Research letter

Red wines countering the metabolic syndrome

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Abstract: *Aim* is to evaluate effectiveness of red wines as a part of medical rehabilitation in coronary heart disease (CHD) patients with metabolic syndrome (MS).
Material and Methods — Analysis of effectiveness of table dry red wine "Cabernet" (DW) and liquor red wine "Cahors" (LW) as parts of the spa resort treatment, was carried out in group of 119 patients with CHD (36 patients with MS).
Results — In patients without MS in main group (with wine consumption) the domain dynamics demonstrate more beneficial changes in comparison with control group. In patients with MS in main group (with wine consumption) the domain dynamics demonstrate no more beneficial changes in comparison with control group.
Conclusion — The moderate consumption of red wines can be recommended to patients with coronary heart disease rather as a preventive measure to developing metabolic syndrome.

Keywords: metabolic syndrome, medical rehabilitation, red wine.

Introduction

The researches on therapeutic and prophylactic properties of wine primarily connected with its antioxidant action against reactive oxygen species (ROS), which play an important role in the development of coronary heart disease (CHD) [1-5]. Numerous studies point out an important role of wines in prevention of various cardiovascular diseases and metabolic syndrome (MS) [1-9]. Rational argument for the inclusion of red wine in the medical rehabilitation in patients with CHD may be MS protecting effect.

The aim of this study is to evaluate effectiveness of red wines as a part of medical rehabilitation in CHD patients with MS.

Material and Methods

Analysis of effectiveness of red wines as part of spa resort treatment was carried out in group of 119 patients with CHD (36 patients with MS). All patients received individual spa 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 wine consumption).

Main characteristics of table dry red wine "Cabernet" (DW), produced by classical technology from red grape of Cabernet-Sauvignon variety, and liquor red wine "Cahors" (LW), produced by classical technology from couple of red grape of Cabernet-Sauvignon and Saperavi varieties, are: alcohol content (% by volume) is 10.6 and 16.0 accordingly; sugar (mass concentration based on invert, g/l) is 0.0 and 160.0 accordingly; titrated acids (mass concentration in terms of tartaric acid, g/l) is 8.3 and 6.8 accordingly; total phenolic compounds (mass concentration, mg/l) is 1717.0 and 2080.0 accordingly; including anthocyanin (mass concentration, mg/l) is 255.0 and 162.0 accordingly. Reception of wine was carried out once a day in the afternoon. Daily doses in core groups were 200 ml of DW (consist of 21.2 ml of ethanol and 343.4 mg of total phenolic compound) and 100 ml of LW (consist of 16.0 ml of ethanol and 164.2 mg of total phenolic compound). Methods of investigation included an assessment of functional state of the leading physiological systems by 20 domains of International Classification of Functioning, Disability and Health (ICF) [10, 11]. All the objective, laboratory and functional investigations were conducted by standard procedures. The estimation of the ICF domain values was carried out according to the procedure [12].

All studies were performed twice, with fixation of the results (M±m) before and after the treatment. At the same time, we also evaluated domain value dynamics Δ as: Δ = (domain value at initial state of treatment) – (domain value at the end of treatment) and pair correlation coefficient (r) of Δ with course dose of wine components. The statistics significance of Δ and r were estimated at $p < 0.050$ or less.

Table 1. The ICF domain value dynamics (Δ) and pair correlation coefficient with component of consumed wine (r) that indicate influence of red wine in CHD patients with or without associated MS

ICF domains	ICF domain value dynamics, Δ (in points) and pair correlation coefficient with component of consumed wine, r					
	Patients with MS			Patients without MS		
	Core group 1A (n=14)		Control group 1B (n=22)	Core group 2A (n=38)		Control group 2B (n=45)
	Δ	r	Δ	Δ	r	Δ
1	2	3	4	5	6	7
b2401 Dizziness	1.00±0.14*$		0.68±0.12*	0.79±0.07*$	E, r=0.329 PC, r=0.366 A, r=0.376	0.53±0.10*
b280 Sensation of pain	0.82±0.13*	W, r=0.474 E, r=0.520 PC, r=0.542 A, r=0.549	0.93±0.10*$	0.99±0.06*§	W, r=0.490 E, r=0.561 PC, r=0.585 A, r=0.586	0.65±0.06*§$
b28010 Pain in head and neck	1.00±0.14*$		0.93±0.14*&	0.60±0.10*$	E, r=0.280 PC, r=0.313 A, r=0.323	0.53±0.11*&
b28011 Pain in chest – heartache	0.64±0.16*	W, r=0.532 E, r=0.585 PC, r=0.611 A, r=0.619	0.93±0.11*	1.02±0.11*	W, r=0.516 E, r=0.562 PC, r=0.566 A, r=0.558	0.81±0.09*
b410 Heart functions	0.21±0.08		0.20±0.07*	0.19 0.04*		0.13±0.04
b4100 Heart rate	0.00±0.00		0.00±0.09	0.00±0.03	W, r=0.380 E, r=0.349 PC, r=0.303 A, r=0.278	0.00±0.08
b420 Blood pressure functions	1.00±0.19*$		1.03±0.23*	0.44±0.09*§ $		0.88±0.15*§
b430 Haematological system functions	-0.03±0.17		-0.06±0.07	-0.15 ±0.07*		-0.03±0.10
b4303 Clotting functions	-0.14±0.27		-0.12±0.18	-0.38±0.13*		-0.07±0.20
b4550 General physical endurance	0.35±0.13		0.25±0.11	0.39±0.08*		0.18±0.08
b4551 Aerobic capacity	-0.12±0.29	E, r=-0.440 PC, r=-0.466 A, r=-0.475	0.25±0.21	0.39±0.14	W, r=0.290	0.45±0.13
b4552 Fatiguability	0.92±0.12*	W, r=0.506 E, r=0.486 PC, r=0.466 A, r=0.458	0.93±0.06*	0.89±0.09*		0.75±0.09*
b540 General metabolic functions	0.91±0.29*$	E, r=-0.452 PC, r=-0.504 A, r=-0.523	0.86±0.21*&	0.04±0.09*$	W, r=0.328 E, r=0.283	0.20±0.08&
b5403 Fat metabolism	0.32±0.28		0.28±0.14	0.11±0.14*		0.27±0.13
b5408 General metabolic functions, other specified – MS	1.57±0.38*$	W, r=-0.584 E, r=-0.651 PC, r=-0.685 A, r=-0.696	1.06±0.23*&	0.02±0.02$		0.06±0.04&
d2408 Handling stress and other physiological demands, other specified	0.17±0.15		0.52±0.21	0.20±0.10	A, r=0.316;	0.57±0.16*
All controlled domains	0.42±0.06*		0.38±0.03*	0.31±0.03*	W, r=0.338	0.29±0.03*

Data of Δ presented as mean with standard deviation (M±SD); r, pair correlation coefficient with components of consumed wine; ICF, International Classification of Functioning, Disability and Health; MS, metabolic syndrome; * , statistically significant ($p<0.05$) difference of domain values before and after treatment, i.e., significant Δ of domain; $, &, § , statistically significant ($p<0.05$) difference between the means in two groups with the same notation (between $ and $, between & and &, between § and §). W, significant ($p<0.05$) pair correlation coefficient with wine course dose (drinks); E, significant ($p<0.05$) pair correlation coefficient r with ethanol course dose (ml); PC, significant ($p<0.05$) pair correlation coefficient with total polyphenol compound course dose (mg); A, significant ($p<0.05$) pair correlation coefficient with anthocyanin course dose (mg).

Results and Discussion

The mean values of domains had the similar level at initial state in all groups of patients. The data that are indicate influence of wine are presented in *Table* 1.

The medical rehabilitation in both core groups of patients with CHD is characterized by high efficiency, which is in agreement with the data obtained earlier on beneficial effect of the Cabernet-Sauvignon alcohol free concentrate [9]. We have shown that patients without MS have the better rehabilitation prognosis for a complex of controlled ICF domains. Influence of wine on functional state in core group 1A (patients with MS) demonstrated the same beneficial trend than in control group 1B (3 beneficial effects versus 3 harmful). In core group 2A (patients without MS) we can see another picture – 11 beneficial effects of red wines versus 3 harmful effects.

The significant negative dynamics of b4303 "Clotting functions" in patients without MS (in the main group 2A) and the tendency to negative dynamics of this function in patients with MS (in the main group 1A) could be formally evaluated as undesirable effect of the wine. But the analysis showed that a decrease in the prothrombin index, which led to negative dynamics of b4303 "Clotting functions" in patients with CHD is more likely to be sought and can't be assessed as an undesirable result of the wine influence.

Under the influence of red wines, the cholesterol level in patients with MS significantly decreased from 5.89 (±0.36) to 4.50 (±0.33). In patients without MS, under the influence of red wines, a decrease in the level of cholesterol from 5,30 (±0.22) to 5.16 (±0.25) was also noted, but that dynamics is not statistically reliable. In patients with MS, the significant positive dynamics of b540 "General metabolic functions" and the b5408 "General metabolic functions, other specified – MS" were noted only when LW was used, whereas this effect was not observed with DW. Our data is in good accordance with clinical data on the normalization of the profile of blood lipids under the influence of red wine [13-16].

In patients without MS a positive correlation of the dynamics of b540 "General metabolic functions" with the course doses of red wine (r=0.328) and ethanol (r=0.283) were found. Mild to moderate alcohol consumption (15-20 ml of ethanol daily), especially wine, is associated with a lower prevalence of MS, but the relative contribution of wine's alcohol and polyphenol components to beneficial effect is unclear [3].

Our data indicate rather a prophylactic than therapeutic effect of red wine in relation to MS. It is the prophylactic effect on the development of MS components that is in good agreement with meta-analysis data indicating the predominantly preventive effect of such an important component of wine on development of cardiovascular diseases [17].

The investigated effects of red wines in CHD patients with MS and of white wines in hypertensive patients with MS [5] are in good accordance to beneficial reputation of Mediterranean diet rich in wine.

Conclusion

The positive effects of polyphenols indicate that red wines consumption is more preferable than strong alcoholic beverages consumption. The moderate consumption of red wines can be recommended to patients with CHD, as a preventive measure to developing MS. The clinical significance of these findings needs further investigation.

Conflict of interest

The authors declare no conflict of interest. This study is designed as a range of joint research work of above mentioned author's affiliation institutions and in no way was supported by any sponsors.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Dhala NS, Temsah RM, Netticadan T. The role of oxidative stress in cardiovascular diseases. *J Hypertens* 2000; 18: 655-673. https://www.ncbi.nlm.nih.gov/pubmed/10872549.

2. Rodriguez-Mateos A, Vauzour D, Krueger CG, Shanmuganayagam D, Reed J, Calani L, et al. Bioavailability, bioactivity and impact on health of dietary flavonoids and related compounds: an update. *Arch Toxicol* 2014, 88: 1803-1853. https://doi.org/10.1007/s00204-014-1330-7.

3. Corder R, Mullen W, Khan NQ, Marks SC, Wood EG, Carrier MJ, Crozier A. Oenology: Red wine procyanidins and vascular health. *Nature* 2006; 444: 566-571. https://doi.org/10.1038/444566a.

4. Dayoub O, Andriantsitohaina R, Clere N. Pleiotropic Beneficial effects of epigallocatechin gallate, quercetin and delphinidin on cardiovascular diseases associated with endothelial dysfunction. *Cardiovasc Hematol Agents Med Chem* 2013; 11(4): 249-264. https://doi.org/10.2174/1871525712666140309233048.

5. Mizin VI, Iezhov VV, Severin NA, Yalaneckyy AYa. White wines countering the metabolic syndrome. *Russ Open Med J* 2017; 6: e0405. https://doi.org/10.15275/rusomj.2017.0405.

6. Hnatush AR, Drel VR, Hanay NO, Yalaneckyy AY, Mizin VI, Sybirna NO. The protective effects of natural polyphenolic complexes of grape wine on organisms exposed to oxydative and nitrosative stress under diabetes mellitus. In: Proceedings of the NATO Advanced Research Workshop on "Advanced Bioactive Compounds Countering the Effects of Radiological, Chemical and Biological Agents", Crimea, Ukraine, May 15-17, 2012. G.N. Pierce, V.I. Mizin, A. Omelchenko, eds. Dordrecht: Springer, 2013: 145-162.

7. Gronbaek M, Deis A, Sorensen TI, Becker U, Schnohr P, Jensen G. Mortality associated with moderate intakes of wine, beer, or spirits. *BMJ* 1995; 310(6988): 1165–1169. https://doi.org/10.1136/bmj.310.6988.1165.

8. Goszcz K, Deakin SJ, Duthie GG, Stewart D, Leslie SJ, Megson IL. Antioxidants in cardiovascular therapy: panacea or false hope? *Front Cardiovasc Med* 2015; 2: 29-76. https://doi.org/10.3389/fcvm.2015.00029.

9. Severin NA, Mizin VI, Iezov VV. Functional activity of polyphenolic compounds of red table "Cabernet" wine under metabolic syndrome. *Vestnik Fizioterapii I Kurortologii* 2016; 22(1): 4-8. Russian. https://elibrary.ru/item.asp?id=27315558.

10. International Classification of Functioning, Disability and Health: ICF. Geneva: World Health Organization, 2001. https://www.who.int/classifications/icf/en.

11. ICF Checklist Version 2.1a, Clinician Form. World Health Organization, September 2003. https://www.who.int/classifications/icf/icfchecklist.pdf.

12. Mizin VI, Severin NA, Dudchenko LS, Ezhov VV, Ivaschenko AS, Beliaeva SN, et al. Methodology of evaluation of rehabilitation potency and efficacy under pathology of cardio-respiratory system in accordance to International Classification of Functioning, Disability and Health. T*rudy Akademicheskiy NII Fizicheskich Metodov Lechenia, Medicinskoy Klimatologii I Reabilitacii imeni I.M. Sechenova* 2016; 27: 1-22. Russian.

13. Droste DW, Iliescu C, Vaillant M, Gantenbein M, De Bremaeker N, Lieunard C, et al. A daily glass of red wine associated with lifestyle changes independently improves blood lipids in patients with carotid arteriosclerosis: results from a randomized controlled trial. *Nutr J* 2013; 12(1): 147. https://doi.org/10.1186/1475-2891-12-147.

14. Chiva-Blanch G, Urpi-Sarda M, Ros E, Valderas-Martinez P, Casas R, Arranz S, et al. Effects of red wine polyphenols and alcohol on glucose metabolism and the lipid profile: a randomized clinical trial. *Clin Nutr* 2013; 32(2): 200–206. https://doi.org/10.1016/j.clnu.2012.08.022.

15. Chiva-Blanch G, Urpi-Sarda M, Ros E, Arranz S, Valderas-Martínez P, Casas R, et al. Dealcoholized red wine decreases systolic and diastolic blood pressure and increases plasma nitric oxide: short communication. *Circ Res* 2012; 111(8): 1065–1068. https://doi.org/10.1161/CIRCRESAHA.112.275636.

16. Di Renzo L, Carraro A, Valente R, Iacopino L, Colica C, De Lorenzo A. Intake of red wine in different meals modulates oxidized LDL level,

oxidative and inflammatory gene expression in healthy people: a randomized crossover trial. *Oxid Med Cell Longev* 2014; 2014: 6813-6818. https://doi.org/10.1155/2014/681318.

17. Rodríguez-Monforte M, Sánchez E, Barrio F, Costa B, Flores-Mateo G. Metabolic syndrome and dietary patterns: a systematic review and meta-analysis of observational studies. *Eur J Nutr* 2017; 56: 925-927. https://doi.org/10.1007/s00394-016-1305-y.

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