Adjunctive 17b-estradiol administration reduces infarct size by altered expression of canine myocardial connexin43 protein.

李聰明;張念中

Tsung-Ming Lee;Lin MS;Chou TF;Tsai CH;Chang NC

摘要

Abstract

BACKGROUND: Traffic of potentially harmful cytosolic messengers through gap junctions might cause increased injury during ischemia. The present study was to determine whether the infarct size-reducing effect of adjunctive estradiol administration prior to reperfusion is associated with an attenuated expression of connexin43 at the border of infarction in a canine model. METHODS: Experiments were performed in 48 dogs (n=16 each group), assigned to receive either vehicle (control group), 17beta-estradiol administered before coronary occlusion (early group), or 3 min before coronary reperfusion following 60-min ischemia (late group). Changes in the amount of phosphorylated connexin43 were measured by Western blot. RESULTS: Infarct size was significantly larger in the control (38+/-7% of area at risk) than in the supplemented groups (16+/-6% in the early group; 16+/-8% in the late group, P<0.0001, both). Reperfusion caused a significant elevation in free radicals as measured by lucigenin-derived chemiluminescence. The rise of free radicals was significantly inhibited in animals treated with estrogen, either early or late. The amount of phosphorylated connexin43 was reduced, as assessed by Western blot in control hearts at the border zone. These changes were significantly enhanced by estrogen administration. The magnitude of infarct size positively correlated with the magnitude of phosphorylated connexin43 expression assessed by Western blot (r=0.83, P<0.0001). Confocal microscopy confirmed the changes of junctional complexes. CONCLUSIONS: This result demonstrated that the cardioprotective effect of estrogen as an antioxidant may be associated with the reduced amount of phosphorylated myocardial connexin43 protein.

.