Are erectile functions affected by ABO blood group?

Erdal Benli ¹, Abdullah Çırakoğlu ¹, Ercan Öğreden ², Selamettin Demir ³, Yasemin Kaya ⁴, Mustafa İbas ⁵, Ali Ayyıldız ⁶, Ahmet Yüce ¹

¹ Department of Urology, Ordu University, Faculty of Medicine, Ordu, Turkey;

² Department of Urology, Giresun University, Faculty of Medicine, Giresun, Turkey;

³ Clinic of Urology, Istanbul Hospital, Van, Turkey;

⁴ Department of Internal Medicine, Ordu University, Faculty of Medicine, Ordu, Turkey;

⁵ Intern, Necmettin Erbakan University, Faculty of Medicine, Konya, Turkey;

⁶ Clinic of Urology, Ankara Training Research Hospital, Ankara, Turkey.

Aim: The aim of this study was to investi-Summary gate whether there is a relationship between erectile dysfunction (ED), thought to be a vascular

disease, and ABO blood group.

Material and Method: The study included 350 people abiding by the study criteria who applied to our clinic from April 2012-April 2015. The patients were divided into two groups including those with ED (Group 1) and those without (Group 2). Age, blood group, IIEF-5 score and presence of additional diseases were recorded. Erectile functions were analyzed

according to blood group.

Results: There was no difference between the mean age of 111 patients with ED and that of 239 patients without ED included in the study (p = 0.284). There was no difference between patients in the two groups in terms of smoking, alcohol use, hypertension and diabetes (p > 0.05). Among patients in the ED group, the mean IIEF-5 score according to blood group was 19.8 ± 5.04 in the 0 blood group, 16.5 ± 5.2 in the A blood group, 17.2 ± 5.3 in the B blood group and 13.3 ± 3.02 in the AB blood group. The IIEF-5 scores of individuals in the 0 blood group were significantly high compared to individuals in other blood groups (p = 0.004). Logistic regression analysis found that compared to the 0 blood group, the erectile dysfunction risk was 3.9 times greater for the A blood group, 3.5 times greater for the B blood group and 4.7 times greater for the AB blood group (p = 0.001) (Table 3).

Conclusion: The risk of erectile dysfunction was significantly increased for individuals in the A, B and AB blood groups compared to individuals in the 0 blood group.

KEY WORDS: ABO blood group; Erectile dysfunction; Vascular disease.

Submitted 6 May 2016; Accepted 31 May 2016

Introduction

Erectile dysfunction (ED) is defined as either continuous or repeated lack of erection, or lack of sustained erection, necessary for satisfying sexual relations (1). The penis includes a very rich and specialized vascular system. The complete endothelium furnishing this vascular system plays an important role in erectile tissue function. Disruption of the complete endothelial may cause development of atherosclerotic vein diseases, in addition to affecting erectile functions. Studies have shown that risk factors such as aging, hypertension, diabetes, smoking, central obesity and dyslipidemia increasing the risk of atherosclerotic coronary artery disease (CAD) are also important risk factors for ED. For both CAD and ED, early indicators of the common vascular disease of atherosclerosis may occur in erectile tissue (2, 3).

The relationship between ABO blood groups and some diseases was first reported by Alexzender for the first time in 1921 (4). Later studies have reported a close relationship between vascular diseases like coronary artery disease and thrombosis, and also a variety of cancers such as pancreatic and bladder cancer (5, 6). According with the demonstrated correlation with many vascular diseases, the correlation between ABO blood groups and another vascular disorder such as ED has not been investigated. In this study we aimed to investigate whether there was a correlation between ABO blood groups and erectile dysfunction.

MATERIALS AND METHODS

The data belonging to 972 patients applying to our clinic from April 2012 to April 2015 were retrospectively investigated. The study included 350 patients with age, blood group, IEFF-5 score and presence of additional diseases recorded. Permission was obtained from the local ethics committee of Ordu University (decision no. 2015/1). The exclusion criteria for the study included congestive heart failure, hyperprolactinemia, hypogonadism, renal function disorders, peripheral or autonomic neuropathy, psychiatric problems and treatment for sexual function disorders. Patients were divided into two groups; those requiring treatment due to lack of or to unsustained erections (ED group) and those with problem-free sexual relations (control group).

The erectile functions of patients were determined using the International Index of Erectile Function-5 (IIEF-5). Each question on this from is scored from 1 to 5. If the patient could not fill out the form, help was given by the same person. The total IIEF-5 score is calculated by adding the scores (from 1-5) given to 5 questions. According to total points sexual function was defined as normal (22-25), mild (17-21), moderate (12-16) and severe dysfunction (1-11).

RESULTS

The mean age of all patients included in the study was 62.34 ± 8.51 (41-84) years. The mean age of the 111 patients in the ED group was 63.05 ± 8.5 (41-84) years, while the mean age of patients in the control group without ED complaints was 62 ± 8.5 (43-84) years. There was no difference between the groups in terms of age (p = 0.284).

Apart from cardiac disease, there was no difference between patients in the ED group and those in the non-ED group in terms of demographic characteristics (Table 1). The distribution of individuals with erectile dysfunction in terms of blood groups is shown in Table 2.

The mean IIEF-5 score of patients in the ED group according to blood group was found as 19.8 ± 5.04 for 0 blood group, 16.5 ± 5.2 for A blood group, 17.2 ± 5.3 for B blood group and 13.3 ± 3.02 for AB blood group. The mean IIEF-5 score for individuals with the 0 blood group was identified to be significantly high compared to other blood groups (p = 0.004).

The presence of $\dot{E}D$ was found in 15.7% of patients with 0 blood group, in 41.6% of patients with A blood group, in 39.3% of patients with B blood group and in 46.7% of patients with AB blood group (p < 0.001). Logistic regression analysis showed that compared to the 0 blood group the risk of erectile dysfunction was 3.9 times increased for A blood group, 3.5 times increased for B blood group and 4.7 times increased for AB blood group (p = 0.001) (Table 3).

Statistical analysis

Descriptive statistics for continuous variables are given as mean, standard deviation, minimum and maximum values, while for categorical variables these are given as number and percentage. To determine whether there was a difference in ED presence for continuous variables, the Student t test was performed. To determine the correlation between categorical variables, the chi-square test was used. Additionally to determine the possible risk factors affecting erectile dysfunction, multiple logistic regression analysis was performed. For calculations the level of statistical significance was taken as 5% and calculations used the SPSS (ver. 13) statistical package program.

Table 1.Demographic characteristics of participants in the research.

Characteristics		ED n (%)		P-value
(Present/absent)		Present	Absent	
Alcohol	Present	9 (33.7)	18 (66.7)	0.832
	Absent	101 (31.6)	219 (68.4)	
Smoking	Present	38 (33)	77 (67)	0.728
	Absent	73 (31.2)	161 (68.8)	
Diabetes	Present	26 (37.7)	43 (62.3)	0.289
	Absent	84 (31)	187 (69)	
Hypertension	Present	37 (33.3)	74 (66.7)	0.711
	Absent	73 (31.1)	162 (68.9)	
Cardiac disease	Present	29 (43.9)	37 (56.1)	0.27
	Absent	82 (73.9)	202 (84.5)	

Table 2. Distribution of blood groups in ED.

Blood group	Erectile dysfunction n (%)		
	Present	Absent	
0 blood group	21 (18.9%)	113 (47.3)	
A blood group	52 (46.8)	73 (30.5)	
B blood group	24 (21.6)	37 (15.5)	
AB blood group	14 (12.6)	16 (6.7)	

Table 3.Results of logistic regression analysis.

	Odds ratio (OR)	95.0% C.I.		P-value			
		Lower	Upper				
Age	1.009	.979	1.040	0.556			
A blood group	3.949	2.143	7.279	0.001			
B blood group	3.504	1.712	7.173	0.001			
AB blood group	4.742	1.960	11.473	0.001			
OR: Odds ratio; CI: Confidence interval. For blood group 0 is the reference category.							

DISCUSSION

The results of our study found a relationship between ED and ABO blood groups and ED was identified to have increased incidence in A, B and AB blood groups compared to 0 blood group. The clearly increased ED risk in the AB blood group may be related to the synergic effect caused by the presence of A and B antigens together. The increased risk identified in the study using multivariate analysis shows the ED risk is independent of promoting factors such as alcohol, smoking and hypertension.

The penis, with a very rich vein network, is one of the richest organs in terms of endothelium per unit area (7). Healthy endothelium releases material with antifibrinolytic and anticoagulant properties, as well as strong vasodilatator materials like NO. Disruption of the completeness of the endothelium disrupts these functions and synthesis of vasoconstrictor materials like thromboxane A2, endotelin, and angiotensin 2 increases. Additionally loss of the permeability and antithrombocyte properties of endothelium is proposed to trigger the atherosclerotic process (8). As a result, studies related to atherosclerotic vascular diseases have frequently used measurements of endothelial functions. Diseases that form a risk for vascular disease, like hypertension, hypercholesterolemia, diabetes and obesity, affect the endothelin in the vein walls, by affecting homeostasis function (9). As a result the process beginning with endothelial disruption is reported to show itself in a variety of diseases such as angina, stroke and CAD where tissue perfusion is disrupted (9, 10). The degree of endothelial dysfunction is related to the severity of these diseases experienced by the patient (11).

Endothelial dysfunction is shown to be an effective factor in the development of ED (12). This effect is thought to be due to effects on the vein elasticity of erectile tissue and on the release of endothelial factors like NO released by endothelium (13, 14). A study by *Davignon et al.* proposed

that one of the earliest indicators of atherosclerosis is

changes in NO activity (15). Thus, ED is thought to occur

as a part of the systemic vascular disease of atherosclerosis

(16). Many studies on this topic have shown a close relationship between ED and vascular diseases. In fact, some studies have proposed ED is the first symptom of systemic vascular disease. Montorsi et al. in a study reported that problems related to ED began 3 years before the occurrence of coronary artery disease, while Ponholzer et al. reported such problems began 10 years before stroke (17, 18). While explaining the reasons for this, the researchers used the artery diameter hypothesis. According to this hypothesis, as the size of penile arteries (1-2 mm) is small compared to coronary arteries (3-4 mm), the same level of atherosclerotic/endothelial damage causes greater reduction in perfusion in erectile tissue compared to coronary or other veins (19). As a result ED may occur in erectile tissue as the first indicator of systemic atherosclerosis (20, 21). Researchers have proposed that erectile tissue may be a sensitive indicator of systemic atherosclerotic diseases (7). The reason for the relationship between ABO blood groups and ED identified in our study may be related to endothelial dysfunction and related atherosclerosis occurring in erectile tissue. Many studies supporting this hypothesis have shown a relationship between atherosclerotic vascular diseases and ABO blood groups (1). Atherosclerotic vascular diseases like myocardial infarct, peripheral vascular diseases, intermittent claudication, and venous thromboembolism are reported to be encountered more frequently in the non-0 blood groups compared to the 0 blood group (22, 23). A study by Carpenggiani et al. investigated the blood groups of 4901 patients undergoing coronary angiography due to atherosclerotic CAD and reported that atherosclerotic coronary disease was most frequently observed in non-0 blood groups (24). This conclusion may explain our results. Probably blood groups cause atherosclerotic results or endothelial dysfunction leading to development of ED. The reason for the relationship between ABO blood groups and atherosclerotic vascular diseases is not fully known. The genetic nature of the ABO blood groups may affect this. There are many hypotheses to explain this situation. One of these is the ATP-binding cassette 2 (ABCA2) gene known to be important for cholesterol balance and carried in the 9q34 locus of chromosome 9 together with ABO blood groups (25, 26). The study by Carpeggiani et al. identified a significant relationship between non-0 blood group and hypercholesterolemia and family history (24). In human and animal models, hypercholesterolemia is shown to disrupt smooth muscle relaxation linked to endothelium, enzyme activity of endothelial nitric oxide synthesis (eNOS) and penile angiogenesis resulting in ED (16, 27). Another hypothesis is related to adhesion molecules such as sICAM-1 (high soluble intercellular adhesion molecule-1), sPselectin (soluble P-selectin) and sE-selectin (soluble Eselectin) which affect ABO blood groups and are thought to cause endothelial disruption (28).

Another opinion gaining great interest is related to blood groups affecting von Willebrand factor (vWF) and factor 8 levels causing development of atherosclerosis (29). These factors, known as adhesion molecules, are reported to be

effective on thrombocyte leukocyte interaction, adhesion of thrombocytes to veins, migration of leukocytes into veins and development of atheroma plaque; in short on the development of atherosclerosis (30, 31). Studies have identified higher vWF and F8 levels in individuals with A and B blood groups compared to 0 blood group (32, 33). The study by *Sarode et al.* reported that A and B blood groups were effective on adhesive activity of vWF (34). Again a study by *Ray et al.* on acute coronary syndrome and a study by *Convay et al.* on thromboemboli and stroke diseases reported a close relationship between ABO blood group and vWF (35, 36).

In short there are many studies in the literature showing the close relationship between ABO blood groups and atherosclerotic vascular diseases (37). In fact a study by *Kaya et al.* reported that ABO blood groups may be related to the complications of atherosclerosis, in addition to the development of atherosclerosis (38).

In our study, A, B and AB blood groups were found to be related to the risk of a person experiencing erectile dysfunction. As mentioned in many studies above, due to the relationship shown between vascular diseases and ABO blood groups, the relationship with ED thought to be a vascular disease is not surprising. We consider that this effect progresses through endothelial dysfunction and atherosclerotic processes. We consider that endothelial damage affects synthesis of a variety of materials like NO known to play an important role in erections, disrupts the effect of endothelium on vascular tonus, narrows the venous lumens due to atherosclerosis and finally affects blood flow to erectile tissue.

There are some limitations to this study. These include its retrospective nature, reflecting results from a single center and that laboratory results from patients including lipid profile, serum F8 and vWF level were not examined.

CONCLUSION

This study found a close relationship between A, B and AB blood groups and ED. We believe this correlation is due to effect of the complicated process resulting in endothelial dysfunction, similar to the correlation previously reported for blood groups and atherosclerotic events. In spite of the limitations of the study, we believe this study is very important in being the first study to show the relationship between ABO blood groups and ED. This may be important in terms of taking preventive precautions related to atherosclerotic vein diseases known to be related to ED.

REFERENCES

- 1. NIH Consensus Development Panel on Impotence. Impotence. NIH Consensus Development Panel on Impotence. Am Med Assoc. 1993; 270:83-90.
- 2. Fung MM, Bettencourt R, Barrett-Connor E. Heart disease risk factors predict erectile dysfunction 25 years later: the Rancho Bernardo Study. J Am Coll Cardiol. 2004; 43:1405-11.
- 3. Sullivan ME, Keoghane SR, Miller MA. Vascular risk factors and erectile dysfunction. BJU Int. 2001; 87:838-45.
- 4. Kumar T, Puri G, Laller S, et al. Association of ABO blood grouping with oral lichen planus. Univ Res J Dent. 2014; 4:93-6.

- 5. Engel O, Soave A, Peine S, et al. The impact of the ABO and the Rhesus blood group system on outcomes in bladder cancer patients treated with radical cystectomy. World J Urol. 2015; 33:1769-76.
- 6. Pelzer U, Klein F, Bahra M, et al. Blood group determinates incidence for pancreatic cancer in Germany. Front Physiol. 2013; 4:118.
- 7. Billups KL, Bank AJ, Padma-Nathan H, et al. Erectile dysfunction is a marker for cardiovascular disease: results of the minority health institute expert advisory panel. J Sex Med. 2005; 2:40-50.
- 8. Drexler H. Factors involved in the maintenance of endothelial function. Am J Cardiol. 1998; 82:3S-4S.
- 9. Heiss C, Schroeter H, Balzer J, et al. Endothelial function, nitric oxide, and cocoa flavanols. J Cardiovasc Pharmacol. 2006; 47:S128-35.
- 10. Sullivan ME, Thompson CS, Dashwood MR, et al. Nitric oxide and penile erection: is erectile dysfunction another manifestation of vascular disease? Cardiovasc Res. 1999; 43:658-65.
- 11. Widlansky ME, Gokce N, Keaney JF Jr, et al. The clinical implications of endothelial dysfunction. J Am Coll Cardiol. 2003; 42:1149-60.
- 12. Grover SA, Lowensteyn I, Kaouache M, et al. The prevalence of erectile dysfunction in the primary care setting: importance of risk factors for diabetes and vascular disease. Arch Intern Med. 2006; 166:213-9.
- 13. Rubanyi GM. The role of endothelium in cardiovascular homeostasis and diseases. J Cardiovasc Pharmacol. 1993; Suppl 4:S1-14.
- 14. Gratzke C, Angulo J, Chitaley K, et al. Anatomy, physiology, and pathophysiology of erectile dysfunction. J Sex Med. 2010; 7:445-75.
- 15. Davignon J, Ganz P. Role of endothelial dysfunction in atherosclerosis. Circulation. 2004; 109:27-32.
- 16. Ryu JK, Kim WJ, Koh YJ, et al. Designed angiopoietin-1 variant, COMP-angiopoietin-1, rescues erectile function through healthy cavernous angiogenesis in a hypercholesterolemic mouse. Sci Rep. 2015; 9222
- 17. Montorsi P, Montorsi F, Schulman CC. Is erectile dysfunction the "tip of the iceberg" of a systemic vascular disorder? Eur Urol. 2003; 44:352-4.
- 18. Ponholzer A, Temml C, Obermayr R, et al. Is erectile dysfunction an indicator for increased risk of coronary heart disease and stroke? Eur Urol. 2005; 48:512-8.
- 19. Montorsi P, Ravagnani PM, Galli S, et al. Association between erectile dysfunction and coronary artery disease: Matching the right target with the right test in the right patient. Eur Urol. 2006; 50:721-31.
- 20. Montorsi P, Ravagnani PM, Galli S, et al. Association between erectile dysfunction and coronary artery disease. Role of coronary clinical presentation and extent of coronary vessels involvement: the COBRA trial. Eur Heart J. 2006; 27:2632-9.
- 21. Kaiser DR, Billups K, Mason C, et al. Impaired brachial artery endothelium-dependent and -independent vasodilation in men with erectile dysfunction and no other clinical cardiovascular disease. J Am Coll Cardiol. 2004; 43:179-84.
- 22. Franchini M, Capra F, Targher G, et al. Relationship between ABO blood group and von Willebrand factor levels: from biology to clinical implications. Thromb J. 2007; 5:14.
- 23. Hørby J, Gyrtrup HJ, Grande P, et al. Relation of serum lipoproteins and lipids to the ABO blood groups in patients with intermittent claudication. Cardiovasc Surg (Torino). 1989; 30:533-7.
- 24. Carpeggiani C, Coceani M, Landi P, et al. ABO blood group alleles: A risk factor for coronary artery disease. An angiographic study. Atherosclerosis. 2010; 211:461-6.
- 25. Yip SP. Sequence variation at the human ABO locus. Ann Hum Genet. 2002; 66:1-27.

- 26. Schmitz G, Kaminski WE. ABCA2: a candidate regulator of neural transmembrane lipid transport. Cell Mol Life Sci. 2002; 59:1285-95.
- 27. Ryu JK, Shin HY, Song SU, et al. Down regulation of angiogenic factors and their down stream target molecules affects the deterioration of erectile function in a rat model of hypercholesterolemia. Urology. 2006; 67:1329-34.
- 28. Preston AE, Barr A. The Plasma Concentration of Factor Viii in the Normal Population. II. The Effects of Age, Sex and Blood Group. Br J Haematol. 1964; 10:238-45.
- 29. Wu O, Bayoumi N, Vickers MA, et al. ABO(H) blood groups and vascular disease: a systematic review and meta-analysis. J Thromb Haemost. 2008; 6:62-9.
- 30. Ruggeri ZM. The role of von Willebrand factor and fibrinogen in the initiation of platelet adhesion to thrombogenic surfaces. Thromb Haemost. 1995; 74:460-3.
- 31. Bowen DJ. An influence of ABO blood group on the rate of proteolysis of von Willebrand factor by ADAMTS13. J Thromb Haemost. 2003; 1:33-40.
- 32. Zagashvili IuV, Zalepukhina OE, Papaian LP, et al. Factor VIII activity in healthy subjects with respect to a blood group according to the ABO system. Klin Lab Diagn. 2004; 3:46-7.
- 33. Thompson IM, Tangen CM, Goodman PJ, et al. Erectile dysfunction and subsequent cardiovascular disease. JAMA. 2005; 294:2996-3002.
- 34. Sarode R, Goldstein J, Sussman II, et al. Role of A and B blood group antigens in the expression of adhesive activity of von Willebrand factor. Br J Haematol. 2000; 109:857-64.
- 35. Ray KK, Francis S, Crossman DC. Measurement of plasma von Willebrand factor in acute coronary syndromes and the influence of ABO blood group status. J Thromb Haemost. 2004; 2:2053-4.
- 36. Conway DS, Pearce LA, Chin BS, et al. Plasma von Willebrand factor and soluble p-selectin as indices of endothelial damage and platelet activation in 1321 patients with nonvalvular atrial fibrillation: relationship to stroke risk factors. Circulation. 2002; 106:1962-7.
- 37. Tarján Z, Tonelli M, Duba J, et al. Correlation between ABO and Rh blood groups, serum cholesterol and ischemic heart disease in patients undergoing coronarography. Orv Hetil. 1995; 136:767-9.
- 38. Kaya A, Tanboga IH, Kurt M, et al. Relation of ABO blood groups to coronary lesion complexity in patients with stable coronary artery disease. Anadolu Kardiyol Derg. 2014; 14:55-60.

Correspondence

Erdal Benli, MD (Corresponding Author) drerdalbenli@gmail.com

Abdullah Çırakoğlu, MD

dr_cirakoglu@yahoo.com

Ahmet Yüce, MD

ahmetyuce7@gmail.com

Department of Urology, Ordu University, Faculty of Medicine, Ordu, Turkey

Ercan Öğreden, MD

9isik061@mynet.com

Department of Urology, Giresun University, Faculty of Medicine, Giresun, Turkey

Selamettin Demir, MD

drselami1978@hotmail.com

Clinic of Urology, Istanbul Hospital, Van, Turkey

Mustafa İbas, MD

ibasmustafa91@hotmail.com

Intern, Necmettin Erbakan University, Faculty of Medicine, Konya, Turkey

Ali Ayyıldız, MD

urology52@gmail.com

Clinic of Urology, Ankara Training Research Hospital, Ankara, Turkey