

The Lollipop with Lemon Aroma May Be Promising in Nausea and Vomiting in Pregnancy

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ABSTRACT

OBJECTIVE: To determine the effect of lemon-flavored lollipop on nausea and vomiting of pregnancy.

STUDY DESIGN: This prospective case-control study included 67 first trimester pregnant women. The 12-hour Pregnancy-Unique Quantification of Emesis and Nausea score was calculated at the time of presentation to the hospital. The study group (32 cases) was given lemon-flavored lollipops while the control group (35 cases) did not receive lollipops. The Pregnancy-Unique Quantification of Emesis and Nausea scores of the patients were recalculated on the morning of the post-treatment day.

RESULTS: The Pregnancy-Unique Quantification of Emesis and Nausea scores of the study group were higher ($p=0.013$) than in the control group on the day of admission. Pregnancy-Unique Quantification of Emesis and Nausea scores were similar between the groups on the day after hospital admission ($p > 0.005$). The Pregnancy-Unique Quantification of Emesis and Nausea difference values obtained by extracting the Pregnancy-Unique Quantification of Emesis and Nausea score on the day after hospital admission from the presentation Pregnancy-Unique Quantification of Emesis and Nausea score were higher in the study group ($p=0.0046$). Lemon-flavored lollipops were found to decrease nausea and vomiting of pregnancy.

CONCLUSION: Lemon-flavored lollipops can be given especially to pregnant women who are concerned about the possible teratogenic effects of drug use in pregnancy. Lemon-flavored lollipops are cheap and easily accessible and therefore promising as a non-pharmacological complementary treatment for nausea and vomiting of pregnancy.

Keywords: Nausea, Nausea and vomiting of pregnancy, Lemon, Lollipop, Vomiting

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Introduction

Nausea and vomiting of pregnancy (NVP) i.e. morning sickness of pregnancy is a quite common condition affecting the mother and the fetus. Prevalence of NVP is reported to be as high as 50-80% (1). It does not only decrease the quality of life but also cause women to miss work (2,3). However, when

NVP is not treated, it can progress to hyperemesis gravidarum (HG), which is a more severe form of nausea and vomiting, and control of symptoms can become a real challenge (4). Although the etiopathogenesis is unknown, various factors such as a supraphysiologic increase in serum levels of human chorionic gonadotropin, estrogen, and progesterone compared to unaffected pregnancies, immunologic factors, ethnic and genetic factors, and finally psychologic background are thought to have a role (5).

Lifestyle changes, diet, pharmacological and non-pharmacological complementary treatments are administered in the prevention and treatment of NVP. However, some pregnant women prefer non-pharmacological alternatives over classic pharmacologic treatment due to safety concerns related to the fetus (6). Various vegetable oils and aromas are among the listed non-pharmacological complementary treatments which can be delivered by either inhalation, massage or via the oral route (7). Lemon aroma inhalation has previously been claimed to be an effective non-pharmacological complementary treatment for nausea and vomiting on NVP and other patient populations such as bone marrow transplant patients undergoing infusion of cryopreserved peripheral blood stem cells (8,9).

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The aim of the present study is to investigate the effect of lemon-flavored lollipops (round candy with a stem) on nausea and vomiting in first-trimester pregnant women who were hospitalized for NVP.

Material and Method

This prospective case-control study was conducted at two centers; Bursa Karacabey and Mustafakemalpaşa State hospitals between June 2016 and August 2018 and was approved by Bursa Higher Specialization Training and Research Hospital Ethics Committee (2011-KAEK-25 2016/10-01) and informed written consent was obtained from each participant. The study was conducted in accordance with the Declaration of Helsinki are needed. Power 81%, the Pregnancy -Unique Quantification of Emesis and Nausea (PUQE) scores of the study and control groups at the beginning and on the first day were 1.23, the significance level (alpha) 0.05, the coefficient of variation on the original scale 0.3 and the sample size was 33 + 33 calculated with PASS 11 program. The group to be included in the first patient who met the inclusion criteria was determined by the simple random method. Accordingly, control group 1 patient and patient 2 were included in the study group. The odd-numbered patients were taken into the control group and the even-numbered patients were included in the study group. The study included women aged 18-45 years with a singleton pregnancy between 6-14 weeks. The gestational week was determined according to the date of the last menstrual period. If there was a difference of more than 1 week between the date of the last menstrual period and ultrasonographic measurements, the ultrasonography measurements were accepted in determining the gestational week. The diagnosis of NVP was a diagnosis of exclusion such that: Patients with multiple pregnancy, molar pregnancy, or a systemic disease (pancreatitis, hepatitis, cholecystitis, etc.) that could cause nausea and vomiting, those with a suspicion of food poisoning, patients suffering from nausea due to psychiatric disease and women with hyperemesis gravidarum were excluded from the study. Pregnant with loss of more than > 5% of weight, findings of dehydration, ketosis, and electrolyte abnormalities were accepted as hyperemesis

gravidarum. Patients who could not tolerate oral food intake due to nausea and vomiting were admitted for hospitalization. Urine and blood tests were requested from the patients before treatment. All the admissions were during daytime working hours. The PUQE score (9) was calculated at admission before treatment (Table I).

At the admission, parenteral fluids, antiemetics, and vitamin treatment were started. A total of 3000 cc intravenous fluid was administered per day. 10 mg of metoclopramide HCL was given as an antiemetic and vitamins B and C were administered in the fluid infusions. Vitamin B was administered first to prevent thiamin deficiency and was followed by dextrose infusion. Parenteral treatments, vitamins, and antiemetic drugs were administered to both groups. The study group was given a total of 2 lemon-flavored lollipops Topitop® (11g round candy with stem, Kent Gıda, Turkey) with the first to be sucked at 17:00 and the second to be sucked at 23:00. The control group was not given lollipops. The PUQE scores of the patients were again measured at 08:00 in the morning the next day.

In addition to demographic data such as age, gravida, parity, curettages, the number of living children, and physical characteristics such as height and weight, routine laboratory workup included serum ALT (alanine aminotransferase), AST (aspartate aminotransferase), urea, creatinine, LDH (lactate dehydrogenase), hemoglobin, hematocrit, and TSH (thyroid-stimulating hormone), in addition to urinary ketone semi-quantification.

Statistical analysis

Constant variables were expressed as mean ± standard deviation or median (minimum: maximum). Categorical variables were expressed as n (%). A normal distribution of the quantitative data was checked using the Kolmogorov-Smirnov test. Whether the variables were compliant with a normal distribution was also checked with the Kolmogorov-Smirnov test. The chi-square test was used in the comparisons of the categorical variables between the groups. The independent *t*-

Table I: Pregnancy-unique quantification of emesis score

Circle the answer that best suits your condition in the last 12 hours?				
1. How long have you felt nauseated or sick to your stomach in the last 12 hours?				
Not at all (1)	≤ 1 h (2)	2-3 (3)	<4-6 h (4)	>6 h (5)
2. In the last 12 hours, have you vomited or thrown up?				
≤7 times (5)	5-6 times (4)	3-4 times (3)	1-2 times (2)	I did not throw up (1)
3. In the last 12 hours, how many times have you had retching or dry heaves without bringing anything up?				
None (1)	1-2 times (2)	3-4 times (3)	5-6 times (4)	≥7 times (5)

test was used in the comparison of constant variables between the groups. The SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) program was used for the statistical analyses. The statistical tests were conducted with a 95% confidence interval and $p < 0.05$ was considered as a statistically significant difference.

Results

A total of 67 pregnant women were randomly recruited in the study, with 32 of them as the study group and the other 35 as controls. No differences were found between the groups in terms of age, gravida, parity, history of abortion, number of living children, gestational week, body weight, height, and BMI ($p > 0.005$) (Table II).

Alanine aminotransferase, AST levels were higher in the study group (respectively $p=0.015$ and $p=0.032$). No differ-

ences were found between the groups in urea, creatinine, hematocrit, hemoglobin parameters (Table III).

When the groups were compared in terms of PUQE scores, the scores of the study group cases at admission were found to be higher ($p=0.013$). PUQE scores calculated the day after hospital admission hospital were similar in the groups ($p > 0.005$). The mean PUQE difference value obtained by subtracting the PUQE score calculated one day after hospitalization from the PUQE score at admission was higher in the study group ($p=0.0046$) (Table IV).

Discussion

No classical pharmacologic antiemetic therapy for NVP or HG can be accepted sufficiently safe in early pregnancy despite the decades of experience and use of these medications without any detected harm. This is especially true when it is considered that long term harm is neither proven nor rebutted

Table II: Comparison of the demographic data among the groups

	Study group (n=32)	Control group (n=35)	p
Age (years)	26.31±6.02	25.60±5.55	0.414
Primigravida	10 (31%)	12 (34%)	0.743
Primipara	12 (38%)	13 (37%)	0.705
No abortion history	27 (84%)	31 (88%)	0.695
At least 1 live child	20 (63%)	22 (63%)	0.740
GA (day)	55.12±13.98	60.28±14.87	0.967
Weight (kg)	62.44±14.69	59.63±11.34	0.165
Height (cm)	160.96±7.23	159.94±5.96	0.113
BMI (kg/m ²)	23.95±4.76	23.72±5.33	0.930

GA: Gestational age, BMI: Body mass index

Table III: Comparison of the laboratory findings among the groups

	Study group (n=32)	Control group (n=35)	p
TSH	1.08±0.74	1.13±0.78	0.556
ALT	16.59±7.27	16.59±7.27	<0.001
AST	19.43±6.45	16.85±4.08	0.015
LDH	143.23±22.97	150.60±52.98	0.032
Urea	18.51±4.94	21.20±6.01	0.456
Creatinine	0.49±0.10	0.47±0.10	0.964
Hematocrit	36.16±3.07	37.48±2.79	0.540
Hemoglobin	12.20±1.17	12.60±1.03	0.771
No ketonuria	22 (69%)	21 (60%)	0.336

TSH: Thyroid stimulating hormone, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase

Table IV: The comparison of Pregnancy-unique quantification of emesis scores of the cases

	Study group (n=32)	Control group (n=35)	p
Admission PUQE	11.65±2.36	10.17±2.40	0.013
1 st day PUQE	5.25±1.96	5.00±2.20	0.461
PUQE difference	6.40±2.67	5.17±2.24	0.046

PUQE: Pregnancy-unique quantification of emesis

by any epidemiologic studies. Many of these classic medications are in pregnancy category C. A considerable number of pregnant women consider using “natural” alternatives over these medications.

Among the non-pharmacologic alternative vegetable oil and aromatherapies, ginger, peppermint, and lemon essential oil are used in preventing the NVP (10-12). Anti-emetic effect of lemon is known for long and no harm during pregnancy is reported so far (13,14). Lemon in essential oil form (citrus lemon) prepared to be dispersed in the bedroom air has shown to decrease NVP (15). The lemon odor was reported to decrease nausea and vomiting symptoms by 40% (16). Smith et al. reported a fresh lemon odor to be effective in decreasing NVP symptoms (17). Yavari Kia et al. suggested that the lemon inhalation for 4 days was effective in decreasing NVP symptoms when compared to controls (8).

Although it is not known that the mechanism of chemotherapy-induced nausea and vomiting is alike with NVP, it has been reported that the oral capsules of Citrus aurantium decreased chemotherapy-induced nausea in patients with ovarian cancer (18). In addition, Ozdemir et al. reported that giving lollipops with a strawberry aroma to the patients receiving infusions of cryopreserved peripheral blood stem cells (PBSC) during bone marrow transplantation decreases treatment-related nausea and vomiting symptoms (9). Dimethyl sulfoxide, an ingredient of cryopreserved autologous peripheral stem cells (PBSC) is thought to reach mucosal surfaces like the oral cavity and causes garlic-like foul odor-producing nausea and vomiting. Gustatory branches of the olfactory and fascial nerve, glossopharyngeal nerve and vagus nerves are thought to transmit these signals to the hypothalamus and limbic system. Probably the same mechanisms operate in lemon lollipops.

It is known that ketones produced during long term starvation are excreted by exhalation and urination in the form of acetone halitosis and ketonuria. The excretion of ketones via exhalation and ketonemia itself cause foul mouth odor, nausea, and vomiting which in turn causes starvation and ketone production again in a vicious cycle. An aroma inhalation or an aromatic taste may be used to suppress the mouth odor and break this cycle. Lemon inhalation is thought to produce this effect by the olfactory center through olfactory receptor and cause a state of physical and mental well-being (8). The same effect may be true for suction of lemon aroma in the form of lollipops.

Although there are reports that lemon inhalation decreases NVP, there are no studies on the effect of oral administration of a lemon-flavored lollipop. Lollipops are readily available and much cheaper and acceptable than lemon-flavored oils. We, therefore, investigated the effect of lemon-flavored lollipops (round candy with stem) on NVP cases in this study. The decrease in PQUE scores in the study group compared to controls

in our study indicates that lemon-flavored lollipop may be advised to women with NVP as a snack in between the meals.

However, the small case number and placebo-uncontrolled nature of our study preclude any definitive conclusion to be derived. Nevertheless, we think that our study may be promising for further placebo-controlled clinical research with a higher number of cases.

Conclusion

Lemon-flavored lollipops were found to decrease NVP in our prospective case-control study. Using lemon-flavored lollipops is a promising non-pharmacological complementary treatment in cases of NVP as a cheap and easily accessible alternative.

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Author Contribution:

IB: Project development, data collection, analysis, interpretation of data, manuscript writing, revising the manuscript to be published. FK: Data collection, analysis, revising the manuscript to be published

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