The effects of steroids on endothelial function

To the Editor,

We read the article about the effects of high-dose steroid treatment used to treat acute demyelinating diseases on endothelial and cardiac functions entitled "The effect of highdose steroid treatment used for the treatment of acute demyelinating diseases on endothelial and cardiac functions." published in Anatol J Cardiol 2017; 17: 392-7 by Çaldır et al. (1) with great interest. The main argument of the authors was that steroids cause endothelial dysfunction. The authors used brachial artery flow-mediated dilatation (FMD) and carotid intima-media thickness (cIMT), which are indirect techniques, to measure endothelial dysfunction. They said that FMD changes that occurred 3 months after steroid treatment might indicate endothelial dysfunction. But we think that this result is not reliable, as FMD is not a valuable indicator without cIMT change. Endothelial dysfunction due to steroid use is related to arterial hypertension. It is not possible to diagnose endothelial dysfunction without a pathological examination performed after 3 months of steroid use. Also, inflammation is another important point of endothelial dysfunction. Inflammation involves the bonding of leukocytes from the bloodstream to the vessel wall via selectins, vascular cell adhesion molecules, intercellular adhesion molecules, chemokines, and interleukins (2). It has been demonstrated in many experimental and clinical studies that steroids have anti-inflammatory effects (2, 3). Certainly steroids, as strong anti-inflammatory agents, can have positive effects on endothelial dysfunction (2). Another study reported that steroids also have antiproliferative effects on smooth muscles (4). Inhibition of smooth muscle cell proliferation also decreases intimal hyperplasia, and so, endothelial dysfunction (2, 5). In this aspect, it is therefore projected that steroids are beneficial for endothelial dysfunction. We await the opinions of the authors on this topic.

Orhan Gökalp, Şahin İşcan, Hasan İner, Ali Gürbüz
Departmant of Cardiovascular Surgery, Atatürk Education and Research Hospital, İzmir Katip Çelebi University; İzmir-*Turkey*

References

1. Çaldır MV, Çelik GK, Çiftçi Ö, Müderrisoğlu İH. The effect of high-dose steroid treatment used for the treatment of acute demyelinating diseases on endothelial and cardiac functions. Anatol J Cardiol 2017; 17: 392-7.
2. Zakkar M, Luong le A, Chaudhury H, Ruud O, Punjabi PP, Anderson JR, et al. Dexamethasone arterializes venous endothelial cells by inducing mitogen-activated protein kinase phosphatase-1: a novel anti-inflammatory treatment for vein grafts? Circulation 2011; 123: 524-32.
3. Gökalp O, Yürekli I, Kıray M, Bağrıyanık A, Yetkin U, Yürekli BS, et al. Assessment of protective effects of pheniramine maleate on reperfusion injury in lung after distant organ ischemia: a rat model. Vasc Endovascular Surg 2013; 47: 219-24.
4. Park TG, Yoo HS. Dexamethasone nano-aggregates composed of PEG-PLA-PEG triblock copolymers for anti-proliferation of smooth muscle cells. Int J Pharm 2006; 326: 169-73.
5. Gökalp O, Yürekli I, Mavioğlu L, Kıray M, Bağrıyanık A, Kestelli M, et al. The effect of ascorbic acid on proliferation of vascular smooth muscle cells and intimal hyperplasia. Turkiye Klinikleri J Med Sci 2013; 33: 126-31.

Address for Correspondence: Dr. Orhan Gökalp
Altınvadi Cd. No: 85 D: 10 35320
Narlıdere/İzmir-*Türkiye*
E-mail: gokalporhan@yahoo.com

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Author`s Reply

To the Editor,

We would like to thank you for your interest in our study entitled "The effect of high-dose steroid treatment on the treatment of acute demyelinating diseases on endothelial and cardiac functions," published Anatol J Cardiol 2017; 17: 392-7 (1).

Steroids are molecules that have been proven to have anti-inflammatory effects as a result of reducing the activity of pro-inflammatory cytokines, adhesion molecules, and inflammatory cells in in vitro and in vivo studies. However, the positive results on endothelial cells are almost exclusively reported in cell cultures and animal experiments, and their efficacy on in vivo endothelium is contradictory (2). It is thought that the creativity effect of endothelial functions in vivo is masked due to the negative effects of increased blood pressure, cholesterol and blood glucose levels, and adverse metabolic effects, such as weight gain (3). In our study, the increase in systolic blood pressure and body mass index at the first week and third month support these findings. Pulse steroid therapy may have resulted in impaired endothelial function with acute and chronic indirect effects. Our study also investigated the question of whether pulsed steroid treatment produced endothelial dysfunction by direct or indirect effect.

Carotid intima-media thickness (cIMT) is the earliest sign of atherosclerosis, which increases in the long-term and is not directly related to endothelial dysfunction. The major studies have been carried out with 3 to 15 years of follow-up. The main limitation of our study is the short follow-up period of 3 months (4, 5). Like the contradictory effects of steroids on endothelial dysfunction, cIMT also has complex in vivo effects. Although they have antiproliferative effects for smooth muscle cells, they increase subintimal lipid storage due to increased metabolic adverse effects and oxidative stress factors, and may cause an increase in cIMT in the long-term (3, 6).

Mehmet Vedat Çaldır, Güner Koyuncu Çelik[1], Özgür Çiftçi[2], İbrahim Haldun Müderrisoğlu*
Department of Cardiology, Faculty of Medicine, Başkent University; Konya, Ankara*-*Turkey*
[1]Department of Neurology, Beyhekim State Hospital; Konya-*Turkey*
[2]Department of Cardiology, Koru Private Hospital; Ankara-*Turkey*

References

1. Çaldır MV, Çelik GK, Çiftçi Ö, Müderrisoğlu İH. The effect of high-dose steroid treatment used for the treatment of acute demyelinating diseases on endothelial and cardiac functions. Anatol J Cardiol 2017; 17: 392-7.
2. Zielińska KA, Van Moortel L, Opdenakker G, De Bosscher K, Van den Steen PE. Endothelial Response to Glucocorticoids in Inflammatory Diseases. Front Immunol 2016; 14: 592.
3. Iuchi T, Akaike M, Mitsui T, Ohshima Y, Shintani Y, Azuma H, et al. Glucocorticoid excess induces superoxide production in vascular endothelial cells and elicits vascular endothelial dysfunction. Circ Res 2003; 92: 81-7.
4. Naqvi TZ, Lee MS. Carotid intima-media thickness and plaque in cardiovascular risk assessment. JACC Cardiovasc Imaging 2014; 7: 1025-38.
5. Nambi V, Chambless L, He M, Folsom AR, Mosley T, Boerwinkle E, et al. Common carotid artery intima-media thickness is as good as carotid intima-media thickness of all carotid artery segments in improving prediction of coronary heart disease risk in the Atherosclerosis Risk in Communities (ARIC) study. Eur Heart J 2012; 33: 183-90.
6. Faggiano A, Pivonello R, Spiezia S, De Martino MC, Filippella M, Di Somma C, et al. Cardiovascular risk factors and common carotid artery caliber and stiffness in patients with Cushing's disease during active disease and 1 year after disease remission. J Clin Endocrinol Metab 2003; 88: 2527-33.

Address for Correspondence: Dr. Mehmet Vedat Çaldır
Başkent Üniversitesi Konya Hastanesi Kardiyoloji Bölümü
Hocacihan Mah. Saray cad. No: 1, Selçuklu, Konya-*Türkiye*
Phone: +90 332 257 06 06/2116 E-mail: vcaldir@hotmail.com

An unusual side effect of weight loss pills in a young man; acute myocardial infarction due to cayenne pepper pills

To the Editor,

As obesity becomes widespread, alternative treatments are sought, and the improper use of cayenne pepper pills increases with easy availability of these pills. The main components of cayenne pepper pills are capsaicin and its derivatives, which cause sympathetic discharge and increase energy consumption and fat burning. Since these agents can cause vasospasm, the number of the cases with cardiotoxic effects reported in the literature has increased.

A 21-year-old male patient presented at the emergency department with compressive chest pain ongoing for 1 hour. The physical examination revealed that the patient was feeling anxious, heart rate was 110 beats/minute and blood pressure was 100/60 mm Hg. Electrocardiography indicated ST segment elevations in leads II, III, aVF, and V2-V6 derivations. Echocardiography showed hypokinetic septum, anterior, and apical walls. Following treatment with acetylsalicylic acid, clopidogrel, and enoxaparin, 100 mg tissue-plasminogen activator was administered within 90 minutes. The patient had no risk factor for coronary artery disease and no exposure to emotional or physical stress. His body mass index was measured at 30 kg/m^2. The patient stated that he had taken "La Jiao Shou Shen" cayenne pepper pills that he had bought via the Internet twice a day for 2 days and that he had taken the last dose 1 hour before the onset of his chest pain. The patient was transferred to our center. Coronary angiography revealed normal coronary vessels. Laboratory analysis yielded cardiac troponin I >50 ng/mL (normal range: 0–0.01 ng/mL), creatinine kinase MB >300 U/L (normal range: 0–25 U/L). The patient's chest pain subsided and did not recur, and cardiac markers decreased. Provocative tests couldn't be carried out during angiography, but it was thought that the myocardial infarction and electrocardiographic changes were probably secondary to coronary vasospasm associated with cayenne pepper pills. Oral 120 mg daily verapamil was added to his therapy. No signs of ischemia were found in the effort myocardial perfusion scintigraphy performed 1 month later. The patient has had no problems in follow-up of 1 year.

In addition to its analgesic, anticancer, anti-inflammatory, and antioxidant effects, nowadays capsaicin is increasingly used improperly for weight loss as it increases sympathetic activation and accelerates metabolism (1, 3). Capsaicinoids lead to increased heart rate, blood pressure, and dysrhythmic discharges with increased adrenaline (3). Activation of the capsaicin receptor, also known as transient receptor potential vanilloid subfamily member 1 (TRPV1), has direct cardiovascular effects (1–3). Szolcsányi et al. (4) demonstrated that endothelin-mediated capsaicin induced dose-dependent coronary vasospasm in isolated working rat hearts. Akçay et al. (5) reported coronary vasospasm cases induced by analgesic-purpose, topical capsaicin. In patients with coronary vasospasm-mediated myocardial infarction, coronary arteries are observed as normal and these patients are usually young patients without atherosclerotic risk factors. Usually, improperly used, external agents or psychological stress is the trigger. Management and treatment are similar to those of coronary atherosclerosis (2, 5). Although arterial vasospasm can be revealed with provocative tests, these tests have high risk during the course of myocardial infarction and cannot always be performed, as in our case.

The use of improper alternatives, especially herbal therapies, for weight loss is increasing. Society should be warned about this issue.