

**ORIGINAL ARTICLE**

Effects of Dietary Yogurt: Changes in Blood Components on Healthy Men Smokers

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식이 요거트의 효과: 흡연남성에게서 요거트에 의한 혈액성분의 변화

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ARTICLE INFOReceived March 27, 2020
Revised 1st May 22, 2020
Revised 2nd June 3, 2020
Accepted June 5, 2020**Key words**Fibrinogen
Immune
Smoker
White blood cells
Yogurt**ABSTRACT**

Smoking is associated with increased inflammation and is a risk factor for a range of diseases. Conversely, yogurt has beneficial effects on health. This study examined the effects of yogurt consumption on the hematological parameters and fibrinogen levels in smokers. The participants were categorized into four groups. Non-smokers were assigned to the control and yogurt groups while smokers were assigned to the smoking and combined (yogurt plus smoking) groups. The participants consumed yogurt, and either smoked or did not smoke for three weeks. The changes in hematological parameters and fibrinogen levels were examined. In the combined group, the proportion of neutrophils and fibrinogen levels increased significantly, whereas the lymphocyte proportion decreased. The eosinophil proportion increased significantly in the Smoking group, but no change was observed in the combined group. In addition, the mean corpuscular hemoglobin concentration increased in the smoking and combined groups, indicating that smoking may affect the lifespan of red blood cells. In conclusion, this study showed that yogurt consumption might influence the immune function by modulating the levels of neutrophils, lymphocytes, and fibrinogen in smokers. Furthermore, the absence of any increase in the eosinophil proportion in the combined group, unlike in the smoking group, suggests that yogurt consumption may have an inhibitory effect on allergic reactions.

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INTRODUCTION

Blood is a sensitive marker for various changes that occur in response to physiological and pathological conditions [1], therefore, investigations into hematological changes are critical in the diagnosis of diseases.

Cigarette smoke contains more than 7,000 chemicals, including various oxidizing agents [2]. Smoking is associated with the occurrence of hypertension and inflammation, and is a risk factor for diseases including cancer and cardiovascular diseases [3-5]. Fibrinogen is a plasma glycoprotein that plays a role in the coagulation system. Fibrinogen levels in the blood increases during inflammatory responses, it is a known proinflammatory mediator already used as a marker of arterial thrombosis [1]. Several studies have investigated

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the effects of probiotic dairy products on health [6]. Yogurt is a probiotic-containing fermented food product, known to have beneficial effects on health, such as decreasing cholesterol and inflammation, when consumed daily [7, 8]. Yogurt exhibits protective effects in acute lung injury and lung cancer [9, 10]. However, it has been reported that habitual yogurt consumption does not necessarily improve the health-related quality of life [11]. Although studies for effects of cigarette use and yogurt on health have previously been performed separately, to our knowledge our investigation into the effects of yogurt consumption in smokers is rare. Therefore, this study attempts to respond to this gap in the literature by investigating the possible effects of yogurt consumption in smokers, using hematological parameters and fibrinogen levels.

MATERIALS AND METHODS

1. Subjects and duration of research

Healthy males aged between 20 and 26, comprising of 18 non-smokers and 18 smokers and not using any medication, were selected for the study (Table 1). Of the smokers, only those using 10 cigarettes per day were included. This study was conducted for three weeks. Approval was gained from the Institutional Review Board of Gimcheon University (GU-201805-HRBRA-06-02-P), signed informed consent was obtained from all participants.

2. Procedure

These participants were divided into 4 groups: Control (no change to routine), Yogurt (160 g of yogurt added to the daily diet), Smoking (10 cigarettes per day), and Combined (160 g of yogurt plus 10 cigarettes per day): 9 subjects were allocated to each group. The yogurt and combined groups consumed 80 g of yogurt

Table 1. Subject characteristics before study

	Control (N=9)	Yogurt (N=9)	Smoking (N=9)	Combined (N=9)	ANOVA
					P-value
Age	21.9±1.4	22.0±1.9	21.8±1.9	21.6±1.6	0.91
Body weight (kg)	70.0±16.1	73.1±8.5	73.6±14.4	69.9±13.9	0.88
Waist circumference	30.8±4.2	31.7±2.4	30.5±3.4	31.4±3.7	0.56
Blood pressure (systolic) (mmHg)	116.4±14.2	118.0±13.5	123.8±10.2	123.8±6.3	0.39
Blood pressure (diastolic) (mmHg)	85.9±4.9	81.8±4.8	84.7±3.9	82.3±7.6	0.41
WBC ($\times 10^3/\mu\text{L}$)	6.5±2.1	6.9±0.7	7.0±2.1	7.4±1.7	0.39
Neutro (%)	54.0±7.9	55.3±5.9	56.1±10.4	50.4±6.5	0.51
Lympho (%)	34.1±8.9	34.2±5.9	33.7±10.6	38.4±6.3	0.55
Mono (%)	7.8±1.8	6.9±1.7	7.3±1.0	7.8±1.6	0.72
Eosino (%)	3.3±2.0	2.7±2.1	2.1±1.1	2.7±1.7	0.64
Baso (%)	0.8±0.1	0.9±0.4	0.8±0.5	0.7±0.3	0.8
RBC ($\times 10^6/\mu\text{L}$)	5.09±0.39	5.25±0.33	5.07±0.37	5.15±0.26	0.83
Hgb (g/dL)	15.5±0.8	15.9±0.8	15.5±0.9	15.7±0.7	0.69
Hct (%)	44.7±2.0	45.9±2.5	45.0±3.2	45.5±1.6	0.85
MCV (fL)	87.9±3.6	87.7±2.3	88.9±2.4	88.5±2.4	0.92
MCH (pg)	30.5±1.3	30.4±1.0	30.7±0.8	30.5±0.9	0.98
MCHC (g/dL)	34.7±0.7	34.7±0.4	34.5±0.8	34.4±0.6	0.63
Plt ($\times 10^3/\mu\text{L}$)	302±59	292±24	259±35	318±57	0.06
MPV (fL)	10.4±0.5	10.7±0.8	11.1±0.7	10.2±0.8	0.09
Fibrinogen (mg/dL)	247.6±57.9	198.1±28.1	252.9±53.8	219.0±12.7	0.56

Data are mean±SD. The Kruskal–Wallis test was used to compare four groups for statistical analysis. Significance level $P<0.05$. Abbreviations: SD, standard deviation; WBC, white blood cell; Neutro, Neutrophil; Lympho, Lymphocyte; Mono, Monocyte; Eosino, Eosinophil; Baso, Basophil; RBC, red blood cell; Hgb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; Plt, platelet; MPV, mean platelet volume.

twice a day, after breakfast and dinner. Commercialized yogurt contains the bacterial species *Lactobacillus bulgaricus*, *Lactobacillus bifidus*, and *Streptococcus thermophilus*. Before this study began, ethylenediamine tetraacetic acid (EDTA) whole blood samples, for complete blood count (CBC) tests and citrated plasma, for fibrinogen measurements, were collected from the subjects. CBC tests were conducted with Sysmex Xn-9000 (Sysmex, Kobe, Japan) and fibrinogen levels were measured with the STA-R analyzer (Diagnostica Stago, Asnières sur Seine, France). This study was conducted for three weeks. The frequency and nature of diet of four groups remained per usual. The yogurt group consumed 80 g of yogurt twice per day, the smoking group smoked 10 cigarettes per day, and the combined group consumed 80 g of yogurt twice per day, in addition to smoking 10 cigarettes per day. After three weeks, EDTA blood samples were collected and CBC and fibrinogen measurement tests were conducted.

3. Statistical analysis

This study was conducted for 9 participants per group. Therefore, we implemented the Wilcoxon signed rank test, a nonparametric method for paired data. The Kruskal-Wallis test, nonparametric alternative to one-way ANOVA, was used to compare four groups (GraphPad Software, San Diego, CA, USA).

RESULTS

1. White blood cells

The total number of white blood cells showed no significant change in any of the 4 groups. Total numbers of white blood cells in smokers was higher than that in non-smokers, although this was not significant. The white blood cell differential counts, however, did showed significant changes in the proportion of specific cell groups, for example, neutrophils, lymphocytes, and eosinophils, over the course of the experiment (Table 2). In the combined group, neutrophil levels increased and lymphocytes decreased. The eosinophil number increased in the smoking group, but this increase was not observed in the combined group.

2. Red blood cells

The number of red blood cells showed no significant changes in any of the 4 groups, but in the red blood cell index, the mean corpuscular hemoglobin concentration (MCHC) showed significant increases in both smoking and combined groups (Table 3). The hemoglobin levels were also acquired but had to be discarded for all 4 groups due to change of control group. The CBC tests were performed by an external laboratory; a systematic error may have affected the results of the hemoglobin

Table 2. Changes of white blood cells

		Control (N=9)	P	Yogurt (N=9)	P	Smoking (N=9)	P	Combined (N=9)	P
WBC ($\times 10^3/\mu\text{L}$)	Pre	6.5 \pm 2.1	0.82	6.9 \pm 0.7	0.18	7.0 \pm 2.1	0.42	7.4 \pm 1.7	0.99
	Post	6.4 \pm 0.9		6.5 \pm 0.8		6.5 \pm 0.9		7.3 \pm 1.9	
Neutro. (%)	Pre	54.0 \pm 7.9	0.07	55.3 \pm 5.9	0.95	56.1 \pm 10.4	0.16	50.4 \pm 6.5	0.03
	Post	49.5 \pm 6.2		55.2 \pm 6.1		50.0 \pm 9.1		54.5 \pm 5.0	
Lympho (%)	Pre	34.1 \pm 8.9	0.16	34.2 \pm 5.9	0.95	33.7 \pm 10.6	0.43	38.4 \pm 6.3	0.02
	Post	38.4 \pm 7.2		34.1 \pm 5.8		38.1 \pm 8.4		34.4 \pm 4.7	
Mono (%)	Pre	7.8 \pm 1.8	0.73	6.9 \pm 1.7	0.94	7.3 \pm 1.0	0.13	7.8 \pm 1.6	0.38
	Post	7.8 \pm 1.6		6.9 \pm 1.4		8.3 \pm 1.8		7.5 \pm 1.8	
Eosino (%)	Pre	3.3 \pm 2.0	0.86	2.7 \pm 2.1	0.29	2.1 \pm 1.1	0.02	2.7 \pm 1.7	0.78
	Post	3.4 \pm 2.6		2.9 \pm 2.4		2.9 \pm 1.4		2.7 \pm 1.7	
Baso (%)	Pre	0.8 \pm 0.1	0.46	0.9 \pm 0.4	0.93	0.8 \pm 0.5	0.36	0.7 \pm 0.3	0.73
	Post	0.9 \pm 0.2		0.9 \pm 0.4		0.7 \pm 0.4		0.8 \pm 0.2	

Data are mean \pm SD. The Wilcoxon signed rank test was used for statistical analysis. Significance level $P < 0.05$. Abbreviations: See Table 1; Pre, before study; Post, after study.

Table 3. Changes of red blood cells

		Control (N=9)	<i>P</i>	Yogurt (N=9)	<i>P</i>	Smoking (N=9)	<i>P</i>	Combined (N=9)	<i>P</i>
RBC ($\times 10^6/\mu\text{L}$)	Pre	5.09 \pm 0.39	0.91	5.25 \pm 0.33	0.99	5.07 \pm 0.37	0.43	5.15 \pm 0.26	0.91
	Post	5.10 \pm 0.34		5.23 \pm 0.29		5.15 \pm 0.29		5.14 \pm 0.26	
Hgb (g/dL)	Pre	15.5 \pm 0.8	0.44	15.9 \pm 0.8	0.55	15.5 \pm 0.9	0.06	15.7 \pm 0.7	0.14
	Post	15.8 \pm 0.9		16.1 \pm 0.9		16.0 \pm 0.7		16.0 \pm 0.6	
Hct (%)	Pre	44.7 \pm 2.0	0.86	45.9 \pm 2.5	0.89	45.0 \pm 3.2	0.36	45.5 \pm 1.6	0.95
	Post	45.0 \pm 2.2		46.0 \pm 2.2		45.8 \pm 2.1		45.8 \pm 1.9	
MCV (fL)	Pre	87.9 \pm 3.6	0.06	87.7 \pm 2.3	0.33	88.9 \pm 2.4	0.67	88.5 \pm 2.4	0.09
	Post	88.4 \pm 3.9		88.2 \pm 2.3		89.0 \pm 2.0		89.1 \pm 1.6	
MCH (pg)	Pre	30.5 \pm 1.3	0.04	30.4 \pm 1.0	0.02	30.7 \pm 0.8	0.04	30.5 \pm 0.9	0.01
	Post	30.9 \pm 1.4		30.9 \pm 1.1		31.1 \pm 0.7		31.2 \pm 0.9	
MCHC (g/dL)	Pre	34.7 \pm 0.7	0.11	34.7 \pm 0.4	0.11	34.5 \pm 0.8	0.04	34.4 \pm 0.6	0.02
	Post	35.1 \pm 0.8		35.1 \pm 0.7		34.9 \pm 0.5		35.0 \pm 0.7	

Data are mean \pm SD. The Wilcoxon signed rank test was used for statistical analysis. Significance level $P<0.05$. Abbreviations: See Table 1; Pre, before study; Post, after study.

Table 4. Changes of platelets

		Control (N=9)	<i>P</i>	Yogurt (N=9)	<i>P</i>	Smoking (N=9)	<i>P</i>	Combined (N=9)	<i>P</i>
Plt ($\times 10^3/\mu\text{L}$)	Pre	302 \pm 59	0.43	292 \pm 24	0.84	259 \pm 35	0.07	318 \pm 57	0.12
	Post	310 \pm 59		298 \pm 29		271 \pm 26		334 \pm 55	
MPV (fL)	Pre	10.4 \pm 0.5	0.07	10.7 \pm 0.8	0.69	11.1 \pm 0.7	0.39	10.2 \pm 0.8	0.48
	Post	10.6 \pm 0.6		10.9 \pm 0.8		11.2 \pm 0.8		10.1 \pm 0.7	

Data are mean \pm SD. The Wilcoxon signed rank test was used for statistical analysis. Significance level $P<0.05$. Abbreviations: See Table 1; Pre, before study; Post, after study.

levels.

3. Platelets

Platelet size is known to be related to cardiovascular disease [12]. Therefore, we investigated the effects of yogurt consumption and smoking on platelet number and size. However, no significant changes occurred, in any group, to either the number of platelets or the mean platelet volume (MPV) (Table 4).

4. Fibrinogen

The fibrinogen levels showed significant increase in the combined group only ($P<0.05$), all other groups showed non-significant changes (Figure 1).

DISCUSSION

The study was conducted to determine if probiotic yogurt, which is known to be beneficial to the human body, could have an effect on the health of moderate

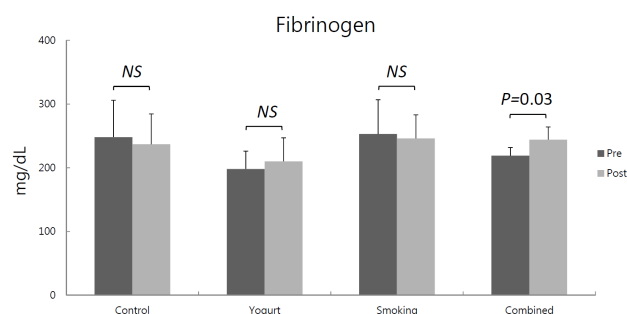


Figure 1. Changes in Fibrinogen level in the blood. Participants were divided into 4 groups. Non-smokers were assigned to the control and yogurt groups while smokers were assigned to the smoking and combined groups. The yogurt and combined groups consumed 80 g of yogurt twice a day, after breakfast and dinner. The smoking and combined groups used 10 cigarettes per day. Participants consumed yogurt and/or smoked for three weeks, after which the citrated plasma were collected from the subjects and were measured for fibrinogen levels. The Wilcoxon signed rank test was used for statistical analysis. significance level $P<0.05$. Abbreviations: Pre, before study; Post, after study; NS, not significant.

smokers. We observed changes in white blood cells, red blood cells, and platelets in the blood, taking place over the course of a three-week study. Our study found that the number of white blood cells in smokers, though not

significant, was higher than in non-smokers, consistent with previous findings [13, 14]. An increase in white blood cells is known to be associated with the occurrence of various diseases [15]. Neutrophils are known to have an innate immune function through phagocytic action [1], thus, a decrease in neutrophils can lead to decreased immune functionality. In a study investigating the effects of cigarettes on neutrophil characteristics, neutrophils exposed to cigarette smoke extract (CSE) were more likely to undergo cell death and to have a compromised ability to ingest pathogens [16]. This corroborates the findings of this study: that smoking affects the number of neutrophils in the blood. In the combined group, the number of neutrophils increased significantly, whereas lymphocytes showed a significant decrease in number. These results were similar to those of previous studies, for example, Nishimura et al. [17] reported changes in white blood cell number after eight weeks of yogurt intake. They showed that, in the yogurt ingesting group, the neutrophil number increased for up to four weeks, before returning to their initial level. Contrastingly, lymphocyte numbers decreased, before recovering at their initial level. The findings of our study, conducted for three weeks, are therefore consistent with the study of Nishimura. Fibrinogen is a known pro-inflammatory protein, increasing the acute-phase of the response. Previous studies have reported that plasma fibrinogen levels increase in smokers [18, 19]. Despite initially predicting to observe a strong increase in fibrinogen in the smoking group, our study showed meaningful increase in the combined group only. Agerholm-Larsen et al suggested that yogurt consumption increases blood fibrinogen levels due to temporary immunostimulation caused by the bacterial strain in the fermented milk product, and reported fibrinogen levels within the normal range and no increase in the CRP [20]. In this study, we found that the increased fibrinogen levels in the combined group were within the normal range. Further, the fibrinogen levels in the yogurt group also increased, however, this change was

not significant. The hs-CRP levels in the yogurt and combined groups did not change significantly, and were within the normal range (data not shown). Therefore, it can be suggested that the increase in fibrinogen levels in the combined group was due to a temporary immunostimulation caused by yogurt consumption. A recent study on fibrinogen reported that the protein is associated with the development of the early innate immune system, and works to rapidly block and neutralize invading pathogens [21]. The significant increase in the number of neutrophils, and the level of fibrinogen, in the combined group appears to be a temporary reaction caused by the immunostimulant effects of the bacteria contained in the yogurt, which could indicate that the ingestion of yogurt by smokers could boost the immune response. These results are consistent with those of previous studies which suggest that yogurt increases immune response [22, 23]. The number of eosinophils in the blood increase as a response to allergic reactions or parasitic infections [1]. Some studies have shown that smoking is related to allergy occurrence [24, 25]. Previous studies, investigating *Lactobacillus* and allergies, have found that *Lactobacillus* may exhibit protective effects [26, 27]. Our study showed a significant increase in the number of eosinophils in the smoking group, after three weeks, which was not seen in the combined group. This may mean that yogurt can work to suppress allergic responses caused by smoking.

In addition, the red blood cell (RBC) index, showed an increase in MCHC in both the smoking and combined groups. The MCHC is an average concentration of hemoglobin in a RBC. If the surface area of cell decreases relative to the volume, the MCHC increases and the RBC becomes a spherocyte. Spherocytes have reduced deformability, which can easily cause hemolysis and often results in a reduction of cell lifespan. In the previous studies, the MCHC showed a greater increase in anemic-smokers than non-anemic smokers as well as in the smoking group, which appears to be the result of increased carbon

monoxide presence in smokers, resulting in reduced oxygen supply to tissues [28–30].

Consequently, smoking may cause the decrease of neutrophils, and the increase of lymphocytes, and eosinophils. Yogurt may be able to modulate immune function by promoting an increase of neutrophils, decrease of lymphocytes, and the increase of fibrinogen when smoking. The potential inhibition of eosinophil increase in smokers also showed that yogurt could have a protective function against an allergic response. Smoking was also found to negatively impact the lifespan of RBCs. These results would seem to predict that smokers' yogurt intake can help control their immune function. There are several limitations to this study, however. The small sample size will, unfortunately, mean we can draw no definitive conclusions. Additionally, the short duration of the study does not enable us to determine the long-term impacts of pro-biotic foodstuffs on the health of smokers, which could be an interesting future project. Further studies may be conducted using larger groups of participants, increasing the study duration, and examining more test parameters. It will be able more information related to yogurt consumption to be attained, and allow the comparison of the effects of yogurt consumption with other lactic acid bacteria. Comparison between light and heavy smokers, and non-smokers, may also be considered.

요약

흡연은 염증 증가와 관련이 있으며 다양한 질환의 위험 인자이다. 요거트는 건강에 이로운 영향을 미치는 것으로 알려져 있다. 이 연구에서는 요거트 섭취가 흡연자들의 혈액학적 변수와 섬유소원 수치에 미치는 영향을 조사하였다. 연구대상자들은 네 개의 군으로 나누었는데 비흡연자는 대조군과 요거트군으로, 흡연자는 흡연군과 복합군(흡연하면서 요거트 섭취)으로 분류하였다. 연구대상자들은 3주 동안 요거트 섭취와/또는 담배를 피웠으며 3주 후에 혈액학적 변수와 섬유소원의 수치 변화를 조사하였다. 연구 결과, 복합군에서 호중구와 섬유소원의 수치가 의미 있게 증가한 반면 림프구 수치는 감소했다. 호산구 수치는

흡연군에서 의미 있게 증가했지만 복합군에서는 변화가 없었다. 또한 흡연군과 복합군에서 평균혈색소농도가 증가하여 흡연이 적혈구 수명에 영향을 미칠 수 있음을 나타냈다. 결론적으로, 이 연구는 요거트 섭취가 흡연자들의 호중구, 림프구, 섬유소원의 수치를 조절함으로써 면역 기능에 영향을 미칠 수 있다는 것을 보여주었고 흡연군과 달리 복합군에서는 호산구 수치가 증가하지 않음으로써 요거트 섭취가 알레르기 반응에 억제 효과를 가지게 할 수 있다는 것을 나타냈다.

Acknowledgements: This work was supported by the 2018 Gimcheon University Research Grant.

Conflict of interest: None

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