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ESTABLISHING LINKS BETWEEN ALCOHOL INTAKE, COGNITIVE FUNCTIONS AND TYPE 2 DIABETES

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Abstract In the present report, we studied the associations that might exist between alcohol consumption, cognitive functions and diabetic pathology in patients with type 2 diabetes (T2D). The alcohol intake of 219 patients diagnosed with diabetes was classified into 6 groups: nondrinkers, 0.1-9.9, 10.0-14.9, 15.0-29.9, 30.0-49.9 and ≥ 50.0, according to the total amount (grams/day) of alcohol consumption. Our results mainly confirm that moderate alcohol consumption can reduce some of the neuropathological aspects of T2D, as demonstrated by the decrease in glycemic levels in patients that consumed higher levels of alcohol (30.0-49.9 g/day), when compared to non-drinkers (p=0.04) or groups in which individuals consumed 0.1-9.9 g/day (p=0.01) and 10.0-14.9 g/day (p=0.02). Regarding the results of cognitive testing, we noticed a significant increase in the values of the MMSE score a lower dose of alcohol intake (0.1-9.9 g/day) was compared with higher doses: 30.0-49.9 g/day (p=0.008) and ≥ 50.0 g/day (p=0.047).

Key words: Type 2 diabetes, alcohol intake, cognitive functions.

INTRODUCTION

Type 2 diabetes (T2D) is a very common disorder, increasing in prevalence around the world, mainly because of the so-called "westernization" of lifestyle (Popescu et al., 2013). It represents a major cause of cardiovascular diseases and all-cause mortality, with exponential increase in the last few years (Wei et al., 2000).

Studies examining the role of alcohol in T2D have yielded contradictory results, with some authors describing an increased risk of diabetes in alcohol consumers, (Kao et al., 2001; de Vegt et al., 2002; Ajani et al., 2000), other authors have reported an opposite, protective effect of alcohol intake, manifested though a reduced incidence of T2D, both with moderate or even higher levels of consumption (Nakanishi et al., 2003; Wannamethee et al., 2002). No correlation between the levels of alcohol intake and T2D risk were also reported (Monterrosa et al., 1995; Hodge et al., 2003). Positive and negative effects of alcohol ingestion on glucose homeostasis have been previously documented (Carlsson et al., 2003). Despite an increased number of some very comprehensive meta-analyses (Carlsson et al., 2005; Koppes et al., 2004) and reviews (Howard et al., 2004; Baliunas et al., 2009), the exact role of alcohol intake in the incidence and mechanism of T2D are still insufficiently known.

It is now generally accepted that T2D is a strong risk factor for cognitive decline and dementia (Cukierman et al., 2005). There are recent theories that alcohol consumption may influence cognitive decline in the patients with T2D (Townsend et al., 2009), especially considering the results of some reference articles, such as the Rotterdam study, which demonstrated that light to moderate alcohol consumption is associated with a reduced risk of dementia in individuals aged 55 years or older (Ruitenberg et al., 2002).

In the present report, we were interested in studying the associations that might exist between alcohol consumption, cognitive functions and diabetic pathology in patients with T2D.

MATERIALS AND METHODS

The subjects of this study were 219 patients (71 females and 148 males; age: 54.2 years ± 6.72) with T2D. Diabetes was diagnosed when fasting glycemia was ≥126 mg/dl (American Diabetes Association, 2010). Patients were recruited from the University Hospital of Psychiatry "Socola", Iasi, Romania, and 207 of them were chronic alcohol abusers, fulfilling DSM diagnostic criteria of alcohol dependence, while 12 were non-drinkers and were used as non-standard controls.

We estimated alcohol intake from self-reported drinking habits. The consumption for each beverage type was multiplied by the ethanol content – one can/bottle/glass of beer = 12.8 g, one glass of white or red wine = 11.0 g, and one glass of liquor = 14.0 g, to give the grams of alcohol per day for each beverage. Beverage-specific intake was then summed to give the total average grams of alcohol per day (Conigrave et al., 2001). Alcohol intake was classified into 6 groups: nondrinkers, 0.1-9.9, 10.0-14.9, 15.0-29.9, 30.0-49.9 and ≥ 50.0, according to the total amount (grams/day) of alcohol intake.

Cognitive testing was performed in the morning, between 10-12 a.m. In addition, self-reported weight and height were used to calculate the Body Mass Index (BMI) as weight in kilograms divided by the square of height in meters.

This study was conducted according to provisions of the Helsinki Declaration and all the patients signed a written consent for participation in this study.

Data analysis

The results were analyzed using one-way analysis of variance (one-way ANOVA). All results are expressed as mean ± SEM. $P < 0.05$ was regarded as statistically significant.

RESULTS

In this study, we were interested in the variations of glycemia levels relative to the quantity of alcohol ingested. As can be seen in Table 1, there was a slight decrease in the glycemic levels in the groups of patients that consumed higher levels of alcohol, such as the fifth group (30.0-49.9 g/day), when compared to non-drinkers ($F(1,32)=7$, $p=0.04$), second (0.1-9.9 g/day) ($F(1,93)=23$, $p=0.01$) or the third group (10.0-14.9 g/day) ($F(1,34)=14$, $p=0.02$). We observed a significant decrease in glycemia in the group that ingested the higher levels of alcohol (≥50.0 g/day), as compared to the second (0.1-9.9 g/day) ($F(1,131)=13$, $p=0.02$) and third (10.0-14.9 g/day) ($F(1,72)=7$, $p=0.039$) groups.

We observed a significant decrease in the mean age of the patients with high levels of alcohol consumption, such as in the case of the fifth (30.0-49.9 g/day) and sixth groups (≥ 50.0), when compared to non-drinkers or to the second group (0.1-9.9 g/day) of patients ($F(1,94)=17$, $p=0.01$) and ($F(1,131)=34$, $p=0.006$, respectively).

In the case of BMI values, we observed its slight decrease in the higher doses of alcohol intake, as demonstrated by the significant decrease of BMI in the fifth group of patients (30.0-49.9 g/day) when compared to the third (10.0-14.9 g/day) ($F(1,35)=17$, $p=0.01$) (Table 1).

Table 1. The characteristics of the 219 patients, according to alcohol intake levels

Alcohol consumption (g/day)						
	Nondrinkers	0.1–9.9	10.0–14.9	15.0–29.9	30.0–49.9	≥ 50.0
Subjects (n)	12	73	14	35	23	60
Age (y)	55.6 ± 2.1	57.5 ± 1.89	55.14 ± 4.93	51.94 ± 2.75	52.43 ± 3.38	52.21 ± 2.12
BMI (kg/m2)	26.82 ±3.96	27.76 ± 0.52	29.29 ± 1.64	27.06 ± 1.19	26.85 ± 1.02	27.34 ± 0.77
Glycemia (mg/dL)	162.5 ±15.5	159.2 ± 2.36	160.28 ± 6.66	159.14 ± 3.28	151.83 ± 3.5	155.28 ± 2.39
Blood pressure (mmHg)						
Diastolic	75 ± 5	78.9 ± 1.55	85.35 ± 3.03	79.71 ± 2.59	75 ± 2.74	78.58 ± 1.71
Systolic	135 ± 5	127.6 ± 2.26	137.14 ± 7.35	132.71 ± 4.43	124.09 ± 4.97	129.75 ± 3.04
Total cholesterol (mmol/l)	185.5 ±46.5	190.94 ± 4.65	167.64 ± 11.9	168.2 ± 5.6	178.86 ± 6.95	175.52 ± 4.33
HDL cholesterol (mmol/l)	42.5 ± 6.5	46.34 ± 0.89	44.92 ± 2.31	47.97 ± 1.45	45.52 ± 1.77	46.18 ± 0.99
LDL cholesterol (mmol/l)	124.5 ±44.5	121.34 ± 5.01	102.71 ± 10.4	101.22 ± 4.69	106.87 ± 5.01	110.24 ± 3.54
Triglyceride (mmol/l)	92.5 ± 42.5	106.57 ± 6.1	121.42 ± 28.9	101.71 ± 12.5	136.04 ± 22.1	96.57 ± 4.96
Cognitive testing						
MMSE	20.34 ± 2	20 ± 0.26	20.84 ± 0.6	21.11± 0.47	21.8 ± 0.5	21.01 ± 0.33
MOCA	19.27 ± 0.6	19.24 ± 0.32	19.18 ± 0.55	19.03 ± 0.52	19.69 ± 0.48	18.94 ± 0.37

Regarding the blood pressure values, we noticed an increase with moderate consumption of alcohol when compared to lower or higher intake, as can be seen from the significant differences in systolic blood pressure between the third group of patients (10.0-14.9 g/day) and the second (0.1-9.9 g/day) ($F(1,85)=24$, $p=0.01$) or the fifth (30.0-49.9 g/day) ($F(1,34)=12$, $p=0.01$). As regards the values of diastolic blood pressure, we observed a significant decrease with an alcohol intake between 10.0-14.9 g/day (third group) and the non-drinkers ($F(1,24)=15$, $p=0.02$) and the fifth group (30.0-49.9 g/day) ($F(1,34)=58$, $p=0.002$).

In the case of the total cholesterol, we observed that moderate consumption of alcohol resulted in lowered levels, as in the case of the group with an intake around 10.0-14.9 g/day (third group) when compared to very low levels (0.1-9.9 g/day) ($F(1,85)=38$, $p=0.005$) or higher levels (30.0-49.9 g/day) ($F(1,35)=7$, $p=0.038$) of consumption (Table 1). Similar aspects were observed in the case of LDL cholesterol, where the third group of patients (10.0-14.9 g/day) showed significant decreased levels when compared to non-drinkers ($F(1,24)=5$, $p=0.049$), the second (0.1-9.9 g/day) ($F(1,85)=22$, $p=0.01$) and the sixth groups (≥ 50.0 g/day) ($F(1,72)=7$, $p=0.04$).

Interesting results were also observed in the case of triglyceride levels, considering that the lower levels were obtained in patients with a higher intake of alcohol (≥ 50.0 g/day), as compared to the second (0.1-9.9 g/day) ($F(1,131)=15$, $p=0.02$), third (10.0-14.9 g/day) ($F(1,72)=20$, $p=0.01$) or fifth (30.0-49.9 g/day) ($F(1,81)=61$, $p=0.001$) groups.

Regarding the results of the psychometric testing, we noticed a significant increase in the values of the MMSE score when we compared a lower dose of alcohol intake (0.1-9.9 g/day) with the higher ones: 30.0-49.9 g/day ($F(1,94)=30$, $p=0.008$) and ≥ 50.0 g/day ($F(1,131)=3$, $p=0.047$) (Table 1).

DISCUSSION

The results presented here suggest that moderate al-

cohol consumption can reduce some neuropathological aspects of T2D, as demonstrated by the decrease in glycemic levels in the groups of patients that consumed increased levels of alcohol (30.0-49.9 g/day) when compared to non-drinkers or groups with 0.1-9.9 or 10.0-14.9 grams of alcohol intake per day. The possible explanations for the published contradictory results with regard to the association between alcohol consumption and T2D could be due to the somewhat small number of patients used in some of the studies, the positive and negative effects that alcohol cand exert on glucose homeostasis (while alcohol could enhance insulin sensitivity, it could have diabetogenic influences through toxic effects on the pancreas), the misclassification of self-reported alcohol consumption (e.g. self-reported alcohol information is generally known to be underreported), differences in drinking patterns (e.g. binge drinking could affect glucose homeostasis differently than consumption that is more evenly distributed), differences between the type of alcoholic beverages consumed, as well as the different follow-up periods or comparisons between follow-up and one-time measurements (Carlsson et al., 2003; Wei et al., 2000). In this study, the consumption for each beverage type was multiplied by its ethanol content, resulting in the classification of patients with T2D into 6 groups according to the total amount (g) of alcohol intake per day.

When it comes to the results of the main studies in this area of research, the very complex report of Carlsson et al. (2003) should be mentioned, which demonstrated on a more than 22 000 Finnish Twin Cohort, during 20 years follow-up, that moderate alcohol consumption (~ 29 g/day) was associated with a reduced incidence of T2D, as compared with low consumption (<5 g/day). In another very recent study by Heianza et al (2013), it was reported that among current drinkers, an intake pattern of <1 drink regularly, over 6 times a week, is associated with the lowest risk of developing diabetes. Although Carlsson et al. (2003) showed that moderate alcohol consumption can reduce the risk of T2D, the authors stated that binge drinking and high alcohol consumption can increase the risk of T2D in women (Carlsson et al., 2003). In regards to gender, there are some controversies as well. Increased risk has been confirmed for men (Kao et al., 2001; Nakanishi et al., 2003), while in women, moderate drinking exerted a protective effect (de Vegt et al., 2002; Carlsson et al., 2003). Additionally, it was showed in post-menopausal women that the consumption of 30 g alcohol per day had some beneficial effects, especially on insulin concentration and sensitivity (Davies et al., 2002). Also, it was shown that light to moderate alcohol intake can be associated with a lower risk of T2D among women aged 25 to 42 years, although this benefit may not persist at higher levels (Wannamethee et al., 2003).

Wei et al. (2000) showed in a prospective study on 8 663 patients an elevated risk of developing T2D in nondrinkers and men with high alcohol intakes when compared with moderate alcohol intake. More importantly, they stated that men with a high alcohol intake might be able to reduce their risk of developing diabetes if they drink less.

Another reference report in this area of research was conducted by Conigrave et al. (2001), who designed a 12-year prospective study including almost 50 000 U.S. male health professionals and in which they demonstrated that frequent alcohol consumption results in increased protection against T2D, even if the level of consumption per drinking day is low. Very importantly, they also showed that the beverage choice did not alter in any way the aforementioned risk. Similarly, Rimm et al. reported in 1995 a reduced incidence of T2D in drinkers when compared with non-drinkers in a cohort of approximately 40 000 male health professionals, who were followed for six years period.

Regarding the mechanisms that could explain this possible protective effect of moderate alcohol intake in diabetes, some authors stated that it could be associated with improved glucose response to ingested carbohydrates, as well as with enhanced insulin sensitivity (Lazarus et al., 1997; Facchini et al., 2004), although this was not confirmed by other authors (Todoroki et al., 1994). Additionally, alcohol intake could decrease glycemic levels during postprandial

period, by reducing gluconeogenesis (Avogaro et al., 1993). It was reported that the tannic acid content of red wine might actually improve insulin sensitivity (Conigrave et al., 2001).

Regarding the results we obtained in our study, we noticed a significant decrease in terms of glycemia in the group that ingested higher levels of alcohol (≥ 50.0 g/day), as compared to those with consumption levels around 0.1-9.9 and 10.0-14.9 g/day. The main mechanisms behind these processes may include reduced insulin binding and resistance (Siller et al., 1998; Wei et al., 2000), decreased insulin mediated glucose uptake and changed glucose tolerance (Lee et al., 1998; Conigrave et al., 2001).

There is increased awareness regarding the relevance of the cognitive status in the relations and mechanisms of alcohol consumption in diabetic pathology. In a the study performed by Townsend et al. (2009) on older women with T2D, it was shown that moderate alcohol intake was associated with better initial cognition, but not with reduced rates of cognitive decline. They concluded that among women with T2D, consumption of at most 1 alcoholic drink per day could result in better initial general cognition, but not with reduced rates of cognitive decline. They showed that very long-term moderate intake of alcohol before and after diagnosis of diabetes was positively associated with both general cognition and verbal memory at the initial interview. Launer et al. (1996) reported decreased risk of poor cognitive function among men with diabetes who drank 1 or 2 drinks per day when compared with non-drinkers. We noticed a significant increase in the values of the MMSE score when we compared a lower dose of alcohol intake (0.1-9.9 g/day) with higher ones, such as 30-49.9 g/day or even more than 50 g alcohol per day.

When it comes to the mechanisms that could explain some of the aforementioned effects, these could include the fact that moderate alcohol intake is associated with decreased levels of markers of inflammation, which leads us to the connections between oxidative stress and inflammatory processes. We have previously demonstrated the relevance of the oxidative stress status in neuropsychiatric disorders (Stefanescu et al., 2012, Padurariu et al., 2013; Irimia et al., 2013; Ciobica et al., 2011a,b, 2012).

We recently showed that BMI is an important confounder in the relationship between alcohol consumption in diabetes and cognitive function (Toarba et al., in press). Research groups have reported a protective effect of alcohol consumption in overweight subjects (Facchini et al., 1994, Carlsson et al., 2003).

Another important aspect is the connection established between alcohol intake and coronary heart disease mortality in patients with older onset diabetes, Valmadrid et al. (1999) demonstrated an overall beneficial effect of alcohol consumption in lowering the risk of death due to coronary heart disease. A protective effect of moderate alcohol consumption on ischemic stroke was demonstrated (Sacco et al., 1999). In addition, it seems that the protective effects of moderate alcohol consumption on myocardial infarction are genetically influenced (Hines et al., 2001).

Clearly, there is a delicate balance between the beneficial and harmful effects of alcohol (the latter being incontestable, as demonstrated very recently by Dobson et al. (2012), who showed that chronic prenatal ethanol exposure increases adiposity and disrupts pancreatic morphology in adult guinea pig offspring). Therefore, decisions about alcohol consumption should consider the full range of benefits and risks to a distinctive individual (Conigrave et al., 2001).

CONCLUSION

Our results presented here suggest that moderate alcohol consumption can reduce some of the neuropathological components of T2D and could improve some aspects of cognitive function. However, studies with larger samples and longer follow-up times are necessary in order to understand the association between alcohol intake, cognitive functions and T2D.

REFERENCES

Ajani, U.A., Hennekens, C.H., Spelsberg, A. and J.E. Manson (2000). Alcohol consumption and risk of type 2 diabetes mellitus among US male physicians. *Arch Intern Med* **160**, 1025-1030.

American Diabetes Association (2010). Standards of Medical Care in Diabetes. *Diabet. Care*. **33**, 11-61.

Avogaro, A. (1993). Alcohol, glucose metabolism and diabetes. *Diabetes Metab Rev* **9**, 129–146.

Baliunas, D.O., Taylor, B.J., Irving, H., Roerecke, M., Patra, J., Mohapatra, S. and J. Rehm (2009). Alcohol as a risk factor for type 2 diabetes: A systematic review and meta-analysis. *Diabetes Care* **32**, 2123-32.

Carlsson, S., Hammar, N., Grill, V. and J. Kaprio (2003). Alcohol consumption and the incidence of type 2 diabetes: a 20-year follow-up of the Finnish twin cohort study. *Diabetes Care* **10**, 2785-90.

Carlsson, S., Hammar, N. and V. Grill (2005). Alcohol consumption and type 2 diabetes meta-analysis of epidemiological studies indicates a U-shaped relationship. *Diabetologia* **48**, 1051-4.

Ciobica, A., Nastasa, V., Hritcu, L., Padurariu, M. and W. Bild (2011a). Effects of angiotensin II receptor antagonists on anxiety and some oxidative stress markers in rat. *Central European Journal of Medicine* **6**, 331-340.

Ciobica, A., Olteanu, Z., Padurariu, M. and L.Hritcu (2012). The effects of low-dose pergolide on memory and oxidative stress in a 6-OHDA induced rat model of Parkinson's disease. *Journal of Physiology and Biochemistry* **68**, 59-69.

Ciobica, A., Padurariu, M., Dobrin, I., Stefanescu, C. and R. Dobrin (2011b). Oxidative stress in schizophrenia – focusing on the main markers. *Psychiatr Danub* **23**, 237-45.

Conigrave, K.M., Hu, B.F., Camargo, C.A. Jr., Stampfer, M.J., Willett, W.C. and E.B. Rimm (2001). A prospective study of drinking patterns in relation to risk of type 2 diabetes among men. *Diabetes* **50**, 2390-5.

Cukierman, T., Gerstein, H.C. and J.D. Williamson (2005). Cognitive decline and dementia in diabetes – systematic overview of prospective observational studies. *Diabetologia* **48**, 2460-2469.

Davies, M.J., Baer, D.J., Judd, J.T., Brown, E.D., Campbell, W.S. and P.R. Taylor (2002). Effects of moderate alcohol intake on fasting insulin and glucose concentrations and insulin sensitivity in postmenopausal women: a randomized controlled trial. *JAMA*. **287**, 2559-62.

de Vegt, F., Dekker, J.M., Groeneveld, W.J., Nijpels, G., Stehouwer, C.D., Bouter, L.M. and R.J. Heine (2002). Moderate alcohol consumption is associated with lower risk for incident diabetes and mortality: the Hoorn study. *Diabetes Res Clin Pract* **57**, 53-60.

Dobson, C.C., Mongillo, D.L., Brien, D.C., Stepita, R., Poklewska-Koziell, M., Winterborn, A. and A.C. Holloway (2012). Chronic prenatal ethanol exposure increases adiposity and disrupts pancreatic morphology in adult guinea pig offspring. *Nutr Diabetes* **17**, e57.

Facchini, F., Chen, Y-D. and G.M. Reaven (1994). Light-to-moderate alcohol intake is associated with enhanced insulin sensitivity. *Diabetes Care* **17**, 115-119.

Heianza, Y., Arase, Y., Saito, K., Tsuji, H., Fujihara, K., Hsieh, S.D. and S. Kodama (2013). Role of alcohol drinking pattern in type 2 diabetes in Japanese men: the Toranomon Hospital Health Management Center Study 11 (TOPICS11). *Am J Clin Nutr* **97**, 561-8.

Hines, L.M., Stampfer, M.J., Ma, J., Gaziano, J.M., Ridker, P.M., Hankinson, S.E., Sacks, F., Rimm, E.B. and D.J. Hunter (2001). Genetic variation in alcohol dehydrogenase and the beneficial effect of moderate alcohol consumption on myocardial infarction. *N Engl J Med* **344**, 549-55.

Hodge, A.M., Dowse, G.K., Collins, V.R. and P.Z. Zimmet (1993). Abnormal glucose tolerance and alcohol consumption in three populations at high risk of non-insulin-dependent diabetes mellitus. *Am J Epidemiol* **137,** 178-189.

Howard AA, Arnsten JH and MN Gourevitch (2004). Effect of alcohol consumption on diabetes mellitus: a systematic review. *Ann Intern Med* **140**, 211-9.

Irimia, R. A.. Ciobica, C. Stanciu and A. Trifan (2013). The relevance of oxidative stress in cirrhotic patients with different forms of hepatic encephalopathy. *Arch. Biol. Sci., Belgrade* **65**, 1245-1252.

Kao, L.H.W., Puddy, I.B., Boland, L.L., Watson, R.L. and F.L. Brancati (2001). Alcohol consumption and the risk of type 2 diabetes mellitus. *Am J Epidemiol* **154**, 748-757.

Koppes, L.L., Dekker, J.M., Hendriks, H.F., Bouter, L.M. and R.J. Heine (2005). Moderate alcohol consumption lowers the risk of type 2 diabetes: a meta-analysis of prospective observational studies. *Diabetes Care* **28**, 719-25.

Launer, L.J., Feskens, E.J., Kalmijn, S. and D. Kromhout (1996). Smoking, drinking, and thinking. The Zutphen Elderly Study. *Am J Epidemiol* **143**, 219-227.

Lazarus, S., Sparrow, D. and S. Weiss (1997). Alcohol intake and insulin levels: the Normative Aging Study. *Am J Epidemiol* **145**, 909-916.

Lee, K.S., Park, C.Y., Meng, K.H., Bush, A., Lee, S.H., Lee, W.C., Koo, J.W. and C.K. Chung (1998). The association of cigarette smoking and alcohol consumption with other car-

diovascular risk factors in men from Seoul, Korea. *Ann Epidemiol* **8**, 31-38.

Monterrosa, A.E., Haffner, S.M., Stern, M.P. and H.P. Hazuda (1995). Sex difference in lifestyle factors predictive of diabetes in Mexican-Americans. *Diabetes Care* **18**, 448-456.

Nakanishi, N., Suzuki, K. and K. Tatara (2003). Alcohol consumption and risk for development of impaired fasting glucose or type 2 diabetes in middle-aged Japanese men. *Diabetes Care* **26,** 48-54.

Padurariu, M., Ciobica, A., Lefter, R., Serban, I.L., Stefanescu, C. and R. Chirita (2013). The oxidative stress hypothesis in Alzheimer's disease. *Psychiatr Danub*.

Popescu, D.S., Ciobica, A., Arhire, L.I., Mihalache, L., Nita, O., Serban, I.L., Dobrin, R., Ungureanu, D. and M. Graur (2013). Increased prevalence of impaired glucose tolerance in a representative rural population from Deleni, Romania. *Arch. Biol. Sci., Belgrade* **65**, 1579-1584

Rimm, E.B., Chan, J., Stampfer, M.J., Colditz, G.A. and W.C. Willett (1995). Prospective study of cigarette smoking, alcohol use, and the risk of diabetes in men. *BMJ* **310**, 555-559.

Ruitenberg, A., van Swieten, J.C., Witteman, J.C., Mehta, K.M., van Duijn, C.M., Hofman, A. and M.M. Breteler (2002). Alcohol consumption and risk of dementia: the Rotterdam Study. *Lancet* **359**, 281-6.

Sacco, R.L., Elkind, M., Boden-Albala, B., Lin, I.F., Kargman, D.E., Hauser, W.A., Shea, S., and M.C. Paik (1999). The protective effect of moderate alcohol consumption on ischemic stroke. *JAMA* **281**, 53-60.

Stefanescu, C. and A. Ciobica (2012). The relevance of oxidative stress status in first episode and recurrent depression. *Journal of Affective Disorders* **143**, 34-8.

Toarba, C., Hogas, S., Covic, A., Ciobica, A., Serban, I.L., Chirita, R. and M. Graur. The relevance of body mass index in the cognitive status of diabetic patients with different alcohol drinking patterns, *Arch. Biol. Sci., Belgrade*, in press.

Todoroki, I., Shinchi, K.K.S. and K. Imanishi (1994). Lifestyle and glucose tolerance: a cross-sectional study of Japanese men. *Ann Epidemiol* **4**, 363-368.

Townsend, M.K., Devore, E., Kang, J.H. and F. Grodstein (2009). The relation between moderate alcohol consumption and cognitive function in older women with type 2 diabetes. *Diabetes Res Clin Pract* **85**, 322-7.

Valmadrid, C.T., Klein, R., Moss, S.E., Klein, B.E. and K.J. Cruickshanks (1999). Alcohol intake and the risk of coronary heart disease mortality in persons with older-onset diabetes mellitus. *JAMA* **282**, 239-46.

Wannamethee, S.G., Camargo, C.A. Jr., Manson, J.E., Willett, W.C. and E.B. Rimm (2003). Alcohol drinking patterns and risk of type 2 diabetes mellitus among younger women. *Arch Intern Med* **163**, 1329-36.

Wannamethee, S.G., Shaper, A.G., Perry, I.J. and K.G. Alberti (2002). Alcohol consumption and the incidence of type II diabetes. *J Epidemiol Community Health* **7**, 542-548.

Wei, M., Gibbons, L.W., Mitchell, T.L., Kampert, J.B. and S.N. Blair (2000). Alcohol intake and incidence of type 2 diabetes in men. *Diabetes Care* **23**, 18-22.