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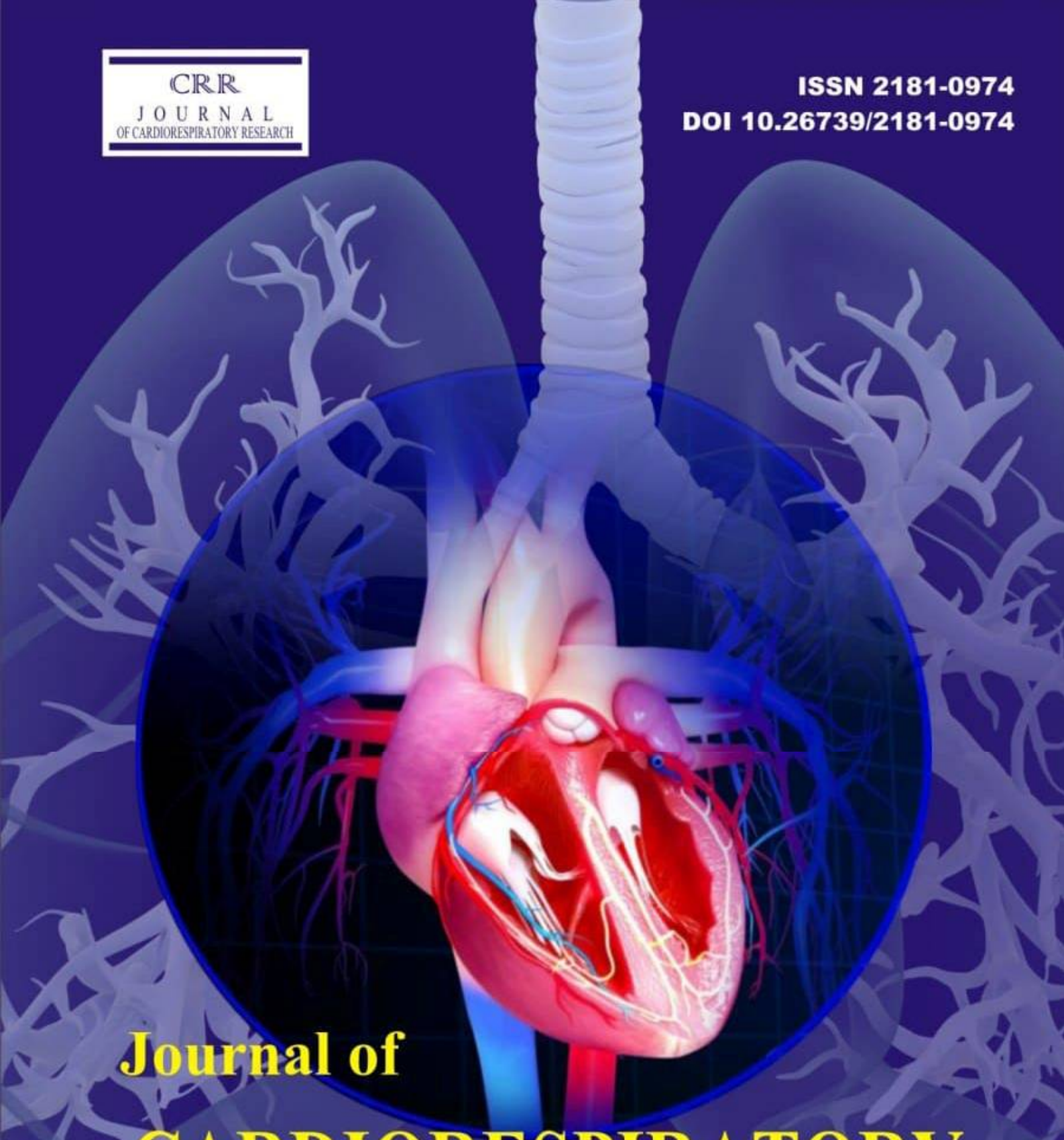

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ЖУРНАЛ КАРДИОРЕСПИРАТОРНЫХ ИССЛЕДОВАНИЙ

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# ЭФФЕКТИВНОСТЬ АМЛОДИПИНА ПРИ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ В СОЧЕТАНИИ С САХАРНЫМ ДИАБЕТОМ 2 ТИПА

**For citation:** Normatov M.B. “EFFICACY OF AMLODIPINE IN ARTERIAL HYPERTENSION COMBINED WITH TYPE 2 DIABETES MELLITUS” Journal of cardiorespiratory research. 2022, vol 3, issue 1, pp. 55-57

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**АННОТАЦИЯ**

Сочетание АГ и сахарного диабета повышает риск развития ишемической болезни сердца, инсульта, почечной недостаточности в 2-3 раза. Поэтому крайне важно рано распознавать и диагностировать как артериальную гипертензию, так и сахарный диабет, для того, чтобы вовремя назначить соответствующее лечение и остановить развитие тяжелых сосудистых осложнений. На ионном уровне инсулин оказывает воздействие на поступление кальция и натрия внутрь клетки, которые влияют на сократимость гладкомышечных волокон сосудов. В результате уменьшения чувствительности к инсулину увеличивается приток кальция в клетку и повышается напряжение гладкомышечных клеток. У таких пациентов снижается реакция коронарных артерий на физиологические раздражители (снижается способность к дилятации), что приводит к нарушению микроциркуляции.

**Ключевые слова:** Артериальная гипертензия, амлодипин, сахарный диабет 2 типа.

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## EFFICACY OF AMLODIPINE IN ARTERIAL HYPERTENSION COMBINED WITH TYPE 2 DIABETES MELLITUS

**ANNOTATION**

The combination of AH and diabetes increases the risk of coronary heart disease, stroke, kidney failure by 2-3 times. Therefore, it is extremely important to recognize and diagnose both arterial hypertension and diabetes mellitus early, to prescribe the appropriate treatment in time and stop the development of severe vascular complications. On the ionic level, insulin affects the entry of calcium and sodium into the cell, which affect the contractility of vascular smooth muscle fibers. As a result of decreased insulin sensitivity, calcium influx into the cell increases and smooth muscle cell tension increases. In such patients, the response of coronary arteries to physiological stimuli is reduced (decreased ability to dilate), which leads to impaired microcirculation.

**Keywords:** Arterial hypertension, amlodipine, type 2 diabetes mellitus

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## QANDLI DIABET 2 TIPI BILAN BIRGALIKDA ARTERIAL GIPERTENZIYA BO’LGAN BEMORLARDA AMPLODIPINNING SAMARADORLIGI

**ANNOTATSIYA**

Gipertoniya kasalligi va qandli diabetning birga kechishi yurak qon-tomir kasalliklari, buyrak yetishmovchiligi xavfini 2-3 barobar oshiradi. Shuning uchun arterial gipertenziyani ham, qandli diabetni ham erta aniqlash va tashxislash, o'z vaqtida tegishli davo muolajalarini belgilash yurak qon-tomir kasalliklar asoratlari rivojlanishini to'xtatishda juda muhimdir. Ion darajasidagi insulin kaltsiy va natriyning hujayraga kirishiga ta'sir qiladi, bu qon tomir silliq mushak tolalarining zo’riqib ishlashiga sabab bo’ladi. Insulinga sezgirlikning pasayishi natijasida hujayraga kaltsiy oqimi kuchayadi va silliq mushak hujayralarining zo’riqishi kuchayadi. Bunday bemorlarda koronar arteriyalarning fiziologik javob reaksiyasi kamayadi (kengayish qobiliyatining pasayishi), bu esa mikrosirkulyatsiyaning buzilishiga olib keladi.

**Kalit so'zlar:** Arterial gipertenziya, amlodipin, qandli diabet 2-tip

**Introduction:** Currently, there is enough drugs used to treat patients at different stages of the cardiovascular continuum. The European guidelines for the treatment of AH in 2007. (ESH and ESC) indicate that adequate hypotensive therapy leads to a significant reduction in cardiovascular risk, and cardiovascular risk decreases in proportion to BP reduction, regardless of age, gender and ethnicity. Diabetes mellitus (DM) type 2, as a comorbid condition, is common in patients with arterial hypertension (AH), significantly increasing morbidity and mortality, mainly cardiovascular. According to many studies, calcium antagonists undoubtedly improved the course and prognosis in this group of patients.

In the pathogenesis and clinic of arterial hypertension (AH), atherosclerosis, diabetes mellitus (DM) and their complications, one of the important aspects is the disorder of structure and function of the endothelium. The development of endothelial dysfunction (ED) in DM patients is initiated by chronic hyperglycemia syndrome. Dihydropyridine-type calcium antagonists (CA) in the experiment and in clinical studies improve endothelium-dependent vasodilation by increasing NO (nifedipine, amlodipine, lacidipine, feldipine).

The use of an acute pharmacologic test with antihypertensive drugs provides an opportunity to evaluate the expected hypotensive effect and predict adverse reactions associated with functional features of central and cerebral hemodynamics of patients with arterial hypertension.

The aim of the study was to develop criteria for the efficacy of amlodipine in arterial hypertension combined with type 2 diabetes mellitus based on acute drug trials and prospective patient follow-up.

**Material and methods**

The study enrolled 88 patients (21 men and 67 women) aged 30 to 75 years (mean age was 61.4±9 years). All patients had AH degree I-II against compensated or subcompensated DM type 2. The duration of diabetes ranged from 1 month to 27 years (on average, 2.6±1.4 years). AH was diagnosed simultaneously with diabetes or preceded it (mean duration of disease was 3.5±1.2 years). After an introductory period of 7-10 days, during which no systematic antihypertensive therapy was administered, patients received amlodipine at an initial daily dose of 5 mg. The efficacy of the drug was evaluated after 10 days, 4 and 12 weeks after the start of therapy. If there was no adequate response to therapy (maintenance of BP 150/90 mmHg or decrease of less than 20 mmHg for systolic BP and/or less than 10 mmHg for diastolic BP), the drug dose was increased to 7.5-10 mg/day. If necessary, indapamide at a dose of 1.5 mg/day was added to therapy after 4 weeks. The use of other antihypertensive drugs was prohibited for the duration of the study.

All patients initially and after 12 weeks underwent general clinical examination, assessment of quality of life (QOL) and psychosomatic status (SF-36, 100-mm visual analogue scale), ECG examination, 24-hour BP monitoring, echocardiography, renal ultrasound, brachial artery reactive hyperemia measurement, lipid spectrum Blood count, blood tests for AST, ALT, fasting glycaemia levels, and individual diaries were kept. The patients then signed an informed consent to participate in the study.

Once efficacy and safety criteria have been established, it is useful to assess in practice the appropriateness of the chosen medicine for the clinical case. Ideally, this is done by conducting a pharmacological trial to assess the efficacy and safety of the treatment in a simulated setting. For example, in the selection of antihypertensive therapy, pharmacological testing with amlodipine and others, as well as with their combinations in a paired stress test, allows the fastest approach to effective and safe treatment.

Peripheral arterial endothelial function was studied using reactive hyperemia tests and the drug amlodipine (2.5 mg under the tongue). To create increased blood flow and reactive hyperemia we performed "cuff test", according to its results we assessed endothelium-dependent vasodilation. Endothelium-independent dilatation was studied after sublingual administration of amlodipine after 30-40 minutes.

**Results and discussion**

Of 88 patients included in the study, 18 patients (20.4%) required an increase in dose from 5 mg to 10 mg, 29 patients (32.9%) additionally received indapamide at a dose of 1.5 mg/day. Adverse reactions were observed in 6 patients: peripheral edema in 4 patients, fever in 2 patients, palpitations in 3 patients, headache in 2 patients. Their severity in most cases was insignificant. in most cases were insignificant and did not require withdrawal of the drug. The results of our study demonstrate the antihypertensive effectiveness of amlodipine: the target BP was reached in 82% of patients, 67% of them on amlodipine monotherapy and 15% in combination with indapamide.

The normalization of BP was confirmed by the results of 24-hour BP monitoring, which revealed a statistically significant decrease in daytime and nighttime systolic and diastolic BP, as well as in the cardiovascular load (area time index). The dynamics of the decrease in BP levels was accompanied by a significant decrease in the time index and area index for both SBP and DBP during the day and night. The manifestation of biphasic rhythm of BP against the background of therapy was assessed by the difference "day-night", as a result of which the proportion of patients with normal diurnal rhythm of BP (dippers) increased from 35 to 60%, and those with insufficient reduction of BP at night (non-dippers) decreased from 65 to 40%.

Peripheral arterial endothelial function was studied using reactive hyperemia tests and the drug amlodipine (2.5 mg under the tongue). The brachial artery responsiveness to the reactive hyperemia test in both groups (with positive and negative amlodipine test) can be regarded as a manifestation of endothelial dysfunction, as a normal increase of the vessel diameter in the endothelium-dependent vasodilation phase should exceed the baseline value by more than 10%, and in the endothelium-independent dilatation phase it should be no less than 20%. An increase in brachial artery diameter (by 8.9%) in endothelium-dependent vasodilation phase and an increase in brachial artery diameter (by 18.1%) in endothelium-independent dilatation phase were observed in Group 1.

The reactive hyperemia test in Group 2 revealed an increase in brachial artery diameter (by 9.2%) in the phase of endothelium-dependent vasodilation; in the phase of endothelium-independent vasodilation an increase in brachial artery diameter (by 15.9%) was detected.

The data obtained testify to the high vasoprotective activity of amlodipine in AH patients, that is characterized by the relief of endothelial dysfunction in AH patients of I-II stages combined with type 2 DM and significant increase of endothelium-dependent vasodilation in brachial arteries during cuff test in AH patients. Individual variability of vascular response to amlodipine makes a careful dose selection with acute pharmacological test under control of BP, heart rate, with mandatory consideration of possible adverse reactions is necessary in primary prescription of the drug. The acute pharmacological test with amlodipine at the beginning of treatment in patients with AH combined with type 2 diabetes provides an opportunity to assess the expected hypotensive effect and predict adverse reactions.

However, the positive group showed significant differences after 1 month of treatment (106.8±1.3 g/m2), whereas the negative group showed significant differences after 3 months.

**Conclusions**

1. Amlodipine is an effective antihypertensive, with 67% achieving the target BP after 3 months on monotherapy, 20% requiring an increase in dose to 10 mg/day and 15% adding indapamid at 1.5 mg/day.

2. Under the effect of amlodipine therapy during 3 months in response to reactive hyperemia there was an increase of vascular diameter by 10.3% ($p<0.01$) in group I, and by 9.9% ($p<0.01$) in group II; endothelium-independent vasodilation by 21.1% ($p<0.01$) in group I, and by 21.9% ($p<0.01$) in group II. Percentage of brachial artery diameter dilatation in reactive hyperemia test was 9.2±1.3% at baseline and 9.9±0.8% after 3 months in patients with negative acute pharmacological test with amlodipine, while in patients with positive acute pharmacological test 8,9±1,2% and after 12 weeks 10,3±0,6%, endothelium-dependent vasodilation of brachial artery significantly increased in these groups, that testifies to the improvement of endothelium functional state against the background of amlodipine therapy.

3. Patients in the group with a positive test result already after 10 days had a statistically significant decrease of SBP and DBP, and after 1 month had reached target values of BP. When estimating the effect of amlodipine treatment on target organs, it was noticed that reliable differences were achieved one month after the treatment in the group with a positive test (106.8±1.3 g/m2), while in the group with a negative test - reliable differences were achieved only after after 3 months

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