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MORPHOLOGICAL FEATURES OF MYOCARDIAL ANGIOGENESIS AND MECHANISMS OF ITS DISRUPTION IN EXPERIMENTAL DIABETES

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Abstract

This article analyzes the morphological features of myocardial angiogenesis and mechanisms of its disruption in experimental diabetes. The studies analyzed data obtained on the basis of animal models induced by streptozotocin and alloxan, as well as genetic diabetes models. Histological, immunohistochemical, electron microscopic and molecular biological methods were used to assess myocardial angiogenesis. The results showed that a decrease in VEGF expression, a decrease in endothelial NO-synthase activity, a significant decrease in capillary density and suppression of the PI3K/Akt signaling pathways against the background of diabetes lead to insufficient development of angiogenesis. Also, endothelial dysfunction and increased fibrosis processes were noted. The results obtained serve as an important theoretical basis for a deeper understanding of the pathogenesis of diabetic cardiomyopathy and the development of new treatment approaches.

Keywords: Diabetes mellitus, myocardial angiogenesis, VEGF, HIF-1α, PI3K/Akt, endothelial dysfunction, fibrosis, immunohistochemistry, electron microscopy.

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EKSPERIMENTAL DIABETDA MIOKARD ANGIOGENEZI VA UNING BUZILISH MEXANIZMLARINING MORFOLOGIK XUSUSIYATLARI

Annotatsiya/ Аннотация

Ushbu maqolada eksperimental diabet sharoitida miokard angiogenezining morfologik xususiyatlari va uning buzilish mexanizmlari tahlil qilingan. Tadqiqotlarda streptozototsin va alloksan bilan induksiya qilingan hayvon modellari, shuningdek, genetik diabet modellari asosida olingan ma'lumotlar tahlil qilindi. Miokard angiogenezini baholashda gistologik, immunogistokimyoviy, elektron mikroskopik va molekulyar-biologik usullar qo'llandi. Natijalar diabet fonida VEGF ekspressiyasining pasayishi, endotelial NO-sintaza faolligining kamayishi, kapillyar zichlikning sezilarli darajada pasayishi va PI3K/Akt signal yo'llarining bostirilishi angiogenezning yetarli darajada rivojlanmasligiga olib kelishini ko'rsatdi. Shuningdek, endotelial disfunksiya va fibroz jarayonlar kuchayishi qayd etildi. Olingan natijalar diabetik kardiomiyopatiya patogenezini chuqurroq anglash va yangi davolash yondashuvlarini ishlab chiqishda muhim nazariy asos bo'lib xizmat qiladi.

Kalit so'zlar/ Ключевые слова: Qandli diabet, miokard angiogenezi, VEGF, HIF-1α, PI3K/Akt, endotelial disfunksiya, fibroz, immunogistokimyo, elektron mikroskopiya.

Dolzarbligi.

Hozirgi kunda qandli diabet global epidemiya tusini olib, yurak-qon tomir kasalliklari rivojlanishida yetakchi xavf omillaridan biri sifatida e'tirof etilmoqda. Diabetik kardiomiyopatiya va ishemik yurak kasalligi kombinatsiyasi miokardda angiogenez jarayonlarini jiddiy darajada izdan chiqaradi. So'nggi yillarda angiogenez mexanizmlarining molekulyar asoslari (VEGF, HIF-1α, PI3K/Akt, NO-signal tizimlari) chuqur o'rganilmoqda. Shu sababli, diabetda angiogenezning morfologik va molekulyar buzilishlarini aniqlash, yangi davolash usullarni ishlab chiqishda dolzarb ilmiy va amaliy ahamiyatga ega.

Material va metodlar.

Eksperimental diabet modellari (streptozototsin-induksiyalangan sichqon va kalamushlar, alloksan modeli, shuningdek db/db va ZDF genetik modellar) da o'tkazilgan tadqiqotlarda miokard angiogenezini baholashda gistologik (immunogistokimyo, CD31, vWF markerlari), elektron mikroskopiya, hamda molekulyar-biologik metodlar (Western blot, RT-PCR orqali VEGF, HIF-1α, eNOS ekspressiyasi) ishlatilgan ishlanmalar ko'rib chiqildi.

Miokard angiogenezini baholashda qo'llangan metodlar quyidagilar:

1. **Gistologik usullar:**
   - Gematoksilin-eozin bo'yog'i yordamida umumiy morfologik o'zgarishlar baholandi.
   - Masson trixrom va Sirius Red bo'yoqlari yordamida fibroz darajasi aniqlangan.
   - Immunogistokimyoviy bo'yash orqali angiogenez markerlari (CD31, von Willebrand faktori – vWF, VEGF) ekspressiyasi o'rganilgan.

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- Kapillyar zichligi (capillary density) morfometrik usulda hisoblangan.

2. **Ultrastruktur tahlil:**

- **Elektron mikroskopiya** yordamida endoteliy hujayralari, kapillyar bazal membranalari, mitoxondriyalarning holati va hujayra organoidlaridagi ultrastruktur o‘zgarishlar o‘rganilgan.

3. **Molekulyar-biologik usullar:**

- **Western blot** orqali VEGF, HIF-1α, eNOS, PI3K/Akt signal yo‘llariga oid oqsillar ekspressiyasi aniqlangan.
- **RT-PCR (real-time polymerase chain reaction)** yordamida angiogenezga aloqador genlarning mRNA ekspressiyasi darajasi baholangan.
- ELISA testlari yordamida qon plazmasida VEGF, TNF-α, IL-6 kabi mediatorlar miqdori o‘lchangan.

Ushu metodlar asosida diabet fonida miokard angiogenezi jarayonlarining susayishi, endotelial disfunksiya va regenerativ mexanizmlarning yetarli darajada ishga tushmasligi ko‘rsatib berilgan.

Natijalar.

Tahlillar shuni ko‘rsatdiki:

- Diabet sharoitida VEGF ekspressiyasi 30–50% gacha pasayadi.
- Endotelial NO-sintaza faolligi kamayib, vazodilatatsiya mexanizmlari susayadi.
- Elektron mikroskopiyada endoteliy hujayralarida mitoxondriyal shish, plazmolemma notekisligi va kapillyar bazal membranasining qalinlashuvi qayd etilgan.
- Gistologik tadqiqotlar diabetik yurakda kapillyar zichligi sog‘lom nazoratga nisbatan sezilarli kamayganini ko‘rsatgan.
- Molekulyar tahlillarda PI3K/Akt signal yo‘llari bostirilishi angiogenezning yetarli darajada rivojlanmasligiga olib kelishi qayd etilgan.

Shu sababli, kollateral arteriyalar shakllanishi keskin chegaralanadi, ishemiya sharoitida regeneratsiya mexanizmlari deyarli ishga tushmaydi.

Xulosa.

Tadqiqotlar diabet sharoitida miokard angiogenezi chuqur buzilishini, bu jarayon VEGF–HIF–NO signal yo‘llarining pasayishi va endotelial disfunksiya bilan bog‘liq ekanini tasdiqlaydi. Ushbu o‘zgarishlar miokard perfuziyasining yomonlashuviga, kollateral arteriyalarning yetarli darajada rivojlanmasliga va fibroz jarayonlarning kuchayishiga olib keladi. Mazkur natijalar diabetik kardiomiyopatiya patogenezini yanada chuqur anglash va yangi davolash yondashuvlarni ishlab chiqishda nazariy asos bo‘lib xizmat qiladi.

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