

Topical Application of Sesame Oil for the Prevention of Chemotherapy-Induced Oral Mucositis: Pilot Study in Seven Hematopoietic Cancer Patients

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Abstract

Background: Oral mucositis is one of the most uncomfortable and common complications of chemotherapy. Inflammation which is initiated by release of free radicals from oral mucosal tissue exposed to anticancer drug is involved in the development of oral mucositis. Therefore, it is expected that antioxidant and anti-inflammatory effect of sesame oil may be effective for the prevention of chemotherapy-induced oral mucositis. In the present study, effects of topical application of sesame oil on the chemotherapy-induced oral mucositis were evaluated.

Methods: Sesame oil of Japanese Pharmacopoeia grade was applied to 7 hematopoietic cancer patients during chemotherapy for 14 days by swabbing more than 3 times a day after ordinary oral hygiene. 4 hematopoietic cancer patients receiving chemotherapy at the same time acted as control. Objective and subjective symptoms, grade of oral mucositis, cytological change of the smear of oral mucosa and subjects' impressions about sesame oil application were evaluated.

Results: Only one subject developed oral mucositis in the sesame oil application group whereas 2 subjects developed oral mucositis in the control group. Additionally, oral mucositis in the subject in sesame oil application group occurred after the termination of sesame oil application and healed by restarting the application of sesame oil. Average grade of oral mucositis of sesame oil application group was lower than that of control group. Cytological examination revealed that inflammatory change was reduced in sesame oil application group compared to control group. 5 of 7 subjects who had experienced mucositis in previous chemotherapy session felt that sesame oil was effective for the prevention of oral mucositis.

Conclusion: Topical application of sesame oil is suggested to be useful for the prevention of chemotherapy-induced oral mucositis. Reduced inflammatory change was considered to be implicated in its preventive effect.

Introduction

Oral mucositis is one of the most uncomfortable and common complications in cancer patients who receive chemotherapy [1]. Pain due to mucositis influences swallowing and mastication, resulting in subsequent malnutrition or dehydration. Bacterial infection of injured oral mucosa may cause the invasion of bacteria into the blood stream. Dose reduction or treatment schedule modification may be necessary when severe oral mucositis develops. Moreover, oral mucositis begets excess costs for supportive care and hospitalization on cancer patients receiving chemotherapy.

Currently oral mucositis is considered to take place in five different phases Initiation, Message generation, Signaling and amplification, Ulceration, and Healing [2]. In the initiation phase, mucosal epithelium, vascular endothelium and connective tissues exposed to anticancer drugs release free radicals. These free radicals not only cause direct tissue injury but also initiate a biological cascade. In the message generation phase, activated transcription factors such as NF- κ B upregulate genes that control synthesis of biologically active proteins including pro-inflammatory cytokines. Anticancer drugs are also capable of activating enzymes that increase the rate of apoptosis. The production of these proteins results in the damage and death of mucosal epithelium, hence making oral mucosa thin and erythematous. Many of these proteins simultaneously enhance message generation and then mucositis proceeds to signaling and amplification phase. For example, tumor necrosis factor- α (TNF- α) -whose level is increased as a consequence of NF- κ B activation in message generation- amplifies NF- κ B activation in addition to direct tissue injury. In turn, NF- κ B activation leads to further production of pro-inflammatory cytokines. Consequently, tissue injury continues to occur beneath the mucosal surface, even after chemotherapy has been completed. Increased vascular permeability induced by inflammation

also enhances cytotoxicity of anticancer drugs [1]. In ulceration phase, tissue injury reaches a climax; the integrity of oral mucosa is lost, followed by stimulation of exposed neuronal endings, which creates clinically significant pain, and colonization of oral resident bacteria on the ulcerated surface. Furthermore, colonized bacteria release cell wall products that penetrate adjoining tissue and stimulate inflammation. When patients have neutropenia, bacteria invade into blood vessels and in the worst-case scenario it results in bacteremia or sepsis. Finally, in the healing phase, proteins that promote migration, proliferation and differentiation of immature cells at the border of the ulcer are released from the extracellular matrix and oral mucositis is eventually healed.

In 2004, the first evidence-based clinical practice guidelines for the management of mucositis were published [3]. The guidelines addressed the importance of basic oral hygiene and oral care protocols in maintaining mucosal health and function. Although specific agents or approaches used in oral care protocols had insufficient evidence to support the guidelines, a lot of attempts, (e.g. topical application of growth factors [4] and agents with anti-inflammatory [5]. Or antimicrobial effects [6]) have been made to manage chemotherapy-induced oral mucositis. After the publication of the guideline, the efficacy of many agents, such as herbal medicine [7], palifermin [8],

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honey and its mixture of beeswax and olive oil- propolis [9], or supersaturated calcium phosphate oral rinse [10], for the prevention and treatment of oral mucositis have been evaluated since management of chemotherapy-induced oral mucositis is an very important issue in oncology nursing.

The authors have been investigating the effect of the application of sesame oil on the oral care of elderly individuals. As anti-inflammatory [11,12] and antioxidant effect [12, 13] of sesame oil, or sesamin, one of its lignans, and antimicrobial effect of fatty acids contained in sesame oils [14] have been reported, it is suggested that sesame oil might be also effective for the prevention of chemotherapy-induced mucositis. Sesame oil is particularly suitable as a natural treatment in oral care because it is widely used as cooking medium in many Asian countries, including Japan. So, it can be used as a readily available 'home remedy' for preventing/containing the development of mucositis. Some Japanese nurses have practically used sesame oil in three cancer patients receiving chemotherapy and reported that development of mucositis was prevented in all of them [15].

In the present study, the authors report the results of topical sesame oil application in seven hematopoietic cancer patients.

The distinct cerebral activation was observed during low-level laser acupuncture (continued wave and 10 Hz-modulated wave stimulation) at KI1 of the left foot in healthy right-handed volunteers [14]. Most of the activated areas, observed by functional magnetic resonance imaging, were involved in the functions of memory, attention, and self-consciousness. The cerebral hemodynamic responses to two laser acupuncture stimulation modes and its mechanism is based on not only afferent sensory information processing but also alteration of hemodynamic properties during external stimulation.

Materials & Methods

Subjects

Eleven patients who had been admitted to the general hospital for the chemotherapy of hematopoietic cancer received an explanation of the study and those whose consents were obtained participated in the study.

Materials

Sesame oil of Japanese Pharmacopoeia grade (Nikko Pharmaceutical, Japan) was used for application. Table 1 shows the fatty acid composition of sesame oil [16].

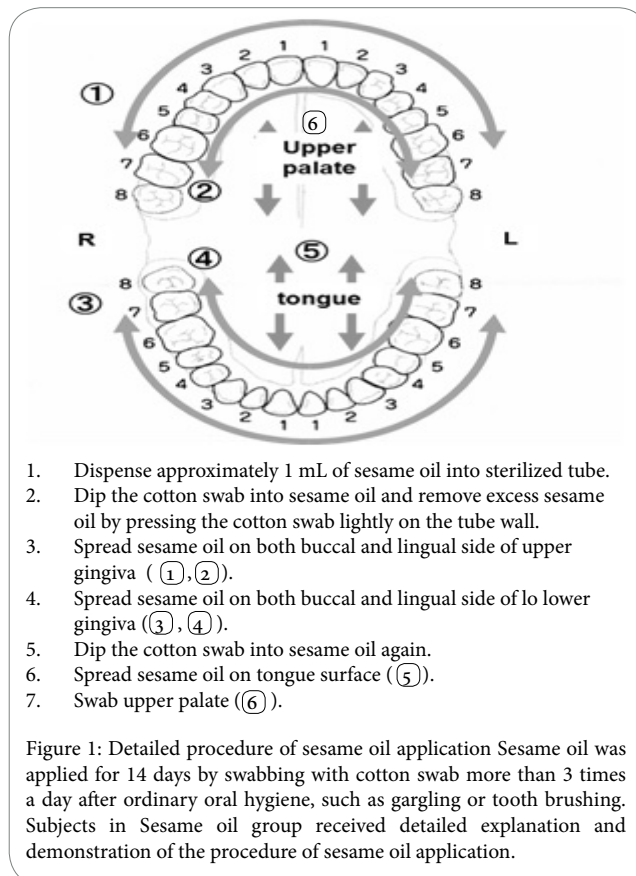
Lauric acid (C12:0)	0.4
Myristic acid(C14:0)	0.5
Palmitic acid(C16:0)	11.2
Stearic acid(C18:0)	3.4
Oleic acid(C18:1)	42.3
Linoleic acid(C18:2)	42.0
Linolenic acid(C18:3)	0.2

Table 1: Fatty acid composition of sesame oil (%).

Procedure

Seven subjects used sesame oil in addition to their ordinary oral hygiene (Sesame oil group). Sesame oil was applied for 14 days by swabbing with cotton swab more than 3 times a day after ordinary

oral hygiene, such as gargling or tooth brushing. Subjects in Sesame oil group received detailed explanation and demonstration of the procedure of sesame oil application (Figure 1). Application was started on the previous day of the beginning of chemotherapy. Subjects in Sesame oil group were asked to record the following data:



1. How many times they applied sesame oil and
2. How many times performed ordinary oral hygiene.

Four hematopoietic cancer patients who received chemotherapy during the same period acted as controls (Control group). Subjects in Control group were asked to perform ordinary oral hygiene and to record the number of oral hygiene.

Evaluation

Information of age, sex, diagnosis, chemotherapy regimen and clinical data of the subjects were obtained from the medical records.

The effect of sesame oil application was evaluated by objective and subjective symptoms, grading of mucositis and cytological evaluation of swabbed oral mucosa. In addition subjects of Sesame oil groups answered to the questionnaire about their impressions on sesame oil application.

Objective and subjective symptoms: Oral cavities of the subjects were observed and recorded once a day by the researcher. Subjects were also asked to record subjective symptoms.

Grading of mucositis: Results of the objective and subjective symptoms were graded according to the grading scale of Mucositis/stomatitis of Common Terminology Criteria for Adverse Events (CTCAE), v3.0 (Table 2) [17].

Grade1	Grade2	Grade3	Grade4	Grade5
Erythema of the mucosa	Patchy ulceration or pseudomembranes	Confluent ulceration or pseudomembranes; bleeding with minor trauma	Tissue necrosis; significant spontaneous bleeding; life-threatening consequences	Death

Table 2: Grading scale of CTC/AE, v3.0.

Cytological examination: Samples for cytological examination of both Sesame oil and Control group were obtained on Day 14 by swabbing the oral mucosa with sterilized cotton swab. Samples were spread on glass slide and fixed immediately with ethanol. Fixed samples were then stained with Papanicolaou's stain solution. Each sample was examined by qualified cytologist who was blinded about the sample source. The samples were examined according to the following criteria [18]:

1. Inflammatory change: (-) No inflammation; (\pm) very small number of inflammatory cells are observed; (+) Inflammatory cells are observed in less than one third of the fields; (++) Inflammatory cells are observed in more than one third of the fields; (+++) Severe inflammatory changes are observed in all fields.
2. Bacterial contamination: (-) No bacterial cell are observed; (\pm) very small number of bacterial cells are observed; (+) Bacterial cells are observed in several fields; (++) Bacterial cells without prominent colony formation are observed in entire background; (+++) Bacterial cells with prominent colony formation are observed in entire background.

Questionnaire: Subjects of Sesame oil group answered a short questionnaire about their impressions on sesame oil application.

Statistical analysis

Average age, lowest leukocyte count, highest CRP value and mucositis grade of Sesame oil group and Control group were compared by Student's t test. Chi squared test was used for the comparison of cytological evaluation. P values of $< .05$ were considered statistically significant. IBM SPSS Statistics version 19 was used for statistical analysis.

Ethical consideration

The study was approved by Ethical Committee of both Graduate School of Nursing, Chiba University and the research facility.

Results

Outline and general status of the subjects

Table 3 shows the outline of the subjects. 4 of 7 subjects in Application group and 3 of 4 subjects in Control group were the patients with acute myelogenous or lymphatic leukemia. Additionally, 3 of 7 subjects in Sesame oil group and 1 of 4 subjects in Control group were the patients with non-Hodgkin lymphoma. Mean age was 63.7 (range 31 to 87) in Sesame oil group and 57.5 (range 43 to 74) in Control group respectively and there was no significant difference. Regimens and phases of chemotherapy differed among the subjects. Methotrexate (MTX), cyclophosphamide (CPA), doxorubicin and etoposide which have higher risks of oral mucositis [19, 21] were administered to 5 subjects in Sesame oil group (Subject A, C, D, E, G) and 2 subject (Subject H, I) in Control group. High dose of MTX or CPA and doxorubicin were administered to one subjects of each group (Subject G in Sesame oil group and subject H in Control group).

Lowest leukocyte count, highest CRP value and number of the episodes of fever over 37.5°C were summarized for each subject (Table 4). After the beginning of chemotherapy, leukocyte count started to decrease and consequently leukocytopenia was observed in most subjects (5 of 7 subjects in Sesame oil group and all subjects in Control group, respectively). Leukocyte count showed the lowest value 7 to 14 days after the beginning of chemotherapy. It fell below $1000/\mu\text{L}$ in 3 of 7 subjects in Sesame oil group and 2 of 4 subjects in Control group. In 2 subjects in Sesame oil group and 1 subject in Control group, the lowest white blood cell count was below $500/\mu\text{L}$. No statistical difference was found in both lowest leukocyte count and highest CRP value.

Elevated CRP value over 2 mg/dL which indicates more than moderate inflammation was also observed in 5 subjects of Sesame oil group and 3 subjects of Control group. 2 subjects in Sesame oil group

	Sesame oil group							Centering			
Subject	A	B	C	D	E	F	G	H	I	J	K
Diagnosis	AML	AML	NHL	NHL (recurrence)	AML	NHL	ALL	ALL	NHL (recurrence)	AML	AML
Sex	M	M	F	F	M	M	F	F	M	M	M
Age	57	62	87	67	79	31	63	74	67	43	46
Regimen	Consolidation therapy #4	Consolidation therapy (HD-AC) #2	CHOP therapy	CHOP therapy	No data	Remission induction therapy	Das /HD-MA	Das+H-CVAD therapy #4	ESHAP therapy #2	IDA-Ara-C therapy #1	Arsenic trioxide therapy
Anticancer agents	Gemtuzumab ozogamicin MTX (Intrathecal injection) Ara-C, PSL	Ara-C PSL	Rituximab CPA Vincristine PSL	CPA Doxorubicin Vincristine PSL	Enocitabine Etoposide Vindesine	Vincristine Daunorubicin CPA Asparaginase PSL	MTX Cytarabine	CPA Doxorubicin Vincristine Dexamethasone Dasatinib	Etoposide Cisplatin Methyl-PSL Ara-C	Idarubicin Ara-C	Arsenic trioxide

Table 3: Outline of the subjects.

HD-AC: High dose Ara-C therapy

Das: Dasatinib

HD-MA: High dose MTX-Ara-C therapy

H-CVAD: Hyper CPA+ Doxorubicin+ Vincristine+ Dexamethasone

IDA: Idarubicin

MTX: Methotrexate

PSL: Prednisolone

Anticancer agents with higher risk of oral mucositis are indicated as bold and underlined letter.

showed fever over 37.5°C. However, no symptoms were caused by sesame oil application.

Group	Subject	Lowest leukocyte count (/μL)	Highest CRP(mg/dL)	No of episode of fever over 37.5°C
Sesame oil	A	550 (Day 10)	4.6 (Day 14)	ND
	B	210 (Day 13)	2.8 (Day 3)	3 (Day 2, 3, 13)
	C	4170 (Day 9)	0.2 (Day 9)	ND
	D	1650 (Day 13)	2.6 (Day -1)	ND
	E	1470 (Day 13)	0.2 Day 6-8)	ND
	F	5960 (Day 14)	1.7 (Day 4)	ND
	G	70 (Day 11)	5.8 (Day 6)	1 (Day 12)
Control	H	390 (Day 21)	5.9 (Day12)	ND
	I	2050 (Day 22)	2.4 (Day -1)	ND
	J	770 (Day 23)	3.1 (Day 14)	ND
	K	2950 (Day 24)	0.7 (Day -1)	ND

Table 4: General condition of the subjects (Day of chemotherapy).
ND :Not detected

Changes in oral mucosa

4 of 7 subjects in Sesame oil group had to stop application of sesame oil due to fever (Subject B, from Day 3 to 5), severe fatigue (Subject E, from Day 2 to 8; Subject G, Day 5), or discharge (Subject C, Day 10). The rest 3 could continue to apply sesame oil to their oral cavity more than 3 times throughout 14 days. Additionally 2 subjects (Subject A, from Day17 to 37; Subject F, from Day 15 to 25) continued sesame oil application after Day 14 since they wished to continue it.

Table 5 shows total and average CTCAE v3.0 grade of each subject during 14 days. None of the subjects of Sesame oil group had developed oral mucositis while they used sesame oil for their oral care. Mucositis of grade 1 appeared in Subject A on the next day of the termination of sesame oil application. His regimen included MTX, an anticancer drug with higher risk of oral mucositis. He started applying sesame oil again on Day 17. Three days after he restarted the application, his mucositis was healed. He continued the application until Day 37. However, on the next day of the last application of sesame oil mucositis reoccurred in his mouth.

In Control group, oral mucositis was observed in 2 subjects (Subject H, I). Mucositis of grade 1 developed in Subject H on Day 4. Although it disappeared by gargling with sodium guaelate solution, uncomfortable feeling in oral cavity still continued and mucositis occurred again on Day 7. Mucositis continued to worsen and consequently CTCAE v3.0 grade also increased from grade 1 to 3 after Day 12. Subject I already had 2 lesions of oral mucositis of grade 1 before chemotherapy; one more lesion developed after chemotherapy started. Anticancer drugs with high incidence of oral mucositis were included in the regimen of both subjects (CPA and doxorubicin for subject H and etoposide for subject I)

However, no statistical significance was found between CTCAE v3.0 grades of Sesame oil and Control group.

Cytological examination

Figure 2 shows the results of cytological examination of Sesame oil

group and Control group on the previous day of chemotherapy (Day 1) and 14 days after chemotherapy started (Day 14).

Group	Subject	Total of CTCAE v3.0 grade	Average of CTCAE v3.0 grade/day
Sesame oil	A	0	0
	B	0	0
	C	0	0
	D	0	0
	E	0	0
	F	0	0
	G	0	0
Control	H	16	1.1
	I	14	1
	J	0	0
	K	0	0

Table 5: CTCAE v3.0 grade during 14 days.

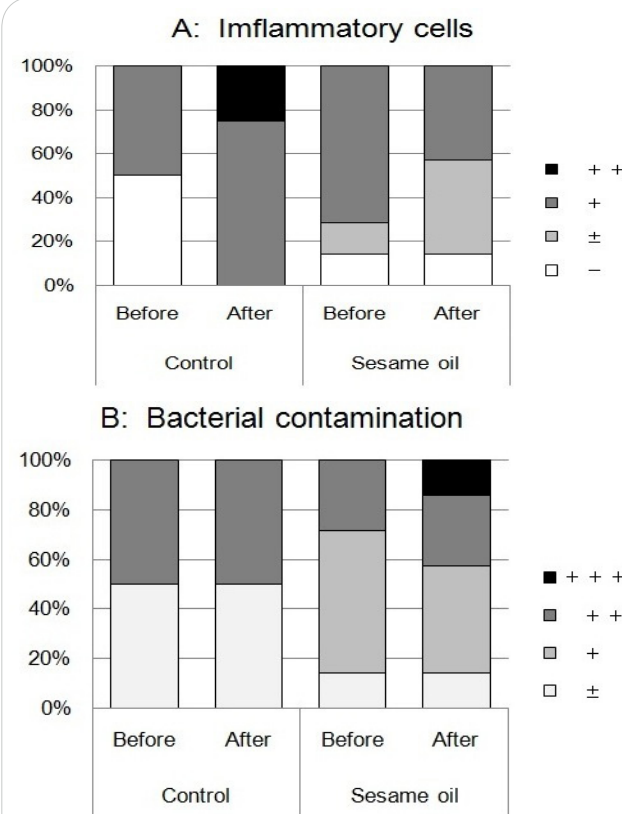


Figure 2: Cytological examination.

Smears of oral mucosa were fixed, stained with Papanicolaou's stain and examined by a qualified cytologist according to the following criteria:

1. Inflammatory change: (-) No inflammation; (±) very small number of inflammatory cells are observed; (+) Inflammatory cells are observed in less than one third of the fields; (++) Inflammatory cells are observed in more than one third of the fields; (+++) Severe inflammatory changes are observed in all fields.

2. Bacterial contamination: (-) No bacterial cell are observed; (±) very small number of bacterial cells are observed; (+) Bacterial cells are observed in several fields; (++) Bacterial cells without prominent colony formation are observed in entire background; (+++) Bacterial cells with prominent colony formation are observed in entire background.

After 14 days, in Sesame oil group, grade of inflammatory change improved in 3 subjects (Subject A, B, F), remained unchanged in 3 subjects (Subject C, E, G) and worsened in 1 subject (Subject D). In case of Control group, although grade of inflammatory change worsened in all subjects, but no statistical significance was found (Figure 2A).

Grade of bacterial contamination was observed to have increased in 2 of 7 subjects (Subject B, G) in Sesame oil group. In the other subjects, it was unchanged (Subject A, C, D, E, F). In Control group, grade of bacterial contamination worsened in 1 subject (Subject I), remained unchanged in 2 subjects (Subject J, K) and decreased in 1 subject (H) (Figure 2B).

Questionnaire

Figure 3 shows the impressions of the subjects in Sesame oil group about sesame oil application. 5 of 7 subjects who had experienced mucositis in previous chemotherapy session felt that sesame oil was effective in preventing oral mucositis. Subject also answered that sesame oil was effective in preventing dry mouth (4 subjects) and tongue coat (2 subjects), and in increasing saliva secretion (2 subjects). All subjects in Sesame oil group told that they would use sesame oil again when they received the next chemotherapy.

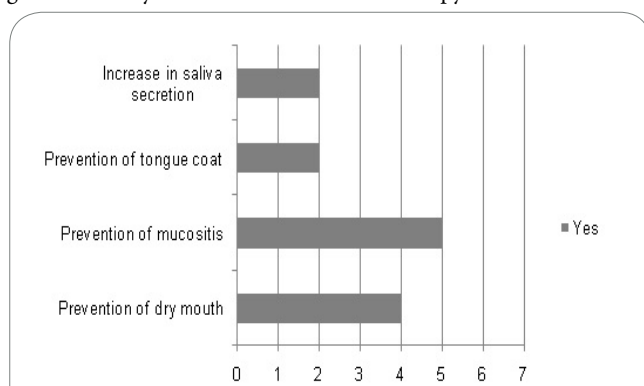


Figure 3: Impression of sesame oil application. Subjects of Sesame oil group answered the short questionnaire about their impressions about sesame oil application.

Discussion

In the present study, topical application of sesame oil seemed to be useful for the management of chemotherapy-induced oral mucositis because of lower incidence of mucositis and lower grade of inflammatory cells in Sesame oil group although no statistical significance was found between Sesame oil group and Control group. Anticancer drugs with higher risk of development of oral mucositis were included in the regimen of 4 subjects in Sesame oil group and 2 subjects in Control group, respectively. Moreover, high dose of MTX or CPA and doxorubicin were administrated to one subjects of each group. Oral mucositis occurred in only one patient in Sesame oil group whereas it developed in both of the two subjects who received chemotherapy regimen with higher risk of oral mucositis.

The clinical course of subject A in Sesame oil group who developed oral mucositis immediately after the termination of sesame oil application suggests the effectiveness of sesame oil application for the prevention of oral mucositis. Since his mucositis was healed after restarting of sesame oil application, sesame oil might also be useful for the treatment of oral mucositis.

It is possible to explain the mechanisms by which topical application of sesame oil prevented oral mucositis based on its pathophysiology. As previously mentioned, release of free radicals by anticancer drugs is the trigger of upregulation of genes coding biologically active proteins including pro-inflammatory cytokines. Sankar et al examined the plasma of the hypertensive patients who were fed sesame oil for 45 days. They found decrease in lipid peroxidation (thiobarbituric acid reactive substances; TBARS) and increase in the activities of erythrocyte superoxide dismutase and reduced glutathione [13]. Therefore, it is suggested that released free radicals become detoxified by superoxide dismutase activated by sesame oil.

Anti-inflammatory effect of sesame oil also may contribute to the prevention and healing of oral mucositis. Inflammation in oral mucosa caused by upregulation of genes regulating synthesis of pro-inflammatory cytokines caused by activation of NF- κ B is a critical event in *message generation and signaling* and *amplification* phase. Cui et al reported that sesamin treatment inhibited the activation of NF- κ B induced by bacterial chemotactic peptide in human monocytic cells. Results of cytological evaluation that inflammatory change was reduced in Sesame oil group support anti-inflammatory effects of sesame oil.

It should be also emphasized that topical application of sesame oil was incorporated into oral care protocol in the present study. Subjects were asked to apply sesame oil after ordinary oral hygiene, such as tooth brushing and gargling. Importance of basic oral hygiene and oral care protocols in maintaining mucosal health and function has already been mentioned in the guideline while basic oral hygiene alone cannot prevent oral mucositis [3]. As leukocytopenia, especially decrease in neutrophil is inevitable in most patients receiving chemotherapy and neutrophil plays an essential role in the defense against bacteria, prevention of excessive proliferation of oral resident bacteria in neutropenic patients is extremely important in avoiding the formation of severe oral mucositis. Here, the antimicrobial activity of fatty acids in sesame oil also helps.

In addition, topical sesame oil application is easy. It can be performed by patients themselves, and saves costs. No prescription is necessary. Taste and mouth feel is acceptable even in the patients who may have nausea because of chemotherapy. More than anything, it is noteworthy that all subjects of Sesame oil group desired continuation of sesame oil application.

Due to small number of subjects and variety of the regimen, the results of this study are not sufficient enough to support the effectiveness of sesame oil. A randomized controlled study with a large sample size is necessary to provide reliable evidence of effectiveness of topical sesame oil application for the management of oral mucositis.

Conclusion

The effectiveness of topical sesame oil application for the prevention of chemotherapy-induced oral mucositis was tested on 7 hematopoietic cancer patients. Their incidences and grades of oral mucositis were lower than that of controls. Cytological examination revealed that inflammatory change was reduced in sesame oil application group. Topical application of sesame oil was suggested to be useful for the prevention of chemotherapy-induced oral mucositis.

Competing Interests

The authors declare that they have no competing interests.

Author contributions

All authors substantially contributed to the study design, collection and interpretation of data, and drafting the manuscript.

References

- Naidu MU, Ramana GV, Rani PU, Mohan IK, Suman A, et al. (2004) Chemotherapy-induced and/or radiation therapy-induced oral mucositis--complicating the treatment of cancer. *Neoplasia* 6: 423-431.
- Sonis ST (2004) Pathobiology of mucositis. *Semin Oncol Nurs* 20: 11-15.
- Rubenstein EB, Peterson DE, Schubert M, Keefe D, McGuire D, et al. (2004) Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. *Cancer* 100: 2026-2046.
- Chi KH, Chen CH, Chan WK, Chow KC, Chen SY, et al. (1995) Effect of granulocyte-macrophage colony-stimulating factor on oral mucositis in head and neck cancer patients after cisplatin, fluorouracil, and leucovorin chemotherapy. *J Clin Oncol* 13: 2620-2628.
- Tanner NS, Stamford IF, Bennett A (1981) Plasma prostaglandins in mucositis due to radiotherapy and chemotherapy for head and neck cancer. *Br J Cancer* 43: 767-771.
- Cheng KK, Molassiotis A, Chang AM (2002) An oral care protocol intervention to prevent chemotherapy-induced oral mucositis in paediatric cancer patients: a pilot study. *Eur J Oncol Nurs* 6: 66-73.
- Matsuoka H, Mizushima Y, Kawano M, Tachibana N, Sawada Y, et al. (2004) [Clinical availability of the herbal medicine, SYOUSAIKOTOU, as a gargling agent for prevention and treatment of chemotherapy-induced stomatitis]. *Gan To Kagaku Ryoho* 31: 2017-2020.
- Vadhan-Raj S, Trent J, Patel S, Zhou X, Johnson MM, et al. (2010) Single-dose palifermin prevents severe oral mucositis during multicycle chemotherapy in patients with cancer: a randomized trial. *Ann Intern Med* 153: 358-367.
- Abdulrhman M, Elbarbary NS, Ahmed Amin D, Saeid Ebrahim R (2012) Honey and a mixture of honey, beeswax, and olive oil-propolis extract in treatment of chemotherapy-induced oral mucositis: a randomized controlled pilot study. *Pediatr Hematol Oncol* 29: 285-292.
- Quinn B (2013) Efficacy of a supersaturated calcium phosphate oral rinse for the prevention and treatment of oral mucositis in patients receiving high-dose cancer therapy: a review of current data. *Eur J Cancer Care (Engl)* 22: 564-579.
- Cui Y, Hou X, Chen J, Xie L, Yang L, et al. (2010) Sesamin inhibits bacterial formylpeptide-induced inflammatory responses in a murine air-pouch model and in THP-1 human monocytes. *J Nutr* 140: 377-381.
- Hsieh PF, Hou CW, Yao PW, Wu SP, Peng YF, et al. (2011) Sesamin ameliorates oxidative stress and mortality in kainic acid-induced status epilepticus by inhibition of MAPK and COX-2 activation. *J Neuroinflammation* 8: 57.
- Sankar D, Rao MR, Sambandam G, Pugalendi KV (2006) Effect of sesame oil on diuretics or Beta-blockers in the modulation of blood pressure, anthropometry, lipid profile, and redox status. *Yale J Biol Med* 79: 19-26.
- Huang CB, George B, Ebersole JL (2010) Antimicrobial activity of n-6, n-7 and n-9 fatty acids and their esters for oral microorganisms. *Arch Oral Biol* 55: 555-560.
- Sato S (2007) The effect of sesame oil on the prevention of chemotherapy induced oral mucositis (in Japanese). *Akita J Rural Med* 52: 43.
- Narasimhamurthy K, Raina PL (1999) Long term feeding effects of heated and fried oils on lipids and lipoproteins in rats. *Mol Cell Biochem* 195: 143-153.
- The National Cancer Institute (2006) The NCI Common Terminology Criteria for Adverse Events v3.0. 24.
- Endo M, Okada H, Yamamoto H, Mega J (2004) Cytological diagnosis for the dependent elderly by using oral smear-Method for evaluating oral mucosa (in Japanese). *J Japanese Soc Disab Oral Health* 25: 548-557.
- Otmami N, Alami R, Hessissen L, Mokhtari A, Soulaymani A, et al. (2011) Determinants of severe oral mucositis in paediatric cancer patients: a prospective study. *Int J Paediatr Dent* 21: 210-216.
- Wardley AM, Jayson GC, Swindell R, Morgenstern GR, Chang J, et al. (2000) Prospective evaluation of oral mucositis in patients receiving myeloablative conditioning regimens and haemopoietic progenitor rescue. *Br J Haematol* 110: 292-299.
- Raber-Durlacher JE, Weijl NI, Abu Saris M, de Koning B, Zwiderman AH, et al. (2000) Oral mucositis in patients treated with chemotherapy for solid tumors: a retrospective analysis of 150 cases. *Support Care Cancer* 8: 366-371.