

MELATONIN IMPROVES LEFT VENTRICULAR MITOCHONDRIAL DYNAMICS IN RATS

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There is increasing awareness that efficient and regular mitochondrial dynamics improves cardiac function and affects the quality of life. Melatonin is the main pineal gland hormone which ameliorates mitochondrial dynamics in many cardiac disorders. For that purpose, we administrated melatonin to healthy rats all day long to investigate a change in left ventricle mitochondrial dynamics both in the end of the night-time and during daytime. Twenty male Wistar rats (3–4 months old) were randomly assigned into Control (C; n = 10) and Melatonin groups (MEL; 10 mg/kg melatonin, added to drinking water, n = 10). On the 5th day of the study, 5 rats from the groups were randomly selected and euthanized at 08:00 AM, the remaining 5 rats from each group were euthanized at 20:00 PM, and the samples of left ventricle (LV) tissue were harvested. Quantitative real-time PCR and Western-blot analysis demonstrated that melatonin plays a preventive role on mitochondrial fusion and mitophagy through the DRP1/FIS1 and BNIP3/NIX axis, respectively. Additionally, melatonin administration significantly reduced P21 activation, induced cell cycle arrest, P27, finally regulated caspase- depended mitochondrial apoptosis signals in a time-dependent manner. Our results suggest that melatonin may emerge as a therapeutic candidate to protect the bioenergetic dynamics of mitochondria in heart.

Key words: melatonin, heart, apoptosis, mitochondrial dynamics, mitophagy.

МЕЛАТОНІН ПОКРАЩУЄ ДИНАМІКУ МІТОХОНДРІЙ У ЛІВОМУ ШЛУНОЧКУ СЕРЦЯ ЩУРІВ

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Зростає усвідомлення того, що ефективна та регулярна динаміка мітохондрій покращує функцію серця і впливає на якість життя. Мелатонін – це основний гормон епіфізу, який оптимізує динаміку мітохондрій при багатьох порушеннях серцевої діяльності. З огляду на цей факт, ми виводили здоровим щурам мелатонін упродовж усієї доби, щоб дослідити зміни у динаміці мітохондрій лівого шлуночка серця і наприкінці ночі, і протягом дня. Двадцять самців лінії Вістар (віком 3–4 міс) були рандомізовано розподілені у групу контролю (C; n = 10) та групу мелатоніну (MEL; додавання 10 мг/кг мелатоніну до питної води, n = 10). На п'ятий день дослідження рандомізовано обрали по 5 щурів з груп та піддали їх евтаназії о 08:00, а інших тварин, по 5 щурів з обох груп, умертвили о 20:00 і взяли зразки тканини з лівого шлуночка (LV). Результати кількісної ПЦР у реальному часі і Вестерн-блот аналізу продемонстрували, що мелатонін відіграє превентивну роль у злитті мітохондрій та мітофагії по осі DRP1/FIS1 та BNIP3/NIX, відповідно. Крім того, введення мелатоніну значно знизило активацію P21, індукувало зупинку клітинного циклу, P27, зрештою, регулювало сигнали каспазо-залежного мітохондріального апоптозу залежно від часу. Наші результати показують, що мелатонін може бути терапевтичним засобом захисту біоенергетичної динаміки мітохондрій у серці.

Ключові слова: мелатонін, серце, апоптоз, динаміка мітохондрій, мітофагія.

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