Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense*)
Lat. Am. J. Pharm. **42** (7): 1460-70 (2023)

Received: April 11, 2023
Accepted: April 22, 2023

MiR-183-5p Enhances Autophagy by Targeting IRS1/PI3K-Oxidative Stress Signaling Pathway via Affecting Sepsis-Induced Cardiac Dysfunction

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SUMMARY. **This study aimed to research the specific of miR-183-5p on sepsis-induced cardiac dysfunction. The cecal ligation and puncture method (CLP) establish an animal model of sepsis. All animals were randomly divided into five groups, namely, control group, CLP+miR-183-5p mimic NC group, CLP+miR-183-5p mimic group, CLP+miR-183-5p inhibitor NC group and CLP+miR-183-5p inhibitor group. According to the results, compared with control group, CLP+miR-183-5p mimic/inhibitor NC group exhibited focal degeneration and necrosis of myocardial cells, infiltration of inflammatory cells, a dramatically increased apoptosis level of myocardial cells and cardiac ultrasonic parameters decreased evidently. In addition, with the remarkably increased protein expression of IRS1, the protein expressions of p-PI3K and p-mTOR rose in myocardium, while those of LC3II and Beclin declined. Moreover, compared with CLP+miR-183-5p mimic NC group, the myocardial cells showed a pathological improvement tendency, the apoptosis level and the protein expressions of IRS1, p-PI3K and p-mTOR in myocardium dropped markedly, LVAW; d, LVAW; s, LVPW; d and EF, and LC3II and Beclin associated with autophagy evidently rose in CLP+miR-183-5p mimic group. Compared with CLP+miR-183-5p inhibitor NC group, the indicators of CLP+miR-183-5p inhibitor group tended to deteriorate. LPS was utilized to induce myocardial cell injury in in vitro experiments. It was found that miR-183-5p mimic down-regulated the protein expressions of IRS1, p-PI3K, p-Akt and p-mTOR, and up-regulated the expressions of LC3II and Beclin, while miR-183-5p inhibitor had the opposite effect. In a word, miR-183-5p enhanced autophagy by targeting IRS1 to regulate the PI3K/Akt/mTOR signaling pathway, thereby influencing sepsis-induced cardiac dysfunction.**

RESUMEN. Este estudio tuvo como objetivo investigar la especificidad de miR-183-5p en la disfunción cardíaca inducida por sepsis. El método de ligadura y punción cecal (CLP) establece un modelo animal de sepsis. Todos los animales se dividieron al azar en cinco grupos, a saber, grupo de control, grupo NC mimético CLP+miR-183-5p, grupo mimético CLP+miR-183-5p, grupo NC inhibidor CLP+miR-183-5p y grupo NC mimético CLP+miR-183-5p. grupo inhibidor 183-5p. De acuerdo con los resultados, en comparación con el grupo de control, el grupo NC mimético/inhibidor de CLP+miR-183-5p exhibió degeneración focal y necrosis de las células miocárdicas, infiltración de células inflamatorias, un aumento drástico del nivel de apoptosis de las células miocárdicas y una disminución evidente de los parámetros ultrasónicos cardíacos. . Además, con la expresión proteica notablemente aumentada de IRS1, las expresiones proteicas de p-PI3K y p-mTOR aumentaron en el miocardio, mientras que las de LC3II y Beclin disminuyeron. Además, en comparación con el grupo mimético de NC CLP+miR-183-5p, las células miocárdicas mostraron una tendencia de mejora patológica, el nivel de apoptosis y las expresiones proteicas de IRS1, p-PI3K y p-mTOR en el miocardio se redujeron notablemente, LVAW; d, LVAW; s, LVPW; d y EF, y LC3II y Beclin

KEY WORDS: autophagy, cardiac dysfunction, IRS1, MiR-183-5p, oxidative stress PI3K/Akt/mTOR signaling pathway.

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ISSN 0326 2383 (printed ed.)
ISSN 2362-3853 (on line ed.)

asociados con la autofagia aumentaron evidentemente en el grupo mimético CLP + miR-183-5p. En comparación con el grupo NC inhibidor de CLP+miR-183-5p, los indicadores del grupo inhibidor de CLP+miR-183-5p tendieron a deteriorarse. Se utilizó LPS para inducir lesión de células miocárdicas en experimentos in vitro. Se encontró que miR-183-5p imitaba las expresiones de proteínas reguladas a la baja de IRS1, p-PI3K, p-Akt y p-mTOR, y aumentaba las expresiones de LC3II y Beclin, mientras que el inhibidor de miR-183-5p tenía el efecto contrario. En una palabra, miR-183-5p mejoró la autofagia al dirigirse a IRS1 para regular la vía de señalización PI3K/Akt/mTOR, lo que influye en la disfunción cardíaca inducida por sepsis.