Age-related Differences in the Effect of Acute Hyperglycemia on Myocardial Ischemia-Reperfusion Injury

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Background

Age and acute hyperglycemia are known risk factors for myocardial ischemia-reperfusion injury and combined frequently in clinical circumstances. However, there are limited data to examine myocardial ischemia-reperfusion injury in animal models exhibiting these co-morbidities concomitantly. Thus, we investigated the effect of acute hyperglycemia on myocardial ischemia-reperfusion injury in different age-groups and possible mechanisms.

Methods

Three different age groups of male Sprague Dawley rats were included (young-aged, 3 months; middle-aged, 10-12 months; and old-aged, 20-22 months). Rats received 1.2 g/kg of dextrose (hyperglycemic group) or same volume of normal saline (normoglycemic group) according to the group. Rats were subjected to coronary artery occlusion for 45 min followed by reperfusion for 240 min (fig.1). By measuring the infarct size and ejection fraction, we estimated the susceptibility to ischemia-reperfusion injury in rat. Proteins related to apoptosis (C-PARP, Bcl-2, Bax, and cytochrome C) and autophagy (Bnip3, Beclin-1, Atg5, and LC3B-II) were evaluated by western blot assay.

Results

While reduction of ejection fraction after ischemia-reperfusion was aggravated by acute hyperglycemia in all age groups (fig.2), infarct size was increased by acute hyperglycemia in young- and middle-aged rats but not in old-aged rats (fig.3). Acute hyperglycemia increased expression of Bnip3 and Beclin-1 after ischemia-reperfusion in young- and middle-aged rats but not in old-aged rats. Also, increased expression of Bax, Cytochrome C, Atg5, and LC3B-II by acute hyperglycemia occurred only in young- or middle-aged rats (fig 4 & 5).

Conclusion

The results of current study demonstrated that acute hyperglycemia did not aggravate myocardial ischemia-reperfusion injury in old-aged rats, unlike young and middle-aged rats. This heterogeneity may be a consequence of attenuation in changes of apoptotic and autophagic signalling after ischemia-reperfusion injury under acute hyperglycemia in old-aged heart.

Fig 1. Experimental protocol. Rats were divided into 3 groups according to the age; young (Y, 3mo), middle (M, 10-12mo) and old (O, 20-24mo). Each age group of rats were randomly assigned to 4 groups; normoglycemia + sham (NG), hyperglycemia +sham (HG), normoglycemia + ischemia-reperfusion injury (NG+IR) and hyperglycemia + IR (HG+IR).

Fig 2. Changes of LV ejection fraction after ischemia-reperfusion.

Fig 3. Myocardial infarct size expressed as a percentage of LV area at risk.

Fig 4. The expression of proteins related to apoptosis. (a,b,c) C-PARP, (d,e,f) Bcl-2, (g,h,i) Bax (j,k,l) Cytochrome C.

Fig 5. The expression of proteins related to autophagy. (a,b,c) Bnip3, (d,e,f) Beclin-1, (g,h,i) Atg5, (j,k,l) LC3B-II.