

RESOLUTION

Of Scientific and Practical Conference "CardioTIME3.0: endothelial dysfunction and protection of target organs in patients with AH"

November 29, 2022 Kyiv, Ukraine

3300 health care specialists from Ukraine have registered to participate in Teleconference "CardioTIME3.0: endothelial dysfunction and protection of target organs in patients with AH"

The teleconference was held in a multidisciplinary format and brought together doctors of various specialties: cardiologists, neurologists, rheumatologists, general practitioners and family doctors. These doctors face daily the patients with manifestations and consequences of damaging of target organs in case of arterial hypertension (AH).

The purpose of the teleconference is to draw attention to the problem of endothelial dysfunction in the pathogenesis of AH. Instrumental methods for diagnostics of endothelial dysfunction available in real clinical practice and approaches to treatment of endothelial dysfunction for protection of target organs in case of AH were addressed.

Five reports were offered to the participants for review and discussion and they were dealing with the following issues:

- The role of endothelial dysfunction in progression of damaging of target organs in case of AH.
- The role of nitrogen oxide in pathogenesis of endothelial dysfunction.
- The methods of instrumental diagnostics of endothelial dysfunction in case of AH.
- Pathogenetic mechanisms defining damaging of target organs of AH: heart, kidneys and brain.
- Directions for treatment of endothelial dysfunction in case of AH and opportunities for better efficiency of standard treatment of AH.

During the scientific and practical conference "CardioTIME3.0: endothelial dysfunction and protection of target organs in patients with AH" the chat worked, thanks to which each participant had the opportunity to ask a question to the speakers and get the answer. There was a quiz with valuable prizes; they will be delivered to the winners within 3 weeks after the event.

The event is registered at the Testing Center of the Ministry of Health of Ukraine. Event Number: 1008860. All participants will receive a certificate, which gives the right to accrue 5 points to the Continuous Professional Development in accordance with the Order of the Ministry of Health of Ukraine dated 22.02.2019 #446. The registration number of the Continuous Professional Development provider is 1208.

Conclusions and decisions after the discussion of reports:

- 1. Arterial hypertension is the most widespread non-infectious disease of internal organs among adults; it belongs to "diseases of civilization". Almost all patients suffering with AH have discernible endothelium dysfunction. We should mention that age is one of the main factors for NO synthesis decrease. This NO synthesis decrease becomes especially evident at the age from 46 till 60. Nitrogen oxide is the key factor for successful functioning of endothelium. Its deficiency promotes development of endothelial dysfunction causing further development of arterial hypertension and damaging of target organs. On the other hand, AH by itself further worsens endothelial dysfunction due to hyperproduction of free oxygen radicals and reduced bioavailability of NO so the "vicious cycle" is formed.
- 2. The most common criterion for heart failure resulting from AH is left ventricular hypertrophy, which occurs in 92% of patients with AH. The consequences of NO deficiency are arterial wall thickening, hypertension and myocardial ischemia. Myocardial fibrosis occurs on the background of remodulation of myocardium microcirculation vessels. The extent of heart failure in patients with AH can be assessed by MRI, a promising method for diagnosing myocardial lesions and prediction, as well as by routine methods such as ECG and cardiac ultrasound.
- 3. Kidneys are another target organ of AH. As a result of the complex impact of endothelial dysfunction and AH on the kidney, chronic kidney disease (CKD) is formed. A common urine test is the easiest way to diagnose kidney damage in AH. The presence of proteinuria in patients with AH is usually indicative of development of hypertensive nephropathy (AH II stage). In the diagnosis of CKD, the estimated glomerular filtration rate, which is calculated using the formula GFR-EPI, plays an important role. It is also important to estimate the level of microalbuminuria.
- 4. AH and endothelial dysfunction play an important role in development of small vessel disease (SVD) which is one of the markers of brain damage. It is important that SVD begins to develop after 40, so it is not the disease of the aged people only. With aging along with progression of endothelial dysfunction and AH SVD causes increased risk of vascular catastrophes and vascular dementia. The main therapeutic goal in the treatment of a patient with SVD is to improve brain tissue perfusion.
- 5. So endothelial dysfunction and AH require specific treatment. Among the drugs that can indirectly improve the endothelial function are angiotensin-converting enzyme inhibitors, beta-adrenergic blocking agents of the 3rd generation, statins. Patients need L-arginine, which is an integral component of AH therapy, to directly affect the endothelium and improve its function.

For example, efficiency of β_1 - adrenergic blocking agent nebivolol depends on the level of endothelial L-arginine/nitrogen oxide (NO). The efficiency of nebivol may be insufficient in the conditions of endothelial dysfunction and NO deficit.

The addition of L-arginine also improves the results of AH therapy with a combination of enalapril + hydrochlorotiaside by recovery of NO synthesis, as confirmed by the results of a placebo-controlled study.

6. In case of AH the full course of treatment of endothelial dysfunction with L-arginine is equal to 2 months, as far as restoration of damaged endothelium significantly slows down in AH and with age, in dyslipidemia, etc. It is recommended to use a stepwise approach: 10 days of infusion course of L-arginine hydrochloride in a dose of 8.4 g / 200 ml per day with a change to oral solution of L-arginine aspartate in 2-dimensional spoons (2 g of L-arginine) twice a day up to 2 months.

While choosing a drug for the treatment of endothelial dysfunction in AH, it is important to choose the one that is a pharmaceutical drug and contains exactly the levorotatory isomer of arginine, because only L-arginine is a substrate for NO synthesis and has positive clinical effects regarding the protection of target organs in case of AH.

7. In case of SVD manifestations, it is recommended to add a ready-made form of pentoxifylline solution in combination with electrolytes and lactate to improve rheology, reduce blood viscosity and reduce inflammation. Ethylmethylhydroxypyridine succinate in the form of an injection solution, identical to the original, improves brain metabolism and blood circulation of the brain, has the effect of a «daytime» tranquilizer. The fixed combination of electrolytes, citicoline and lactate provides double modulation of nerve impulse transmission in patients with SVD on the background of AH.

For a full course of vascular recovery and synaptic plasticity in patients with SVD, it is recommended to continue the outpatient oral treatment with a levorotatory nitrogen oxide donator (L-arginine aspartate) after the infusion treatment and oral citicoline being supplied by 200 ml to achieve high SVD treatment compliance. The choice of the optimal medicinal preparation of oral citicoline taking into account the presentation (200 ml is the treatment course in one bottle), the associated diseases and the financial capabilities of the patient can positively affect the duration and quality of treatment.

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