Pinocembrin attenuates autonomic dysfunction and atrial fibrillation susceptibility via inhibition of the NF-κB/TNF-α pathway in a rat model of myocardial infarction

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**Introduction**: Atrial fibrillation (AF) is the most prevalent tachyarrhythmia. Previous studies have demonstrated that AF and myocardial infarction (MI) often coexist. MI is a traditional risk factor for AF; however, little is known about the signaling basis. Autonomic remodeling, atrial electrical remodeling, and atrial structural remodeling are considered to be the predominant mechanisms of AF. Inflammatory responses can be activated after MI, followed by elevated inflammatory cytokines. Clinical studies also show that post-MI patients with arrhythmias have higher circulating levels of inflammatory cytokines compared with patients with sinus rhythm, which implies that inflammation may promote the occurrence of arrhythmia. Pinocembrin, an abundant flavonoid isolated from propolis and some plants, shows various biological effects, such as anti-inflammatory, antioxidant, and antimicrobial activities. Studies have showed that pinocembrin has protective effects against cerebral ischemic injury (I/R). Pinocembrin was also found to improve cardiac function, reduce ventricular arrhythmias, and decrease the myocardial infarct area in myocardial I/R rats. However, it remains unknown whether pinocembrin has beneficial effects on atrial arrhythmias, especially in a MI model. In certain studies, pinocembrin suppresses inflammatory responses via the inhibition of the NF-κB pathway. TNF-α, primarily regulated by NF-κB, is closely related to an increased risk of atrial arrhythmias. In the present study, we hypothesized that pinocembrin could attenuate autonomic dysfunction and AF susceptibility, which is possibly associated with the suppression of the NF-κB/TNF-α signaling pathway.

**Methods**: Rats were randomly assigned to three treatment groups: (i) Sham group: Sham + saline; (ii) MI group: MI + saline; and (iii) MI + P group: MI + pinocembrin (5 mg/kg). Pinocembrin or saline was injected intravenously via the tail vein for 6 days.

**Result**: Our results demonstrated that pinocembrin treatment significantly decreased sympathetic activity, augmented parasympathetic activity, improved HRV, prolonged the atrial effective refractory period and action potential duration, shortened activation latency, lowered the frequency of AF incidence, attenuated atrial fibrosis, and decreased the concentrations of NE, TNF-α, IL-1β and IL-6 in the serum and LA. Furthermore, pinocembrin significantly increased the expression levels of Cx43 and Cav1.2 and suppressed the phosphorylation of IκBα and the activation of nuclear NF-κB subunit p65.

**Conclusion**: In conclusion, our findings indicate that pinocembrin treatment decreases autonomic remodeling, lowers atrial fibrosis, ameliorates atrial electrical remodeling, and suppresses MI-induced inflammatory responses, which suggests a potential novel strategy for atrial arrhythmias.