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Research letter

Grape wine chlorogenic acids offset the development of metabolic syndrome

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Abstract: *Goal* is to evaluate effectiveness of chlorogenic acids (CGA) of grape wines as a part of medical rehabilitation in chronic bronchitis (CB) patients with comorbid metabolic syndrome (MS).
Material and Methods — Analysis of effectiveness of CGA of dry white wines "Rkatsiteli" and "Rkatsiteli Alma" and liquor red wine "Cahors" as parts of the health resort treatment was carried out in group of 182 patients with CB (42 patients with MS).
Results and Conclusion — The beneficial effect of grape wine CGA was manifested in relation to dynamics of triacylglycerol, regardless of presence or absence of MS. The greatest metabolic effect of CGA was manifested in patients with MS with positive effect on dynamics of Quetelet index and cholesterol. The moderate consumption of wines rich in CGA can be recommended to patients with chronic bronchitis as a preventive measure to development of metabolic syndrome.

Keywords: metabolic syndrome, medical rehabilitation, grape wine, chlorogenic acids.

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Introduction

Chlorogenic acid (CGA) is a compound found in a wide variety of foods and beverages including fruits, vegetables, olive oil, spices, grape, grape wine and coffee [1]. CGA are mainly esters of quinic acid with caffeic, ferulic, or coumaric acids. Significant amounts of three isomers (in positions 3,4, and 5 of quinic acid) of each of these groups of caffeoylquinic, di-caffeoylquinic, and feruloylquinic acids are usually found, too [2]. CGA reduces food cravings and daily calorie intake, induces body fat loss by increasing thermogenesis as a peroxisome proliferator-activated receptor alpha (PPARa) agonist, just like statins. CGA assists the liver in processing the fatty acids and reduces hepatic triacylglycerol levels, thus resulting in weight loss [3]. CGA shows antioxidant activity against reactive oxygen species (ROS), which play an important role in the development of inflammation and lipid exchange disorders under chronic bronchitis (CB) and comorbid metabolic syndrome (MS) [4, 5, 6]. Rational argument for the inclusion of grape wine CGA in the medical rehabilitation (MR) can be its protecting and therapeutic effects.

The aim of the study is to evaluate effectiveness of chlorogenic acids (CGA) of grape wines as a part of medical rehabilitation (MR) in chronic bronchitis (CB) patients with comorbid metabolic syndrome (MS).

Material and Methods

Analysis of effectiveness of grape wine CGA as part of health resort treatment was carried out in group of 182 patients with CB (including 42 patients with MS) according to CONSORT guidelines. Institutional (Academic Scientific Research Institute of Physical Methods of Treatment, Medical Climatology and Rehabilitation n.a. I.M. Sechenov) review board approvals were obtained. The comparison of CGA effect data was carried out between four groups (see *Table* 1). All patients received individual health resort treatment which involves the use of all necessary medical factors and pharmaceuticals (climatic- and spa-therapy, remedial gymnastics, massage, baths, physiotherapy, supporting medication etc.). Characteristics of treatment program in all four groups were not significantly different (except for the grape wine CGA consumption). Main characteristics of table dry white wine "Rkatsiteli" (DW1) and "Rkatsiteli Alma" (DW2), produced by white (classical, for DW1) and red (Kakhetian, for DW2) technologies from white grape of Rkatsiteli variety, and liquor red wine "Cahors" (LW), produced by red (classical) technology from couple of red grape of Cabernet- Sauvignon and Saperavi varieties are: alcohol content (% by volume) is 12.7, 12.7 and 16.0 accordingly; sugar (mass concentration based on invert, g/l) is 0.0, 0.0 and 160.0 accordingly; titrated acids (mass concentration in terms of tartaric acid, g/l) is 5.7., 7.9 and 6.8 accordingly; total phenolic compounds (mass concentration, determined by a standard Folin-Ciocalteu method, mg/l) is 243.0, 1254.0 and 2080.0 accordingly;

including CGA (mass concentration, determined by a standard HPLC method, mg/l) is 74.0, 32.0 and 70.0 accordingly. Reception of wine was carried out once a day in the afternoon. Daily doses in core groups were 200 ml of DW1 and DW2 (consist of 14.8 and 6.3 mg of CGA) and 100 ml of LW (consist of 7.0 mg of CGA). Course doses of DW1, DW2 and LW were 2722.4±119.2, 2406.8±174.4 and 1318.5±52.3 ml respectively, including course doses of CGA of 201.5±15,3, 76.9±7.7 and 92.2±5.1 mg respectively. The course doses of CGA in core groups 1A and 2A were 135.7±13.1 mg and 124.1±8.2 mg respectively. Methods of investigation included an assessment of functional state of the leading physiological systems by 20 domains of ICF [7, 8]. All the clinic, laboratory and functional investigations were conducted by standard procedures. The estimation of the ICF domain values was carried out according to the procedure [9]. All studies were performed twice, with fixation of the results (M±m) before and after the treatment. We also evaluated parameter value dynamics Δ as: Δ = (value at initial state of treatment) – (value at the end of treatment). The influence of wine components including CGA, total phenolic compounds (PC) and ethanol (E) was estimated by pair correlation coefficient (r) of parameter value dynamics (Δ) with course dose of the components. The statistics significance of Δ and r were estimated at $p<0.05$. The software used for statistical analysis is Microsoft Excel, including multiple regression analysis.

Table 1. The statistically significant ICF domain value dynamics (Δ) and pair correlation coefficient (r) with course doses of ethanol (E) and total phenolic compounds (PC), including CGA

ICF domains	*ICF domain and other parameters value dynamics, Δ and pair correlation coefficient, r*					
	Patients with MS			Patients without MS		
	Core group 1A, with wine consumption (n=24)		Control group 1B (n=18)	Core group 2A, with wine consumption (n=76)		Control group 2B (n=64)
	Δ	r	Δ	Δ	r	Δ
b2401 Dizziness (in points)	0.25±0.12	CGA r=+0.328 E r=+0.390	0.22±0.10 &	0.32±0.06 * §	CGA r=+0.210 PC r=+0.224 E r=+0.224	0.56±0.08 * §&
b28010 Pain in head and neck (in points)	0.50±0.1 * $	CGA r=+0.328 PC r=+0.491	1.11±0.22 * $	0.49±0.10 * §	CGA r=+0.193 PC r=+0.239 E r=+0.239	0.53±0.11 * §
b430 Hematological system functions (in points)	0.11±0.06	CGA r=+0.344	-0.02±0.12	0.07 ±0.04		0.00±0.04
b4301 Oxygen-carrying functions of the blood (in points)	0.09±0.06	CGA r=+0.397 E r=+0.277	0.17±0.10	0.11 ±0.04 *		0.03±0.04
b4303 Clotting functions (in points)	0.33±0.17 $ §	CGA r=+0.277 E r=+0.277	-0.92±0.27 * $ &	-0.21±0.12 §		-0.13±0.18 &
b440 Respiration functions (in points)	0.04±0.04	CGA r=+0.259	0.11±0.07	0.03±0.05	CGA r=+0.167	0.02±0.05
b455 Exercise tolerance function (in points)	0.70±0.1 *	E r=+0.284	0.60±0.08 *	0.70 ±0.07 *	PC r=+0.218 E r=+0.218	0.63±0.05 *
b4550 General physical endurance (in points)	0.17±0.17	CGA r=+0.417 E r=+0.417	-0.22±0.15 &	0.06±0.06		0.23±0.09 &
b4551 Aerobic capacity (in points)	0.66±0.28	E r=+0.264	0.23±0.12	0.77±0.18 * §		0.33±0.09 §
b4552 Fatiguability (in points)	0.88±0.1*	PC r=+0.472	1.22±0.15 *	0.82±0.09 *	PC r=+0.171 E r=+0.171	0.95±0.08 *
b540 General metabolic functions (in points)	1.03±0.2 * &	CGA r=+0.569 E r=+0.485	0.79±0.16 * §	0.08±0.06 &		0.02±0.06 §
b5403 Fat metabolism (in points)	0.60±0.22	CGA r=+0.650 E r=+0.550	0.54±0.20	0.42±0.09 *		0.32±0.17
b5408 General metabolic functions, other specified – MS (in points), including:	1.16±0.3 * $	CGA r=+0.327	1.18±0.25 * &	-0.08±0.07 $		0.00±0.00 &
Δ of Quetelet index, BMI (kg/m²)	0.32±0.13	PC r=+0.294 E r=+0.280	0.46±0.15	-0.06±0.07		0.73±0.57
Δ of cholesterol (mmol/l)	0.51±0.15	CGA r=+0.408 E r=+0.338	0.51±0.25	0.51±0.08 *		0.21±0.13
Δ of triacylglycerol (mmol/l)	0.51±0.1 * $	CGA r=+0.609 E r=+0.419	-0.16±0.20 $	0.26±0.08	CGA r=+0.387 PC r=+0.344 E r=+0.344	0.10±0.07
d2408 Handling stress and other physiological demands, other specified (in points)	0.53±0.25	CGA r=+0.538 PC r=+0.475	0.53±0.22	0.21±0.11 §		0.60±0.13 * §
Complex of all controlled domains (in points)	0.50±0.0 * &	CGA r=+0.527 E r=+0.531	0.40±0.06 *	0.25±0.03 * § &	CGA r=+0.230 PC r=+0.247 E r=+0.247	0.34±0.03 * §
Number of beneficial effects of CGA	14				5	

Data of Δ presented as mean value and standard deviations (M±m); r, pair correlation coefficient with course dose; ICF, International Classification of Functioning, Disability and Health; MS, metabolic syndrome. * – statistically significant (at $p<0.05$) difference of values before and after treatment, i.e., significant Δ of parameter; $^{\$, \&, \S}$, statistically significant (at $p<0.05$) difference between the means in two groups with the same notation (between $^{\$}$ and $^{\$}$, between $^{\&}$ and $^{\&}$, between § and §); CGA, significant (at $p<0.05$) pair correlation coefficient with CGA course dose (mg); PC, significant (at $p<0.05$) pair correlation coefficient with total polyphenol compound course dose (mg); E, significant (at $p<0.050$) pair correlation coefficient r with ethanol course dose (ml); positive value of Δ or r indicates a beneficial effect, and vice versa.

Table 2. The results of regression analysis on triacylglycerols dynamics with course doses of ethanol (E) and CGA

Parameters of multiple regression	*Effect on the dynamics of triacylglycerols in group with MS (N=29)*			*Effect on the dynamics of triacylglycerols in group without MS (N = 91)*		
	Course dose of CGA (Variable X 1), in mg	Course dose of Ethanol (Variable X 2), in mg	Joint action of course doses of CGA and Ethanol	Course dose of CGA (Variable X 1), in mg	Course dose of Ethanol (Variable X 2), in mg	Joint action of course doses of CGA and Ethanol
R – square	0.3767	0.2986	0.3824	0.0949	0.0622	0.0995
F – value (analysis of variance)	16.3207	11.4953	8.0486	9.33016	5.8987	4.8620
Y-intersection	-0.1412	-0.1617	-0.1089	0.0621	0.0667	0.0807
Odds of Variables	X1=0.0041	X2=0.0021	X1=0.0054 X2=-0.0008	X1=0.0017	X2=0.0007	X1=0.0025 X2=-0.0004
P – values of Variables	X1=0.0004	X2=0.0022	X1=0.0717 X2=0.6301	X1=0.0030	X2=0.0171	X1=0.0593 X2=0.5034
Significance of F – value (i.e., P – value for joint action of all variables)	0.0004	0.0022	0.0019	0.0030	0.0171	0.0099

Results and Discussion

The mean values of domains had the levels at initial state which have not statistically significant differences in core and control groups of patients with MS and in core and control groups of patients without MS, too. The initial values of the controlled parameters in the core groups of patients with and without MS did not have statistically significant differences, with the exception of arterial blood pressure, Quetelet index and triacylglycerol level, which are the signs of MS. The same picture was observed in the control groups of patients with and without MS. The distribution of controlled data was close to statistically normal.

The data indicate influence of ethanol and total phenolic compounds including CGA are presented in *Table* 1.

The medical rehabilitation of patients with CB is characterized by high efficiency for complex of all controlled domains in all 4 groups. Influence of grape wine CGA on functional state in core group 1A (patients with MS) demonstrated more beneficial effects than in core group 2A (patients without MS): 14 and 5 beneficial effects correspondingly.

First of all, the beneficial effect of grape wine CGA was manifested in relation to the dynamics of triacylglycerol, regardless of the presence or absence of MS (decrease 28.9% and 11.1% from the baseline in patients with and without MS, accordingly).

As can be seen from *Table* 1, two studied components – CGA and ethanol – had significant positive correlation coefficients with the dynamics of triacylglycerols in both studied groups. We carried out a factor analysis of influence of these components (see *Table* 2).

It was found that in both patient groups (with and without MS) the regression equations for the effect of CGA were an order of magnitude more reliable than the equations for the effect of ethanol. In both patient groups the multiple regression equations for the combined effect of CGA and ethanol were also significant but less reliable than the regression equation of influence of one single factor – CGA. Another studied component – PC – had significant positive correlation coefficient with the dynamics of triacylglycerols in patients without MC, too (see *Table* 1). But the regression equations for the effect of PC on the dynamics of triacylglycerols, single or together with CGA and E, were not reliable (the F – value significance exceeded 0.05) in all studied groups. The regression equations for the effect of CGA, ethanol and polyphenol compound (for single or joint action) on dynamics of Quetelet index (BMI) and cholesterol were not reliable in all studied groups, too.

The greatest metabolic effect of CGA was manifested in patients with MS who also had a positive effect on the dynamics of the Quetelet index (decrease of 1% from baseline) and cholesterol (decrease of 8.1% from baseline).

As a result, a good rehabilitation of the functional state of patients in b540 (General metabolic functions), b5403 (Fat metabolism) and b5408 (General metabolic functions, other specified – MS) domains is noted. The data is in good accordance with effect of coffee CGA consumption [3, 10, 11] and with results of clinical trials [12-15]. The data indicates the possibility of no less effective correction of lipid metabolism using grape wine rich in CGA, not only coffee alone.

The investigated effects in CB patients with MS are in good accordance to beneficial reputation of Mediterranean diet rich in grape wine.

Conclusion

The positive effects of grape wine CGA indicate that wines consumption is more preferable than strong alcoholic beverages, poor of CGA. The moderate consumption of wines rich in CGA can be recommended to patients with chronic bronchitis, as a preventive measure to developing metabolic syndrome. The clinical significance of these findings needs further investigation. Subsequently, our research will be aimed at studying the potential role of gallic and other grape wine acids in medical rehabilitation.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects and its later amendments or comparable ethical standards.

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