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Evaluating the effects of the essential oils *Leptospermum scoparium* (manuka) and *Kunzea ericoides* (kanuka) on radiotherapy induced mucositis: A randomized, placebo controlled feasibility study

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A B S T R A C T

This study evaluated the effects of an essential oil mouthwash on radiation induced mucositis of the oropharyngeal area during treatment for head and neck cancers. Nineteen adult patients completed the randomized placebo controlled trial which involved the use of a gargle containing 2 drops of a 1:1 mix of the essential oils of manuka (*Leptospermum scoparium*) and kanuka (*Kunzea ericoides*) in water. Those in the essential oil gargle group were observed to have a delayed onset of mucositis and reduced pain and oral symptoms relative to placebo (gargling with water) and the control ('usual care') groups. In addition those in the essential oil group were seen to have less weight loss (1% loss) than the other two groups (control 2.5%, placebo 4.5%). However a significant limitation in this study was the small sample size. Although the results from this feasibility study support the hypothesis that very small volumes of manuka and kanuka used in a gargle can provide a positive effect on the development of radiation induced mucositis, further research is required to confirm this finding. Randomization was applied according to the timing of the patient's entering the trial as well as their physical ability to gargle. Confirmation of these findings would pave the way for introduction of a simple, yet effective treatment for a condition which causes considerable discomfort and for which there is currently no definitive treatment.

Introduction

Radiation induced mucositis (RIM) of the oropharyngeal area is an accepted, though distressing, side effect of radiotherapy for head and neck cancers (HAN), affecting between 80 and 100% of patients (Scully et al., 2003b). Personal and health costs can be high due to the nature of the treatment and additional burdens associated with treatment interruption due to side-effect severity (Epstein et al., 2001; Trotti et al., 2004). The main signs and symptoms of the reactions experienced include erythema, ulceration and pain (Mueller et al., 1995). Treatment factors including radiation dose, size of field, site of radiation and concomitant chemotherapy all impact on the severity of reactions experienced (Scully et al., 2003b). Other factors also influence the severity including smoking during treatment and increasing age (Rugg et al., 1990), however gender does not seem to be an influencing factor (Duncan and Grant, 2003).

Identifying agents which can be used to prevent or treat RIM is a primary concern for researchers and clinicians. An oral care solution or product for HAN cancer patients needs to reduce oral flora, have an acceptable taste, reduce oral pH, assist in the re-epithelialization of the mucosa and be non-toxic and non-irritating to the oral tissue (Carl and Emrich, 1991). Usual oral care recommendations at MidCentral Health at the time included baking soda and chlorhexidine or benzydamine hydrochloride mouthwashes. Baking soda is used to help slough off cellular debris and has been found to be effective in reducing the pain and discomfort of radiation induced mucositis (Dodd et al., 2003). Despite its wide spread use there is little empirical evidence to support the use of chlorhexidine as a mouthwash (Plevová, 1999; Scully et al., 2003a,b). Epstein et al. (2001, 1989) note that benzydamine helps to stabilize cell membranes in the mucosal area and has been effectively used as a gargle with minimal side effects. Several recent systematic reviews on this topic have found however that there is insufficient

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evidence to make clinical recommendations for practice and that the best options for managing radiotherapy induced mucositis are good oral hygiene and regular review of the patient (Clarkson et al., 2007; Kwong, 2004; Worthington et al., 2007; Yanovich et al., 2004).

Growth of interest in plants as sources of biological active compounds have included investigations into the use of plant extracts such as chamomile and *Aloe vera* extracts/gel for RIM however the results of these studies have had mixed outcomes (Su et al., 2004; Maddocks-Jennings et al., 2005; Dörr et al., 2005). A group of plant products known to have a range of biological activities, including anti-inflammatory, analgesic and antimicrobial properties (Lis-Balchin, 2005), but which have not previously been investigated for use in RIM, are essential oils (Lis-Balchin, 2005).

Manuka (*Leptospermum scoparium*) and kanuka (*Kunzea ericoides*) are indigenous to New Zealand and have a long history of being used medicinally by both Maori and early European colonists. Most commercial interest in manuka has been related to its use as a floral source for the production of medicinal honeys (Visavadia et al., 2008) and in identification of essential oils high antibacterial triketones (Douglas et al., 2004; Perry et al., 1997). Both these essential oils are known to have antibacterial and antifungal activity and contain constituents, such as sesquiterpenes hydrocarbons, which have anti-inflammatory and analgesic actions (Lis-Balchin, 2005; Lis-Balchin et al., 2000).

This randomized placebo controlled feasibility study evaluated whether gargling with a solution of essential oils of manuka (*L. scoparium*) and kanuka (*K. ericoides*) during radiotherapy had any beneficial effects on the appearance of RIM and the symptoms experienced by patients with HAN cancer. The primary outcomes evaluated were the development of mucositis, the experience of pain and the effects on nutritional status including weight changes. Secondary outcomes evaluated included effects on mood and coping.

Method

Site and participants

The research was conducted at the Regional Cancer Treatment Services (RCTS) in Palmerston North New Zealand. This service is one of six in New Zealand and provides cancer treatment to a population base of 540,000 people. HAN patients account for between 7 and 9% of the 1200 new patients admitted each year. A summary of recruitment and interventions in this trial are shown in Fig. 1. All patients who were having non-palliative radiotherapy which included the oropharyngeal area during the allocated research time were approached. Additional selection criteria were that the patient must be: aged over 18, able to provide informed consent, having radiotherapy for at least four weeks, physically able to gargle, able to complete records accurately, and not allergic to the gargling solution. Consent for participation was also required from each patient's radiation oncologist. Patients were excluded from the trial if they did not meet all of the criteria or later withdrew. If patients were not able to gargle but met all other criteria they were invited to be in the study in the control group. A control group consisting of patients receiving usual oral care interventions was included to compare results of both the active and placebo groups with. Nineteen adult patients who were having radiotherapy to the head and neck area, which included the oropharyngeal area, completed the trial and were included in the data analysis. All patients received their radiotherapy during August 2004–April 2005. Ethical approval was obtained from the Manawatu-Wanganui Regional Ethics Committee and the Charles Sturt University Ethics in Human Research Committee.

Interventions

Essential oils distilled from wild grown plants in the north of the South Island of New Zealand were used in this study as oils from these plants are reported to contain the highest proportions of key anti-inflammatory and analgesic constituents (trans calamenene and viridiflorol) (Perry et al., 1997). Both treatment and placebo groups received their solutions in identical 25 mL amber bottles fitted with dropper caps. Patients in the treatment group were provided with a 1:1 mix of manuka and kanuka oils while those in the placebo group received a bottle of sterile water. The oil or water was further diluted by the patients by mixing the two drops of the liquid to 10–15 mL of warm tap water at the time of gargling. Whilst the essential oil would not disperse completely in the warm water, as the entire volume of water was gargled or swallowed it is taken that the entire dose of essential oil (2 drops) was used at each intervention by each patient. After gargling and circulating the fluid around the mouth for at least 15 s it was spat out and a fresh preparation of the same dilution was then swallowed. The purpose of swallowing the solution was to try and capture as much of the pharyngeal area as possible. Gargling commenced either on the day of radiotherapy or up to two days before depending on when the patient entered the trial. They were asked to gargle 30 min either before or after eating, smoking or drinking as well as before and after each radiotherapy treatment. On radiotherapy days patients would be gargling up to five times with the research gargle as well as possibly having other gargles or oral treatments. Gargling was to continue for a week after completion of radiotherapy.

In this study patient compliance was important therefore the gargling needed to fit in with their schedule of eating, treatment, other oral care regimes and travelling to and from treatment. The post radiotherapy gargle was considered the most important to evaluate whether there was any soothing effect. In this study patients were gargling between 3 and 5 times per day depending on whether they were having radiotherapy. Some patients commented that they found it hard to fit in the five gargles especially if they were travelling some distance to and from treatment. Over the course of a day a patient would swallow up to ten drops of essential oil and gargle with up to ten drops (2 drops per treatment, 3–5 times per day). All patients were to continue with usual oral care as prescribed by their doctor but were asked not to self prescribe other products.

Recruitment and treatment allocation

Potential participants in the study were identified by clinic staff and approached about participation by one of the authors (WM-J) who explained the background to the project and sought consent for participation. A convenience sample of twenty-six patients who met the inclusion criteria and were due to commence radiotherapy treatment during the allocated time consented to be involved in the study. Four patients subsequently withdrew voluntarily from the trial for personal reasons. All participants were provided with a project information sheet which, in addition to general contact and project information, detailed the procedure for diluting the gargle mix and that they should stop using the gargle and notify the research team if they experienced any allergic or other reaction. As patients entered the trial they were allocated to either an active gargle (essential oils), placebo gargle (sterile water) or control group (no gargle) in turn such that the first person was allocated to the essential oil group, the next to the sterile water group and so on. Full randomization however was not possible in this study. If a patient was willing to participate but could not gargle they would be allocated to the control group and the next person allocated to

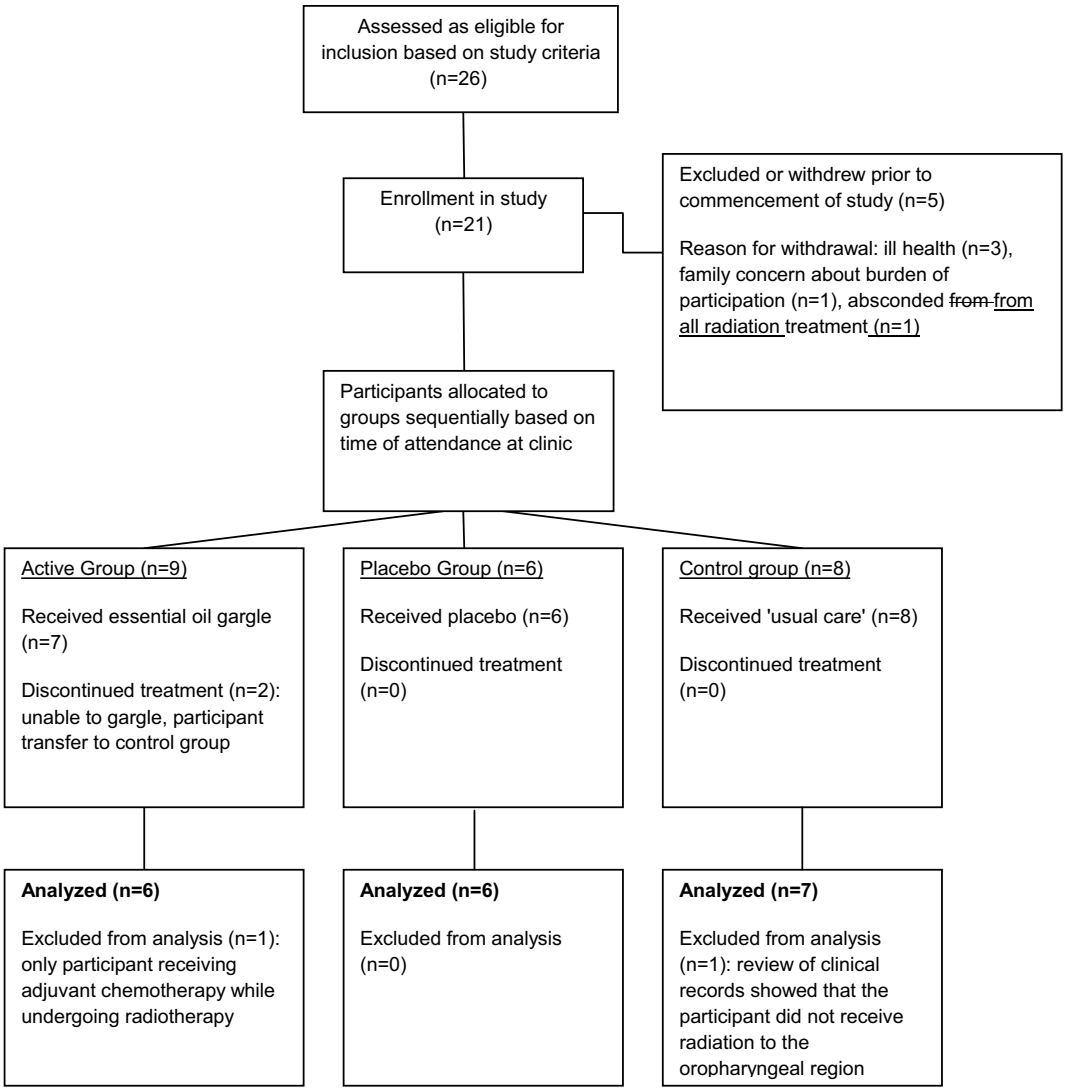

Fig. 1. Flowchart showing recruitment and treatment allocation of study participants.

the appropriate intervention group. The researcher had no prior knowledge of or relationship with any of the patients nor were they involved in their clinical care.

Blinding

Clinical staff and radiation oncologists conducted all objective assessments and were blind as to which treatment arm patients were in. Patients who were allocated a gargle were informed that a range of gargle options were being explored and those in the control group were advised that data was being collected about patient's experiences during radiotherapy. Patients completed a daily diary recording their pain scores, medication use, and other oral symptoms (Fig. 3). Pain was recorded against a 10-point visual analogue scale (VAS, Fig. 2). At the weekly clinical review the radiation oncologist graded the oral mucosa using the adapted Radiation Therapy Oncology Group (RTOG) Scale of Acute Toxicities 0–4 scale (Table 1) as well as recording body weight and general well being. Patient diaries were collected by the researcher at this time as well as a review of clinical notes. Once patients were discharged from the clinic they were followed up by the researcher by phone for at least two weeks to ensure no adverse reactions to the

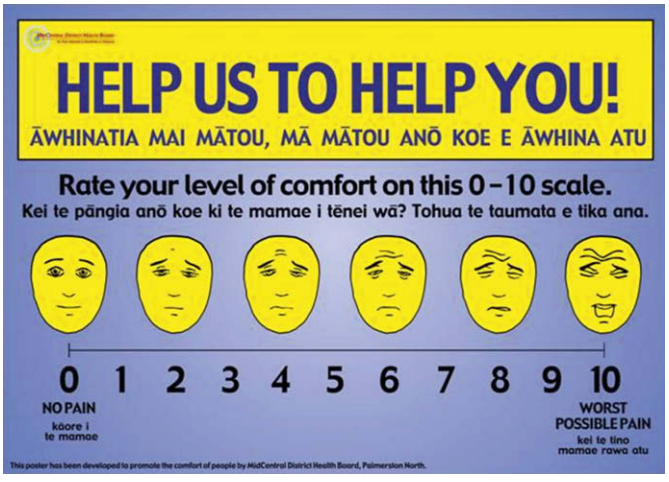

Fig. 2. MidCentral Health Pain Scale (reproduced with permission by the Pain Services at MidCentral Health). Information is provided in both English and Maori.

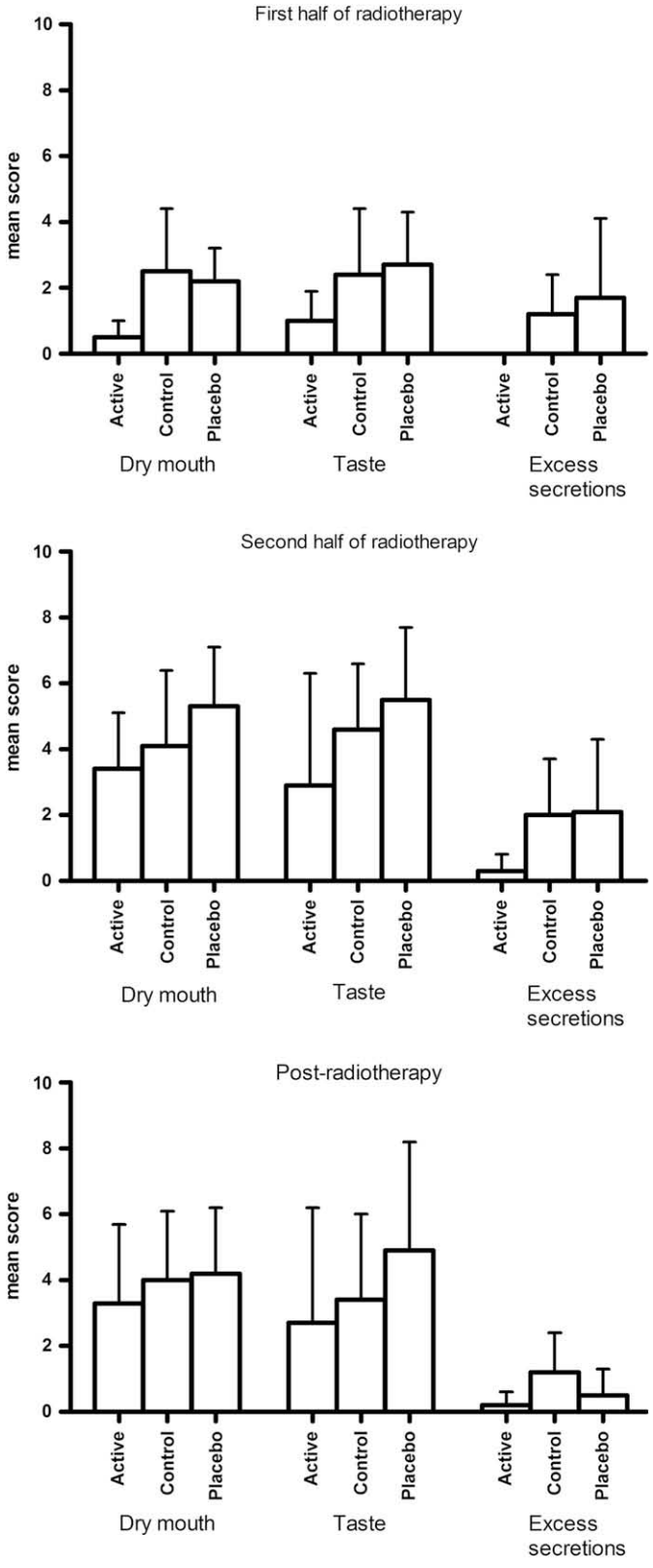

Fig. 3. Data from the retrospective oral symptom survey. Data is presented as the mean and standard deviation for each domain.

study treatments. At this time the patients were also asked to complete a survey recalling the severity of oral symptoms in the first and second halves of treatment, and post-treatment. This data was collected using a pre-printed form listing symptoms representing three domains: dry mouth/cough; altered taste and appetite; and excess secretion/nausea & vomiting with patients asked to rate each item from 0 (not present) to 10 (very severe).

Table 1
Modified Radiation Therapy Oncology Group (RTOG) Scale of Acute Toxicities used by MidCentral Health (New Zealand) for the assessment of the oropharyngeal area following head and neck radiotherapy.

Grade	Oropharyngeal reaction	Oral cavity reaction
0	Odynophagia	Normal
1	Mild dysphagia	Erythema, mild pain, not needing analgesia
2	Moderate dysphagia, liquid diet, requiring narcotic analgesia	Patchy mucositis, inflammation, moderate pain
3	Severe dysphagia, >15% weight loss, artificial feeding and/or hydration	Confluent mucositis, narcotic analgesia
4	Complete obstruction or ulceration	Complete ulceration, haemorrhage or necrosis

At the commencement of their treatment patients received a daily schedule, which included weekly doctors and occasional dietician visits. The principal researcher made contact with each patient on a weekly basis. This would mostly be at the time of the doctor's appointment, but if this was not possible the principal researcher made phone contact or met with the patient at another appointment time. The clinical notes were reviewed each week. Most patients had their initial doctor's appointment after receiving 5–7 of doses. At these appointments the patient would be seen either by the consultant or registrar. Prior to the appointment the principal researcher and patient discussed the diary and if this was full these were collected at this time. It also meant that any queries over diary entries could be clarified. As the waiting was sometimes lengthy (up to an hour) there was plenty of time for general conversation. Whilst the waiting was often time consuming the researcher found it useful as over time a rapport was built up with the patients and they felt involved and committed to the trial. Most of the patients had a family member present and they were usually fully involved in the trial as well, such as reminding the patient to gargle, or to record their diaries.

The weekly review with the doctor followed a standard format where the patient would be weighed by the nurse or nurse aide and then a general enquiry into their well being, eating patterns, fatigue; condition of skin and how they felt they were coping with treatment. There was also time for the patient to ask questions about their treatment. Sometimes a nurse or nurse aid would also sit in on the session in case things were needed. The principal researcher would sit away from the patient and record the review in long hand or electronically. The oropharyngeal area would then be assessed and graded by the doctor. At times they needed reminding to do this by the researcher if they appeared to not be inclined to conduct this. Prior to getting permission from the medical staff for the trial it had been their clear request that whilst they were happy for this trial to proceed, it must not interfere with the usual management of patients and that there was minimal extra workload for any member of staff. Therefore interrater reliability or cross-checking assessments was not possible.

All clinical staff would be aware a patient was in the trial; however they were blind to which arm the patient was in. The consent form and any other documentation relating to the trial were in a distinctive green colour so that it stood out from any other clinical notes. Whilst the researcher did not participate in the assessment in any way, often the patient or doctor asked questions or clarified information. For example a patient may have forgotten how many times they were taking a certain medication and the researcher was able to refer to the patient diary to confirm details, which the doctor could note along with the clinical observations.

From time to time the patient asked the researcher questions about the treatment or medications or passed comments about the clinical staff if they felt they weren't receiving adequate care. The researcher was careful to clarify with each patient that she was not part of the clinical team and that no treatment advice or information could be given. If necessary the researcher recommended that the patient ask to see a member of the clinical staff. Clearly patients and staff were interested in the trial and if there had been any results. The researcher generally responded along the lines that it was too early in the data collection phase to draw any conclusions as to effect. The researcher depended on the help and support of many people within the department including the receptionist, booking clerks, file clerk, medical, radiotherapy and nursing staff. As a guest it would have been virtually impossible for the researcher to conduct the trial without this.

Data analysis

Mean daily values were calculated for pain scores, medication use for each patient and each group of patients. Mean reactions of the oropharyngeal area, the radiation dose when these occurred and the weight changes over treatment were also calculated for each patient and each group. Medication use was calculated as number of units of a standard dose for each medication type. All data was initially collected using Microsoft EXCEL and a Palm pilot and was then transferred to an SPSS (Statistical Package for Social Sciences, v11) for further analysis. Results were compared between each gargle group and the control group as well as comparing other variables such as gender, age, treatment factors and patient related variables. Differences between groups were calculated using ANOVA with Tukey post test. *P* values of ≤ 0.05 were deemed to be statistically significant differences.

Results

Three clinical outcomes were evaluated in this study: the development of mucositis, pain and nutritional effects. The characteristics of the individuals who completed this study are shown in Table 2. Five females and fourteen males completed the study with a mean overall age at the time of commencement of 68.9 years (range 45–81 years). All except one patient denied smoking during treatment. Five patients did not have family staying with them during their treatment.

Development of mucositis

For the purposes of this study the radiation dose when mucositis first appeared was recorded as well as the maximum mucositis score recorded. The oral assessment tool used clinically in the department was used for assessments. This tool is presented in Table 1. It was not appropriate for the researcher to suggest a different tool for this trial. All radiation oncologists are trained by the department to use this tool. From the outset of the study, it was made clear to the principal researcher that staff workload was not to be affected by this study; therefore it was not appropriate for interrater reliability or having 2 people assess the area to occur and usually for only one doctor may be on duty at a time. All nineteen patients experienced some degree of mucositis with 31.6% (6/19) experiencing a grade 1 (out of a maximum of 4) and 63% (12/19) experiencing a grade 2 reaction (see Table 3). One patient experienced a grade 3 reaction and had her treatment halted on two separate occasions to allow her oral area to heal. The active gargle group went for the longest time before a reaction occurred; this was at a mean radiation dose of 3120 cGy. This is the equivalence of 15.6 treatment days at a typical daily dose of 200 cGy. The remaining patients experienced their reactions considerably earlier with the placebo group experiencing their first reactions after just over seven days (1450 cGy) of treatment and the control group experienced their first reaction at 2163 cGy (equivalent to 10.8 treatment days). Difference between the active gargle and the placebo group, and between the active gargle and control group was found to be statistically significant ($p = 0.05$). Irrespective of group allocation all patients had higher mucositis scores during the second half of their radiotherapy treatment and all patients had had least doubled their initial mucositis scores but the end of treatment: active group 0.4 v 1.4 (mean mucositis score for the 1st half of radiation therapy v mean score for the 2nd half of treatment); placebo group 1.0 v 1.3; control 0.5 v 1.

Comparisons between different treatment related factors such as treatment site, dose, presence of dentures, pre-radiation surgery and concomitant chemotherapy were also made. However due to the small sample size of some variables it was not possible to make statistical comparisons. The only treatment variable of note is that patients who had a full set of dentures had lower overall mucositis scores (mean mucositis score of 1.2; $p = 0.023$) compared to patients who had undergone any dental extraction prior to commencing radiotherapy (mean mucositis score 2.2).

Table 2
Patient demographics according to group allocation (all 19 patients who completed the trial). Those in the active group gargled with a diluted 1:1 mix of manuka and kanuka oil while those in the placebo group gargled with water in addition to usual care. The control group received usual care but did not use a gargle solution.

	Active ($n = 6$)	Control ($n = 7$)	Placebo ($n = 6$)	Total ($n = 19$)
Male	5	7	2	14
Female	1	0	4	5
Age 45–60 y	1	4	0	5
Age 61–75 y	2	2	5	9
Age >75 y	3	1	1	5
No surgery pre-radiotherapy	2	3	3	8
Own teeth	2	3	1	6
Teeth removed pre-radiotherapy	1	0	0	1
Dentures	3	2	2	7
Partial dental removal pre-radiotherapy	0	2	3	5
Family member present	6	6	1	13
Treatment site				
Tongue	1	1	0	
Throat	1	1	0	
Submandibular	0	1	0	
Thyroid	0	1	0	
Supraglottis	0	1	0	
Neck lymph	1	2	0	
Jaw	1	0	0	
Cheek	0	0	1	
Larynx	0	0	2	
Floor of mouth	1	0	2	
Maxilla/nose	1	0	1	
Mean radiation dose to OP area cGy	5933 SD = (653)	5300 SD = (814)	6200 SD = (565)	

Table 3
Development of mucositis across treatment according to research group allocation.

	Active (6)	Control (7)	Placebo (6)
cGy at no reaction	3633 (1627)	2417 (1371)	1600 (921)
cGy at 1/4	3666 (1681)	2617 (1502)	1450 (661)
cGy at 2/4	5033 (1713)	3850 (1368)	3760 (2291)
Max. mucositis score	1.7 (0.5)	1.7 (0.5)	1.8 (0.7)
Mean mucositis score 1st half RT	0.4 (0.4)	0.5 (0.6)	1.0 (0.7)
Mean mucositis score 2nd half RT	1.4 (0.3)	1.6 (0.5)	1.3 (0.7)

The experience of pain

Patients scored their oral pain using a 0–10 visual analogue scale up to five times per day during and for two weeks after radiotherapy concluded. Comparisons are made of the mean daily pain score, the radiation dose when a patient first experienced oral pain of 3/10 or higher and the mean daily medications used by patients to control their oral pain are all compared. While not all patients experienced oral pain, each of the research groups had similar mean pain scores which gradually increased over the treatment time. Within the active group ($n = 6$) 2 individuals experience pain scores ≥ 3, in contrast 5 from the control group ($n = 7$) and 4 from the placebo group ($n = 6$) experienced this level of pain. The active group also went the longest until this level of pain was reached: active group 3600 cGy, control group 3000 cGy and placebo group 2100 cGy (typical radiation dose per day is 200 cGy/day). This was also reflected in the daily analgesic use with the active group using a mean of 0.2 units/day during the first half of treatment, 0.4 units/day in the second half and 0.5 units/day post-radiation treatment. For the placebo group the values were 0.4, 0.6 and 0.6 units/day respectively and for the control group 0.4, 0.8 and 0.3 units/day. In all cases where oral pain was experienced, this preceded the visible appearance of mucositis by a day. Regardless of the total length of radiotherapy all patients who experienced pain felt it exactly half way through their radiotherapy. Gender and age did not appear to have an impact on the pain experience and medication use for this group of patients. Those patients who had a family member present throughout their treatment tended to report pain more frequently and rate it higher than those without family members present.

Effects on nutritional status

The development of mucositis will impact on the patient's ability to eat normally. In this study weekly weight change was recorded along with the subjective measurement of taste, appetite, ability to eat, dry mouth, nausea and vomiting and how the patient thought this affected their day-to-day functioning. Weight change was calculated as a percentage of change over base line for each patient and then the mean of the percentages was calculated for each group. No statistically significant weight changes between the groups were recorded with weight change and mean loss of 1% of initial body weight recorded for the active group, 5.2% loss for the control group and 4.1% loss for the placebo group. In addition two patients in the active gargle group gained weight over their treatment.

All patients reported experiencing a range of symptoms oral and appetite related symptoms. Reported symptom severity tended to be lower in the active (essential oil) group particularly for the domain of excess secretions/nausea and vomiting. All patients in the active group with altered taste were either improving or back to pre-radiotherapy levels by week two after completion of treatment. No patients in the control group had improved taste until at least two weeks after treatment had finished. Some patients made the comment that they felt the essential oil solution 'repeated' on them once they swallowed but did not find this unpleasant. Others felt it provided a 'coating' sensation to the mouth. No significant differences were observed related to oral symptoms and gender or other patient variable.

Discussion

Mucositis related to radiotherapy is a significant issue for those with head and neck cancer and there are no definitive treatments for this condition. In this study evidence is presented which suggests that a gargle or mouthwash containing the essential oils of manuka and kanuka may help to delay the development of mucositis and reduce associated health effects (e.g. weight loss, pain and oral symptoms). The most important result for this trial is the time it took for mucositis to first occur with those in the active group experiencing a delay in the appearance of mucositis compared to both placebo and control groups. Recordings of results on pain, analgesia use and oral symptoms were reduced in the active gargle group and once use of the active gargle ceased patients reported an increase in both pain and analgesic use. Together this data supports the hypothesis that the active gargle was having a positive effect on the oral cavity. This is further supported by the observation that two patients in the active group gained weight during the study and one had no weight change; weight loss of up to 10% of body weight is a common phenomenon in those with head and neck cancers and predicted by poorer quality of life indices (Jager-Wittenaar et al., 2007; Petruson et al., 2005; van den Berg et al., 2006). Although the time to development of mucositis in the control groups was similar to that reported in the literature (Trotti et al., 2004), however it is also acknowledged that length of treatment, pre-treatment surgery and other factors can impact on development of mucositis (Porock et al., 2004). As the sample size in this study was relatively small influence of these factors on the study outcomes is unknown.

Overall the active gargle was well tolerated by patients, with no evidence of toxic or side effects relating to swallowing of it. The gargle compliance was high with it being used at least 80% of the required time by all patients using it. That the active group also reported the lowest level of nausea and vomiting suggests that swallowing the gargle did not have an adverse effect on the gastrointestinal systems. In addition comparison of the cost of the essential oils is comparable to the other oral care products used by patients in this study and anecdotally may have higher compliance compared to the other products. Clinical evidence suggests that manuka essential oil is effective in vivo against periodontopathic and cariogenic bacteria (Takarada et al., 2004) and there is growing evidence to suggest that essential oils have a role in improving oral health by causing lysis of oral bacteria and helping reduce the bacterial load (Ouhayoun, 2003; Seymour, 2003).

Due to the small sample size, results relating to the secondary outcomes of mood and coping did not reach significance; therefore they have not been presented here. A discussion paper may be produced from these results at a later stage. Fig. 3 summarizes the results relating to the experience of oral sensations such as taste changes, secretions and dry mouth. None of these results reached statistical significance.

While this study points to the potential of essential oil containing gargles to provide a benefit for those undergoing radiotherapy the data needs to be considered in light of the study limitations. The main limitation in this study is sample size. A post hoc power analysis was conducted on the results obtained for the development of mucositis (the primary outcome) and this indicated that between 4 and 8 patients were needed for each treatment arm depending on the exact outcome measured relating to mucositis (e.g. time at no reaction, time at grade 1, 2 or 3). While the current study falls within this range post hoc power analyses for the other outcomes measured such as weight change, pain data and subjective quality of life measures, suggest that at least 30 patients per treatment arm would be needed. As with any population group undergoing a major medical intervention, and who may be ill, elderly or both recruitment to research studies is difficult. In addition timing of gargling in relation to eating, drinking or smoking was not explored in this study. Within this study participants were advised not to use the gargle within 30 min of eating, drinking or smoking and the gargle was also swallowed in an attempt to coat the upper part of the pharynx which was not

reached by the gargle. This is compounded by attempts to recruit at sites, such as the one used in this study, where the condition of interest makes up only a small proportion of total site attendees. In this study the nature of the condition also resulted in some individuals being unable to continue to participate in some treatment arms and their reallocation to the control group is a threat to randomization.

Whilst it is acknowledged that the essentials do have a distinctive aroma, it was unlikely that patients in different treatment arms were aware of others in the same trial as their individual treatment timings rarely if ever coincided. Patients only knew they were taking part in a trial evaluating different types of oral care, they did not know what the other options were.

Conclusions

The results from this feasibility study support the hypothesis that very small volumes of manuka and kanuka used in a gargle can provide a positive effect on the development radiation induced mucositis. However due to the small sample size in this study it is recommended that the work be repeated in a large randomized clinical trial and should include measuring anti-inflammatory markers such as salivary lactoferrin, oral microbial cultures and assessment of quality of life. Should this treatment be shown to be effective it would provide a cost effective, easy to administer and novel treatment for what is recognized as a cause of significant discomfort and pain in those undergoing radiotherapy for head and neck cancer.

Conflict of interest statement

I have no conflict of interest in the conducting or submitting the results of the research.

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