

# The Effect of Royal Jelly on Oral Mucositis in Patients Undergoing Radiotherapy and Chemotherapy

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This study was conducted to evaluate the effect of royal jelly on oral mucositis in patients undergoing radiotherapy and chemotherapy. The study population consisted of 103 patients undergoing radiotherapy and chemotherapy. Oral mucositis was graded according to the World Health Organization criteria, and patients were divided into 2 groups. All patients received mouthwash therapy with benzydamine hydrochloride and nystatin rinses. In addition, patients in the experimental group received royal jelly. The mean resolution time of oral mucositis in the royal jelly group was significantly shorter than that of the control group. As a result, the study results demonstrate that royal jelly administrated by a certain procedure improved the signs and symptoms of oral mucositis and markedly shortened its healing time. **KEY WORDS:** cancer, chemotherapy, nursing, oral care, oral mucositis, radiotherapy, royal jelly *Holist Nurs Pract* 2014;28(4):242–246

Oral mucositis is an extremely serious and challenging complication of radiotherapy and chemotherapy in patients with cancer.<sup>1</sup> Mucositis can cause pain and dysphagia, xerostomia, and alterations in taste, weight loss, infections, and weakness. These complications can significantly complicate treatment, extend hospitalization, decrease patient quality of life, and increase costs.<sup>2</sup> For this reason, from a public health perspective, oral mucositis is a bigger problem than is currently recognized.<sup>3</sup> Many different interventions, treatments, and agents are used to prevent or treat mucositis.<sup>4–8</sup> However, currently, there is no prevention or therapy for oral mucositis and treatment is essentially palliative. There is clearly a need for additional agents to prevent and mitigate the development of oral mucositis.<sup>4–6</sup>

Royal jelly is a secretory product of the cephalic glands of nurse bees and serves as the most important part of honeybee larvae diet. Royal jelly, one of the

most effective and beneficial remedies for human beings, is widely used both in folk and in mainstream medicines, and it is a controversial dietary supplement. Because of its complex composition, royal jelly has a multitude of pharmacological actions. It has antioxidant, neurotrophic, hypoglycemic, hypocholesterolemic, and hepatoprotective properties. It also has hypotensive and blood pressure regulatory, antitumor, antibiotic, anti-inflammatory, immunomodulatory, and antiallergic, general tonic, and antiaging effects.<sup>9,10</sup> This study was conducted to evaluate the effect of royal jelly administrated by a certain procedure on oral mucositis in patients undergoing radiotherapy and chemotherapy.

## METHODS

### Design and samples

This study was designed as a prospective and randomized clinical trial. The study population consisted of 103 patients undergoing chemotherapy and radiation therapy, due to various types of malignancies, from July 2011 to January 2012. Patients were recruited from the Oncology Department of Medical Faculty, Ataturk University, Erzurum, Turkey. The study was approved by the local ethics commission; patients were included after a written informed consent was obtained.

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Patients were excluded if they had grade 4 mucositis, were abusing alcohol or drugs, had honey bee product allergy, and were noncooperative or not prepared to continue the treatment process.

## Procedure

Mucositis was graded according to the World Health Organization criteria,<sup>11</sup> and patients were divided into 2 groups. Patients in both study groups received mouthwash therapy with benzydamine hydrochloride and nystatin rinses. In addition to mouthwash therapy, patients in the experimental group received royal jelly (Faculty of Agriculture, Ataturk University, Erzurum, Turkey) 2 times per day for a total daily dose of 1 g. Patients in both study groups received mouthwash and/or royal jelly therapy until mucositis resolved. Royal jelly was orally swished for 30 seconds and then swallowed.

Patients were instructed to refrain from eating or drinking for 30 minutes after royal jelly administration. No other prophylactic mouthwashes or treatments of mucositis were allowed.

In the study, the patients, the clinicians, and researchers who examined the subjects and recorded the results were all blind to the subjects' assignment to trial groups. All patients were examined daily by one of the researchers using a flashlight and a tongue depressor. The oral mucosa was divided into 5 sites, including labial mucosa, buccal mucosa, gingivae, the tongue, and soft and hard palates, and the score of mucositis was determined separately for each site. The date of treatment commencement and that of mucositis termination were recorded. On the basis of these dates, the duration of mucositis was calculated and resolution of mucositis was considered complete when there was no evidence of mucositis at any of the sites of the oral cavity.

## Analyses

Data were analyzed with the Student *t* test, Mann-Whitney *U* test, and  $\chi^2$  test by using SPSS software version 11.

## RESULTS

Baseline demographics and disease characteristics of the study population are shown in Table 1. The mean (SD) age of the patients in the royal jelly and control groups was 53.8 (13.08) and 50.69 (25.42), respectively. There were no significant differences in

the baseline demographics and disease characteristics between the 2 groups.

The healing times and mean values of mucositis in the royal jelly and control groups are presented in Tables 2 and 3, respectively. At the beginning of the study, there was no significant statistical difference between the 2 groups regarding mucositis severity (Table 1). The healing time of mucositis was 3 to 4 days in the royal jelly group, except for grade 2 mucositis for 1 case. In the control group, the time required for healing of the lesions was 3 to 5 days for grade 1 mucositis and 13 and 14 days for grade 2 to 3 mucositis (Table 2).

The mean (SD) healing time of grade 1 mucositis was 2.7 (1.1) days for the control group and 1.1 (0.4) days for the royal jelly group. There was a significant difference between the 2 groups ( $U = 64$ ;  $P = .0001$ ) (Table 3).

The mean (SD) healing times of grade 2 mucositis for the control and royal jelly groups were 5.8 (2.7) days and 3 (1.4) days, respectively, which demonstrated a significant statistical difference ( $U = 77$ ;  $P = .0001$ ) (Table 3).

The mean resolution time of grade 3 mucositis in the royal jelly group was significantly shorter than that of the control group, and there was a significant difference between the 2 groups ( $U = 59$ ;  $P = 0.005$ ) (Table 3).

In addition, there was no evidence that royal jelly caused any toxicity. Specifically, there was no suggestion of a differential incidence of nausea, vomiting, anorexia, dysphagia, diarrhea, or constipation.

## DISCUSSION

Oral mucositis is a highly significant and common side effect of chemotherapy and radiotherapy. It reduces patient quality of life, affects nutritional intake, leads to oral and systemic infections, and causes treatment reduction or withdrawal. Currently, there is no predictable prevention or therapy for oral mucositis, and treatment is essentially palliative. The appropriate and effective management of mucositis is therefore a very important factor in improving clinical outcomes for patients.<sup>2-6</sup> Nurses are among the best placed professionals to assess patients at risk by reviewing their patients' current health status. For this reason, they are in a unique position to recognize, assess, and treat the symptoms of oral mucositis through their frequent contact with the patients. Nursing care

**TABLE 1. Patient Demographics and Baseline Disease Characteristics<sup>a</sup>**

|                             | Control Group | Royal Jelly Group |                           |
|-----------------------------|---------------|-------------------|---------------------------|
| Age, mean (SD), y           | 53.03 (13.08) | 50.69 (25.42)     | $t = 0.125; P > .05$      |
| Sex                         |               |                   |                           |
| Female                      | 24 (43.6)     | 31 (58.3)         | $\chi^2 = 2.215; P > .05$ |
| Male                        | 28 (56.4)     | 20 (41.7)         |                           |
| Current smoking history     |               |                   |                           |
| None                        | 26 (50)       | 24 (47.1)         | $\chi^2 = 1.147; P > .05$ |
| Quit smoking                | 26 (50)       | 27 (52.9)         |                           |
| Condition of teeth and gums |               |                   |                           |
| Good                        | 41 (78.8)     | 39 (76.5)         | $\chi^2 = 1.237; P > .05$ |
| Poor                        | 11 (21.2)     | 12 (23.5)         |                           |
| Denture wearer              |               |                   |                           |
| Yes                         | 9 (17.3)      | 5 (9.8)           | $\chi^2 = 1.365; P > .05$ |
| No                          | 43 (82.7)     | 46 (90.2)         |                           |
| Severity of mucositis       |               |                   |                           |
| Grade 1                     | 24 (46.2)     | 25 (49)           | $\chi^2 = 0.098; P > .05$ |
| Grade 2                     | 24 (46.2)     | 22 (43.2)         |                           |
| Grade 3                     | 4 (7.6)       | 4 (7.8)           |                           |
| Cancer stage                |               |                   |                           |
| 1                           | 9 (17.3)      | 4 (7.8)           | $\chi^2 = 7.521; P > .05$ |
| 2                           | 20 (38.4)     | 11 (21.6)         |                           |
| 3                           | 6 (11.5)      | 11 (21.6)         |                           |
| 4                           | 17 (32.6)     | 25 (49)           |                           |
| Cycles of chemotherapy      |               |                   |                           |
| 1                           | 6 (11.5)      | 4 (7.8)           | $\chi^2 = 10.27; P > .05$ |
| 2                           | 22 (42.5)     | 11 (21.6)         |                           |
| 3                           | 5 (9.6)       | 12 (23.5)         |                           |
| 4                           | 8 (15.4)      | 6 (11.8)          |                           |
| 5                           | 4 (7.7)       | 3 (5.9)           |                           |
| 6                           | 7 (13.5)      | 15 (29.4)         |                           |
| Chemotherapeutic agents     |               |                   |                           |
| Alkaloids                   | 30 (57.7)     | 33 (64.7)         | $\chi^2 = 3.167; P > .05$ |
| Anthracyclines              | 1 (1.9)       | 2 (3.9)           |                           |
| Antimetabolites             | 16 (30.8)     | 14 (27.5)         |                           |
| Taxanes                     | 5 (9.6)       | 2 (3.9)           |                           |

<sup>a</sup>The values given are number (percentage) unless indicated otherwise.

protocols for oral mucositis management may allow more patients to receive chemotherapy on schedule and at full dose, as well as reduce potential practice variations that could compromise care, promote cost-effectiveness, and increase the quality of care for patients. Nursing care protocols may help improve patient quality of life, which is typically affected in patients with oral mucositis.<sup>3,12-15</sup> In the present study, oral mucositis management and care protocols have been made by oncologists and nurses, and the oral mucositis care and management were followed until mucositis was resolved. The study results demonstrate that royal jelly improved the signs and symptoms of oral mucositis and markedly shortened its healing time. Generally, the symptoms of oral mucositis

appear 5 to 8 days after starting treatment, and oral mucositis can persist for 7 to 14 days. In some cases, oral mucositis can last longer than 7 to 14 days.<sup>1,3,6</sup> At the beginning of our study, there was no significant statistical difference between the 2 groups regarding mucositis severity. The mean resolution time of mucositis in the royal jelly group was significantly shorter than that of the control group. In fact, after 3 to 4 days, there was no trace of the lesions in any subjects of the royal jelly group, except for grade 2 mucositis in 1 case. In the control group, the time required for healing of grade 1 lesions was 5 days and 13 and 14 days for grade 2 and 3 mucositis. The mean healing time of grade 1 mucositis was 2.7 days for the control group and 1.1 days for the royal jelly group. The mean

**TABLE 2.** The Healing Times of Mucositis<sup>a</sup>

| Day | Control Group |          |         | Royal Jelly Group |          |         |
|-----|---------------|----------|---------|-------------------|----------|---------|
|     | Grade 1       | Grade 2  | Grade 3 | Grade 1           | Grade 2  | Grade 3 |
| 1   | 3 (12.5)      |          |         | 22 (88)           | 3 (13.6) |         |
| 2   | 10 (41.7)     | 1 (4.2)  |         | 2 (8)             | 3 (13.6) |         |
| 3   | 4 (16.7)      | 2 (8.3)  |         | 1 (4)             | 9 (40.9) | 2 (50)  |
| 4   | 5 (20.8)      | 7 (29.2) |         |                   | 6 (27.3) | 2 (50)  |
| 5   | 2 (8.3)       | 4 (16.7) |         |                   |          |         |
| 6   |               | 2 (8.3)  |         |                   |          |         |
| 7   |               | 1 (4.2)  | 1 (25)  |                   |          |         |
| 8   |               | 3 (12.5) |         |                   | 1 (4.5)  |         |
| 9   |               | 1 (4.2)  | 1 (25)  |                   |          |         |
| 10  |               | 2 (8.3)  | 1 (25)  |                   |          |         |
| 13  |               | 1 (4.2)  |         |                   |          |         |
| 14  |               |          | 1 (25)  |                   |          |         |

<sup>a</sup>The values given are number (percentage).

**TABLE 3.** The Mean Healing Times of Oral Mucositis

| Severity of Mucositis | Control Group |              | Royal Jelly Group |              |                     |
|-----------------------|---------------|--------------|-------------------|--------------|---------------------|
|                       | n             | Mean (SD), d | n                 | Mean (SD), d |                     |
| Grade 1               | 24            | 2.7 (1.1)    | 25                | 1.1 (0.4)    | $U = 64; P = .0001$ |
| Grade 2               | 24            | 5.8 (2.7)    | 22                | 3 (1.4)      | $U = 77; P = .0001$ |
| Grade 3               | 4             | 10 (2.9)     | 4                 | 3.5 (0.5)    | $U = 59; P = .005$  |

healing time of grade 2 mucositis was 5.8 days for the control group and 3 days for the royal jelly group. The mean healing time of grade 3 mucositis was 10 days for the control group and 4 days for the royal jelly group. Similarly, in an experimental study, researchers demonstrated that topical application of films that contain royal jelly had a healing effect on severe oral mucositis induced by 5-fluorouracil.

Research indicates that the use of royal jelly films may be more effective in the early stages of oral mucositis than in the late stages.<sup>16</sup>

## CONCLUSION

As a result, assessment of oral mucositis is the first step in the nursing process. The primary goal of the nursing assessment of the oral cavity is to identify changes in the oral mucosa and describe the effect that oral mucositis has on patients' functional status. Our findings suggest that these care protocol and treatments may be useful in resolution or prevention of oral mucositis and demonstrate that royal jelly improved the signs and symptoms of oral mucositis and markedly shortened its healing time.

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