

Gargling with Tea Catechin Extracts for the Prevention of Influenza Infection in Elderly Nursing Home Residents: A Prospective Clinical Study

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ABSTRACT

Objectives: To evaluate the effects of gargling tea catechin extracts on the prevention of influenza infection in elderly nursing home residents.

Design: A prospective study conducted for 3 months from January to March 2005.

Settings/location: A nursing home in Japan.

Subjects: A total of 124 elderly residents of at least 65 years of age were enrolled in the study. Seventy-six residents (83 ± 8.2 years, mean \pm standard deviation; 24 men, 52 women) gargled with tea catechin extract (catechin group) and were compared with 48 age- and sex-matched residents who gargled without tea catechin extracts (control group). All the residents were vaccinated with an influenza vaccine until early December 2004.

Interventions: catechin group: gargling with the tea catechin extract solution (200 $\mu\text{g}/\text{mL}$ catechins, 60% of catechins comprise epigallocatechin gallate); control group: gargling without the catechin extract solution. In both groups, gargling was performed three times daily for 3 months.

Outcome measures: The incidence of influenza infection during the study was compared between the two groups. A safety evaluation was conducted to observe adverse events during the study.

Results: The incidence of influenza infection was significantly lower in the catechin group (1.3%, one resident) than in the control group (10%, five residents) calculated by multivariate logistic regression analysis ($p = 0.028$; odds ratio, 15.711; 95% confidence interval, 1.883–399.658). No adverse events, such as respiratory tract irritation, an obstruction, or allergic bronchial spasm, were observed during the study.

Conclusions: This prospective study demonstrating the effect of catechin gargling on the prevention of influenza infection in the elderly is the first to be reported in the literature. Further randomized, controlled studies are needed to confirm the effects of catechin gargling on the prevention of influenza infection.

INTRODUCTION

Influenza virus infection often causes life-threatening complications, such as pneumonia, in the elderly and is often associated with significant mortality and morbidity.¹ In nursing homes in particular, epidemic outbreaks of influenza still occur during the winter season despite inocula-

tion with influenza vaccine. An advanced prophylactic approach to influenza infection is, therefore, essential both for social welfare and for improvements in the health and quality of life of the elderly.

Catechins are the major components of tea flavonoids and are reported to possess various physiological activities such as antioxidative, anticancer, hypolipidemic, hypoglycemic,

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hypotensive, antibacterial, and antiviral effects.^{2,3} *In vitro* studies have revealed that tea catechin extracts have preventive effects against influenza infection;⁴⁻⁶ however, except for within the Japanese literature, few studies have been conducted on the effects of tea gargling on influenza infection, and the clinical evidence remains equivocal.^{7,8} Similarly, there have been no reports of studies on the effect of gargling with tea catechin extracts on the prevention of influenza infection. Based on this background, we designed a prospective study to evaluate the effects of catechin gargling on influenza infection in elderly nursing home residents.

MATERIALS AND METHODS

A 3-month, prospective cohort study was conducted from January to March 2005 at the White Cross Nursing Home, Higashi-Murayama, Japan. The nursing home is one of the long-term care facilities located in an urban district of West Tokyo. A total of 124 elderly residents at least 65 years of age were enrolled in the study. Prior to entering the study, all the residents in the nursing home were vaccinated with a single lot of influenza vaccine between late October and early December 2004. In accordance with the recommendations of the World Health Organization (WHO) for the 2004–2005 northern hemisphere influenza season, the vaccine used in this study contained the following strains of virus: an A/New Caledonia/20/99 (H1N1), an A/Wyoming/3/2003 (H3N2), and a B/Shanghai/361/2002. Residents were excluded from participation in the study if they had difficulties in gargling by themselves or if they had a history of bronchial asthma; hypersensitivity to tea ingestion; or severe cardiac, respiratory, renal, or hepatic dysfunction. The study was approved by the Ethics Committee at the University of Shizuoka and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all the participants prior to their participation in the study.

Seventy-six residents (83 ± 8.2 years, mean \pm standard deviation; 24 men, 52 women) gargled a solution of tea catechin extracts (catechin group), and were compared with 48 age- and sex-matched residents (83 ± 7.7 years; 16 men, 32 women) who gargled without the tea catechin extract solution (control group). In the catechin group, the residents gargled the tea catechin extract solution with sterilized tap water (200 $\mu\text{g}/\text{mL}$ catechins, 60% of catechins comprised epigallocatechin gallate) three times daily for 3 months. The catechins were formulated as polyphenon E (Mitsui Norin Co., Ltd., Tokyo), and the total catechin content was 90%, including 64% (-)-epigallocatechin gallate, 9.7% (-)-epicatechin, 6.3% (-)-epicatechin gallate, 4.5% (-)-epigallocatechin, 4.2% (-)-gallocatechin gallate, and 0.2% (-)-catechin gallate. The concentration was half that of commercially sold green tea beverages in Japan; therefore, the taste of the catechin extract solution was not very unpleasant for Japan-

ese green tea drinkers. During the follow-up period, registered nurses at the nursing home supervised the participants' activity and encouraged them to maintain their daily gargling.

Influenza infection was identified by RapidTesta[®] FLU II (influenza virus kit, Daiichi Pure Chemicals Co., Ltd., Tokyo, Japan)—a commercially available rapid assay for influenza virus antigens. It took only 15 minutes to identify influenza A and B viruses; the assay was approximately 85% sensitive and 100% specific for the viral antigens.⁹ The procedure was performed on nasal secretions. Using the assay, it was not possible to distinguish between mere carriage of the virus and actual infection. Therefore, the assay was performed only if a resident had an influenza-like illness, defined as a temperature of at least 37.8°C, accompanied by a recent or aggravated cough and one or more of the following signs or symptoms: chills, myalgia, malaise, sore throat, new or increased rhinorrhea or headache, and loss of appetite or diarrhea. The assay was repeated twice if the first assay was negative for viral antigen, and the influenza-like symptoms became worse in spite of the anti-inflammatory medication. If residents were diagnosed as having an influenza infection with the rapid antigen assay, neuraminidase inhibitor was administered as an anti-influenza therapy.

For an estimation of the residents' clinical outcome, the incidence of influenza infection during the study was compared between the two groups. For the safety evaluations, adverse events such as respiratory tract irritation, an obstruction, or allergic bronchial spasm were also checked by registered nurses at each gargling session during the study. All the statistical analyses were performed using SPSS for Windows, version 13.0 (SPSS Inc., Chicago, Illinois). Data for continuous variables are expressed as the means \pm standard deviation. Differences in the quantitative data between the groups were assessed using the Student's *t*-test. The Fisher's exact test was used to compare the differences in qualitative data. The statistical difference in the incidence of influenza infection between the two groups was evaluated by multivariate logistic regression analysis adjusted for the factors including the variables of $p < 0.10$ by the Student's *t*-test or the Fisher's exact test. A $p < 0.05$ was considered to be statistically significant.

RESULTS

The profile of the residents who participated in the study is shown in Table 1. There were no significant differences in age, sex, and the levels of blood hemoglobin, serum alanine aminotransferase, and creatinine between the two groups. The degrees of activity of daily living and the levels of total serum protein were significantly lower in the catechin group than in the control group ($p < 0.05$).

Although all the residents received an influenza vaccination, 4.8% of the residents (six residents) became infected

TABLE 1. PROFILE OF ELDERLY NURSING HOME RESIDENTS WHO PARTICIPATED IN THE STUDY AND COMPARISON OF THE INCIDENCE RATES OF INFLUENZA INFECTION BETWEEN THE GROUP GARGLING WITH TEA CATECHIN EXTRACTS (CATECHIN GROUP) AND THE GROUP GARGLING WITHOUT TEA CATECHIN EXTRACTS (CONTROL GROUP)

	<i>Catechin group</i> n = 76	<i>Control group</i> n = 48
Residents age, years ^a	83 ± 8.2	83 ± 7.7
Men/women	24/52	16/32
Influenza infection*	1.3% (1 resident)	10% (5 residents)
Activity of daily living*		
Independent	20	27
Standing with assistance	48	20
Bedridden	8	1
Blood hemoglobin, g/dL ^a	12 ± 1.5	12 ± 1.4
Total serum protein g/dL ^{a,*}	6.6 ± 0.43	6.8 ± 0.44
Serum ALT, IU/L ^a	15 ± 13	14 ± 8.0
Serum Cr, mg/dL ^a	1.0 ± 0.49	1.0 ± 0.34

^aValues are expressed as mean ± standard deviation.

**p* < 0.05.

ALT, alanine aminotransferase; Cr, creatinine.

with influenza and were identified using the antigen assay as type B. The incidence of influenza infection was significantly lower in the catechin group (1.3%, one resident) than in the control group (10%, five residents); this was determined by the multivariate logistic regression analysis adjusted for factors including degrees of activity of daily living and total serum protein level (*p* = 0.028; odds ratio, 15.711; 95% confidence interval, 1.883–399.658) (Table 2). No adverse events, such as respiratory tract irritation, an obstruction, or allergic bronchial spasm, were observed during the study.

DISCUSSION

The present study is the first to describe the effects of gargling with tea catechin extracts on the prevention of influenza infection in a nursing home for the elderly. The study was conducted in a prospective manner but not randomized; therefore, further randomized, controlled studies will be required to confirm the effects with minimal selection biases.

In fact, in this study, residents could be included in the catechin group if they so wished; residents with lower functional disability or nutritional status who anticipated positive effects preferred to participate in the catechin group. However, functional disability or malnutrition often compromises immune dysfunction and thus enhances susceptibility to infections in the elderly.^{10–12} An overestimation of the influence of these factors would therefore be unlikely. Indeed, as shown by the multivariate logistic regression analysis, the incidence of influenza infection was significantly reduced even with the existence of these confounding factors.

Previous studies that have shown binding to the hemagglutinin of influenza virus and the inhibition of viral adsorption to Madin-Darby canine kidney (MDCK) cells have given an insight into the mechanisms by which tea catechin extracts inhibit the influenza virus.^{3–5} The effects were shown to be dose dependent, even at catechin concentrations less than 200 µg/mL, which is less than that of a typical green tea beverage. We determined the 200 µg/mL catechin concentration on the basis of these experimental studies, and showed the same inhibitory effect in clinical studies. Tea catechins are reported to have low systemic bioavailability and to be well tolerated, except in tea factory workers with occupational asthma induced by the inhalation of green tea dust.^{13–15} The study also showed that no harmful side effects were apparent in the elderly residents during 3 months of gargling. In view of the fact that the sample size was small and that the effects of increasing dose dependency were not investigated, the results of this study should be interpreted with caution. Consequently, further larger-scale and optimal dose-determining studies will be required to confirm the effectiveness and safety of catechin gargling on influenza infection.

CONCLUSIONS

This prospective study demonstrating the effect of catechin gargling on the prevention of influenza infection in the elderly is the first to be reported in the literature. Further randomized, controlled studies are needed to confirm the preventive effects of catechin gargling on influenza infection.

TABLE 2. RESULT OF THE MULTIVARIATE LOGISTIC REGRESSION ANALYSIS

<i>Variables</i>	<i>p value</i>	<i>Odds ratio (95% CI)</i>
Incidence of influenza infection (catechin group vs. control group)	0.028	15.711 (1.883–399.658)
Activity of daily living		
Independent vs. standing with assistance	0.300	0.323 (0.015–2.746)
Independent vs. bedridden	0.534	1.561 (0.042–53.138)
Total serum protein (g/dL)	0.041	0.025 (<0.001–0.507)

CI, confidence interval.

ACKNOWLEDGMENTS

This work was supported by a grant from the Japanese Ministry of Health, Labour and Welfare. The authors have no competing interest. We gratefully thank the residents, nurses, pharmacists, and social workers at the White Cross Nursing Home for their dedicated cooperation.

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