared with manual tooth brushing (Yaacob et al., 2014). As it has been shown that oral hygiene levels and OM are related, such a reduction might, in HSCT recipients, also translate into a reduced incidence and/or severity of oral mucositis (Coracin et al., 2013; Kashiwazaki et al., 2012). However, the intensive action of a powered toothbrush might also increase discomfort during brushing, thereby reducing compliance with the brushing frequency guideline and reducing plaque removal.

Patient acceptance of the use of powered toothbrushes during intensive chemotherapy is unclear, as is their effect on hygiene levels and/or mucositis severity. The MASCC guideline makes no mention of powered toothbrushes, but in clinical practice, nursing staff often discourage powered tooth brushing, fearing it might cause mucosal damage leading to bacteraemia. No well-designed studies so far have examined their use in patients with oral mucositis. Therefore, the objective of this study was to compare manual and powered tooth brushing with respect to a) brushing frequency, b) plaque removal and c) severity of oral mucositis in patients undergoing high-dose chemotherapy and HSCT. A secondary aim was to assess the relationship between plaque scores and oral mucositis.

2 | METHODS

A randomized controlled trial with two arms, comparing manual and powered tooth brushing, was carried out at the Haematology ward of the Radboud University Medical Center between 2007 and 2012. The study was approved by the regional ethical commission (number NL1538_091_06) and was conducted in accordance with the Declaration of Helsinki.

2.1 | Patients

Patients scheduled to undergo autologous HSCT receiving as conditioning regimen either HDM (high-dose melphalan: 200 mg/m²) or BEAM (carmustine 300 mg/m²; cytarabine 100 mg/m²; etoposide 100 mg/m²; plus melphalan 140 mg/m²) were eligible for inclusion. These myeloablative conditioning regimens are associated with a high risk of OM. Edentulous patients, and those not able to understand the Dutch language, were excluded.

Consecutive patients not included in other clinical studies were approached by nursing staff and received written study information. They were included by research assistants only after obtaining written informed consent. Patients were randomly assigned to the test or control group by means of a block randomization (random block size of 4), using closed envelopes prepared by an independent researcher.

2.2 | Baseline recording

At baseline (day of admission, day 1), patients were interviewed and received a dental clinical examination. The structured interview included questions about the patients’ regular oral hygiene behaviour. Dental screening included recording the number of teeth present and recording the Dutch Periodontal Screenings Index (DPSI) (Kashiwazaki et al., 2012). The DPSI is measured using complete periodontal probing and is determined by the maximum score of each of 6 sextants of the dentition. Scores are based on the presence of bleeding (1), combined with retention factors such as calculus (2), presence of pockets of 4–5 mm without (3−) or with (3+) gingival recession, or presence of pockets of ≥6 mm (4). The baseline assessment also included a plaque measurement using the Plaque Control Index (PCI) (O’Leary et al., 1972). A disclosing solution was applied to all tooth surfaces, leaving dental plaque coloured red/blue after rinsing. The presence of dental plaque was recorded (4 locations per tooth), and the PCI plaque score (%) was calculated by dividing the total number of surfaces with plaque by the total number of tooth surfaces.

2.3 | Intervention

The powered toothbrush used in this study was the Oral-B Triumph™ with an Oral-B Sensitive brush head (Procter & Gamble Netherlands BV, Rotterdam, NL). This is a rechargeable oscillating/rotating toothbrush. The manual toothbrush was a conventional Lactona® adult toothbrush with a soft brush head (Lactona Europe BV, Bergen op Zoom, NL). Soft brushes were selected, as recommended for
sensitive teeth and gums, with a view to the likelihood of oral mucositis development with related mucosal sensitivity. The brush(head) was replaced every week.

At baseline, all patients received oral and written instruction for the use of their assigned toothbrush. Patients in the test group were instructed to place the powered toothbrush on each individual tooth for a few seconds, moving along the dental arches until all accessible tooth surfaces had been brushed. Patients in the control group were instructed to use the Bass method (Bass, 1954), with the toothbrush placed at the gum margin at an angle of 45° and making small, vibratory movements, also moving along the dental arches until all accessible tooth surfaces had been brushed.

According to the basic oral care protocol in the haematology department, patients were instructed to brush their teeth 4 times a day and to rinse with water or NaCl 0.9% as preferred. No other mouth rinses or interdental cleaning were advised, and oral hygiene instructions were not repeated or reinforced during the study.

### 2.4 Outcome measures

Starting at baseline (day 1), patients were seen every day during their hospital stay for the HSCT procedure, which lasted between 17 and 21 days. In order to report on the complete groups, only data up to day 17 were included in the analysis. To determine patient compliance with brushing frequency instructions, patients were asked to fill out a daily report of the times they brushed. PCI was measured every day as described for the baseline screening, and the plaque score was recorded. As patients kept their toothbrush in the hospital every day as described for the baseline screening, and the plaque score was recorded. The observer did not mention the plaque score to the patient or make any comments on the level of oral cleanliness. The Oral Mucositis Nursing Instrument (OMNI) was used to assess OM on a daily basis (Potting et al., 2006). The OMNI scores 6 items: erythema, oedema, lesions, pain, oral dryness and saliva viscosity. The overall oral assessment score is the sum of the six scores, with a maximum of 16 points.

The research staff consisted of dental hygiene students, well trained in plaque recording. For OM scoring, they were trained by an experienced researcher (C.P.) and who supervised scoring for at least a week for every observer. Inter-observer consistency for OMNI scoring has been shown to be acceptable (Potting et al., 2006).

### 2.5 Sample size calculation and data analysis

A sample size calculation was performed using a 40% difference in reduction in compliance as a meaningful difference to be observed, with a power of 80% and a significance level of 5%, yielding a group size of 20. Allowing for a 10% drop-out, 23 patients per group were included.

Descriptive statistics were used to summarize sample characteristics and baseline dental measurements. A regression analysis was performed to analyse the effect of PT versus MT on patient compliance, plaque score and oral mucositis. To analyse the effect of type of toothbrush on plaque, a general linear model was applied with an autoregressive correlation structure, to model the correlation between plaque measurements over time within a patient. Independent variables were the percentage of plaque at day 1 and the type of toothbrush. For the dependent variable oral mucositis, the analysis had to incorporate the clear time pattern of oral mucositis in these patients. This was done by first fitting a polynomial curve through the OMNI scores over time. The values for OM as fitted were subtracted from the actual OMNI score, to eliminate the time effect. Next to these reduced OMNI scores, which can be interpreted as the deviation from the mean level of OM for this patient group at a certain point in time, the same analysis was performed as with the previous outcome, but without inclusion of the measurement at day 1.

The relation between percentage of plaque and total OMNI score was analysed using the correlation between the two variables. This was done first per patient, and subsequently, the overall correlation was calculated using a meta-analysis approach (inverse variance weighting of the individual correlations).

### 3 RESULTS

In total, 72 consecutive patients admitted to undergo an autologous HSCT for multiple myeloma (MM), non-Hodgkin or Hodgkin lymphoma (NHL and HL) were approached for participation in the study. After screening, 13 patients were found to be edentulous and were excluded. Five patients refused to participate, because they used a powered toothbrush and did not want to take the risk of being randomized into the control group. Ten patients were not willing to participate for various other reasons. Finally, 46 patients were entered into the study. No participants were lost during the study, and all analyses were performed on all included patients.

Patient characteristics and baseline plaque scores are summarized in Table 1. Overall mean age was 54.2 years (range 21–66), and 30 (65%) were male. At baseline, both groups were similar for number of teeth, DPSI, plaque score and habitual brushing frequency and type of toothbrush used.

Figure 1 presents the results for brushing frequency. Both Figures 1 and 2 include (as a shaded area) the overall mean OMNI scores, providing a visual reference for OM development during the study period. A typical curve of increasing severity up to a peak at day 9–11 after the start of chemotherapy can be observed, followed by a gradual resolution of the mucositis. Tooth brushing frequencies showed similar patterns for both toothbrushes, with the proportion of patients brushing 4 times a day or more dropping from about 40% at day 1, to about 5% at day 10. After peak oral mucositis, this proportion did not increase again. The PT group showed a slightly higher percentage of patients brushing 4 times per day (12.9%), but this was not significant (p = .151; 95% CI[4.8, 30.6]). In the period of peak oral mucositis, only 2 patients completely stopped brushing. More than 50% of patients maintained a brushing frequency of 2 or 3 times per day.
Results for plaque scores are visualized in Figure 2. Both groups again demonstrated a similar pattern. The mean plaque score during the hospitalization period was 34.2% for the PT group and 35.1% for the MT group. The regression analysis of the effect of the use of different toothbrushes on plaque scores during the hospital stay showed a small but significant difference in favour of PT of 0.68% compared to MT ($p = 0.006; 95\% \text{CI} \: -11.89 \text{ to } -2.06$).

Oral mucositis results for the two groups are presented in Figure 3. Again, patterns for PT and MT are comparable. The incidence of severe OM (OMNI score 11–16) was 7/22 (32%) in the PT group versus 10/23 (39%) in the MT group. The regression analysis for OM showed no differences in OM scores between the groups ($p = 0.968; 95\% \text{CI} \: -1.19 \text{ to } 1.14$).

In order to explore whether the outcome was influenced by the fact whether patients continued to use their habitual tooth brushing technique, or were forced to change, Figure 4 shows the results for plaque score and OM-score for the relevant subgroups. Although the patients continuing their habitual manual tooth brushing appear
to leave most plaque, there is no clear indication that experience with the type of toothbrush before the trial influenced the plaque score.

Figure 5 shows the forest plot of the meta-analysis to explore a relationship between plaque score and oral mucositis. The correlation per patient between percentage of plaque and OMNI score during the hospital stay is individually plotted. A significant positive correlation was found between plaque scores and OM severity: $R^2 = .15$, $\tau^2 = 0.10$ ($p < .01$, 95% CI 0.04 to 0.27).

4 | DISCUSSION

The aim of this study was to assess the effect of powered tooth brushing as compared to manual brushing during HSCT hospitalization, on compliance to brushing frequency advice, plaque scores and oral mucositis severity. No differences were found between manual or powered brushing for compliance and oral mucositis. A small significant effect in favour of powered brushing was found for plaque score. Overall, a significant positive correlation was found between plaque score and severity of oral mucositis.

The study included more males than females. This can be explained by the higher prevalence of both NHL and MM in males than in females of about 1.5:1 (Howlader et al., 2017). In this study, most patients were classified as having mild periodontitis, using the DPSI screening index with a score of 3-. This index gives a reliable screening estimate of the periodontal status (Van der Velden, 2009). DPSI values in this study correspond well with recent epidemiological data for this age group in the Netherlands, where about 35% of patients had DPSI 3- (Schuller et al., 2014). Average plaque scores at baseline were about 35%; this corresponds with other studies using the O’leary index (Eckley et al., 2004). Although levels as low as 10%–20% have been suggested as a threshold for good oral hygiene levels (O’Leary et al., 1972), normal levels are more likely to be around 35%–50% (O’Leary et al., 1972; Toda et al., 2019).

Even at the start of their hospital period, only a minority of patients actually brushed 4 times a day, as was advised. Regardless of

**FIGURE 2** Mean plaque scores in manual (MT) and powered tooth brushing (PT) groups as a function of time. The shaded area indicates mean OMNI scores based on the total group (PT and MT).

**FIGURE 3** Mean OMNI score for manual and powered tooth brushing groups as a function of time.

**FIGURE 4** Exploration of the effect of habitual toothbrush use before the trial on outcomes. Mean plaque score (a) and mean oral mucositis score (b) in for subgroups of habitual versus trial tooth brush use. Group indication: experimental/habitual brush type. Habitual brush type was unknown of three patients.
the tooth brushing technique used, the compliance dropped further to about 5%. The reduction occurred at the time of increasing severity of oral mucositis, indicating a role of oral pain and ulcerations in this reduction. It may be concluded that powered tooth brushing neither helped nor hindered compliance. General advice to patients in the Netherlands is to brush two times a day (Kruis, 2011), and it may be hard to change this routine even during hospitalization. Also, the rationale and evidence for the advice of brushing four times a day may be questioned. Current guidelines no longer specify the frequency of brushing or mention 2–3 times per day as advisable (Elad et al., 2015).

A recent Cochrane systematic review concluded that powered tooth brushing was more effective in plaque removal than manual brushing, with an effect size of 11% (Yaacob et al., 2014). The studies on which this review was based were generally performed in healthy populations and using plaque scores distinguishing levels of plaque coverage per surface. Although our study used a more course outcome measure, looking only at the proportion of surfaces with
plaque, a significant effect of about 7% was still present. This indicates that even in this challenging situation powered tooth brushing is more effective than manual brushing. Plaque scores directly after instruction were similar to baseline plaque scores and end of study plaque scores, showing no great effect of instruction or daily visits for plaque assessment on brushing quality. The fact that plaque levels remained very stable throughout the study period, notwithstanding changes in brushing frequency, indicates that brushing efficacy is more relevant for plaque levels than brushing frequency.

The clinical relevance of the difference between MT and PT of 11% as reported in the systematic review has been questioned (16). Also, in our study, although a correlation between individual plaque scores and oral mucositis severity could be observed, this did not translate into a significant effect of powered tooth brushing on oral mucositis. Timing and severity of oral mucositis development in this study are in accordance with literature reports (Raber-Durlacher et al., 2010; Stiff et al., 2006). The observed relationship between plaque levels and oral mucositis is also in agreement with previous reports, either showing a relationship between pretransplantation plaque index and OM incidence (Coracín et al., 2013) or showing a reduced incidence of oral mucositis in patients receiving weekly professional oral prevention during hospitalization (Kashiwazaki et al., 2012). The importance of good oral hygiene is mentioned in different guidelines for OM, which was only based on expert opinions (Lalla et al., 2014). This is the first study that showed a positive correlation between plaque and oral mucositis severity. Whether there is causation involved: either more plaque resulting in higher mucositis scores or the other way around, could not be established in this study. Moreover, the observed correlation was very small and, as mentioned above, an effect of powered brushing could not be observed in OM.

5 | CONCLUSION

Although this study had some weak points, in that it was not blinded, it was performed over the course of several years, due to a slow inclusion rate, and measurements had to be recorded in a hospital setting; with these limitations, we conclude that powered tooth brushing during HSCT resulted in lower plaque scores. Individual plaque scores were related to oral mucositis severity; however, powered tooth brushing did not result in reduced oral mucositis severity. Compliance with the advice to brush 4 times per day was extremely low, but almost all patients continued brushing during peak oral mucositis, and most brushed at least 2 or 3 times per day for the whole period, independent of the toothbrush used. Continuing the use of a powered toothbrush during HSCT may be recommended, as it was well tolerated and slightly more effective.

CONFLICT OF INTEREST

The authors declare no conflict of interest. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

AUTHOR CONTRIBUTIONS

Carin M.J. Potting: Conceptualization; Formal analysis; Investigation; Methodology; Project administration; Writing-original draft. Marie-Helene Kurstjens: Conceptualization; Investigation; Writing-original draft. Renske Thomas: Writing-review & editing.

PEER REVIEW

The peer review history for this article is available at https://pubons.com/pubon/10.1111/odi.13899.

DATA AVAILABILITY STATEMENT

Data available upon request from corresponding author.

ORCID

Stephanie J.M. van Leeuwen https://orcid.org/0000-0002-4522-3705
Marie-Charlotte D.N.J.M. Huysmans https://orcid.org/0000-0002-3036-7554

REFERENCES

Bass, C. C. (1954). An effective method of personal oral hygiene; part II. The Journal of the Louisiana State Medical Society: Official Organ of the Louisiana State Medical Society, 106, 100–112.
Coracín, F. L., Santos, P. S., Gallottini, M. H., Saboya, R., Musqueira, P. T., Barban, A. et al (2013). Oral health as a predictive factor for oral mucositis. Clinics, 68, 792–796. https://doi.org/10.6061/clinics20130611
Curra, M., Soares Junior, L. A. V., Martins, M. D., & Santos, P. (2018). Chemotherapy protocols and incidence of oral mucositis. An Integrative Review. Einstein (Sao Paulo), 16(1), eRW4007. https://doi.org/10.1590/s1679-45082018rw4007
Djuric, M., Hillier-Kolarov, V., Belic, A., & Jankovic, L. (2005). Mucositis prevention by improved dental care in acute leukemia patients. Supportive Care in Cancer, 14(2), 137–146. https://doi.org/10.1007/s00520-005-0867-7
Eckley, C. A., Michelsohn, N., Rizzo, L. V., Toddor, C. E., & Costa, H. O. (2004). Salivary epidermal growth factor concentration in adults with reflux laryngitis. Otolaryngology - Head and Neck Surgery, 131, 401–406. https://doi.org/10.1016/j.otohns.2004.01.020
Elad, S., Raber-Durlacher, J., Brennan, M. T., Saunders, D. P., Mank, A. P., Zidak, Y., Quinn, B., Epstein, J. B., Blijlevens, N. M. A., Waltimo, T., Passweg, J. R., Correa, M. E. P., Dahlöf, G., Garming-Legert, K. U. E., Logan, R. M., Potting, C. M. J., Shapira, M. Y., Soga, Y., Stringer, J., ... Jensen, S. B. (2015). Basic oral care for hematological oncology patients and hematopoietic stem cell transplantation recipients: A position paper from the joint task force of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) and the European Society for Blood and Marrow Transplantation (EBMT). Supportive Care in Cancer, 23(1), 223–236. https://doi.org/10.1007/s00520-014-2378-x
Harris, D. J. (2006). Cancer treatment-induced mucositis pain: Strategies for assessment and management. Therapeutics and Clinical Risk Management, 2, 251–258. https://doi.org/10.2147/tcrm.2006.2.3.251
Howlader, N., Noone, A., Krapcho, M., Miller, D., Bishop, K., Kosary, C. L. SEER Cancer Statistics Review, 1975-2014. National Cancer Institute: 2017.
Kashiwazaki, H., Matsushita, T., Sugita, J., Shigematsu, A., Kasashi, K., Yamazaki, Y., Kanehira, T., Yamamoto, S., Kondo, T., Endo, T., Tanaka, J., Hashino, S., Nishio, M., Imamura, M., Kitagawa, Y., & Inoue, N.
Professional oral health care reduces oral mucositis and febrile neutropenia in patients treated with allogeneic bone marrow transplantation. Supportive Care in Cancer, 20, 367–373. https://doi.org/10.1007/s00520-011-1116-x

Kruis, I. (2011). Advies Carïëspreventie Adviezen. https://www.ivorenrui.nl/Adviezen.html

Lalla, R. V., Bowen, J., Barasch, A., Elting, L., Epstein, J., Keefe, D. M., McGuire, D. E., Migliorati, C., Nicolai-Galitis, O., Peterson, D. E., Raber-Durlacher, J. E., Sonis, S. T., & Elad, S. (2014). MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer, 120, 1453–1461. https://doi.org/10.1002/cncr.28592

Potting, C. M., Mank, A., Blijlevens, N. M., Donnelly, P. J., & van Achterberg, T. (2008). Providing oral care in haematological oncology patients: Nurses’ knowledge and skills. European Journal of Oncology Nursing, 12, 291–298. https://doi.org/10.1016/j.ejon.2008.03.002

Raber-Durlacher, J., Barasch, A., Elad, S., & Barasch, A. (2010). Oral mucositis. Oral Oncology, 46, 452–456. https://doi.org/10.1016/j.oraloncology.2010.03.012

Schuller, A., van Kempen, I., Vermaire, E., Poorterman, J. H. G., Verlinden, A., Hofstetter, H., & Verris, E. (2014). Gebit Fit, een onderzoek naar de mondzondheid en het tandheelkundig preventief gedrag van volwassenen in Nederland in 2013. TNO, 89.

Stiff, P. J., Erder, H., Bensinger, W. I., Emmanouilides, C., Gentile, T., Isitt, J., Lu, Z. J., & Spielberger, R. (2006). Reliability and validity of a patient self-administered daily questionnaire to assess impact of oral mucositis (OM) on pain and daily functioning in patients undergoing autologous hematopoietic stem cell transplantation (HSCT). Bone Marrow Transplantation, 37, 393–401. https://doi.org/10.1038/sj.bmt.1705250

How to cite this article: Potting CMJ, van Leeuwen SJM, Kruis IT, et al. A randomized controlled trial of manual versus powered tooth brushing during haematopoietic stem cell transplantation. Oral Dis. 2022;28:1987–1994. https://doi.org/10.1111/odi.13899