Journal of Health Disparities Research and Practice

Volume 12, *Issue* 4 2018 *Article* 27

2019 STEP-UP SPECIAL ISSUE

Protective Effects of Insulin in Cardiomyocytes Against Iron-mediated Cell Death

Carina Tanaka* Takashi Matsui, M.D., Ph.D., FAHA†

*

†Department of Anatomy, Biochemistry & Physiology, John A. Burns School of Medicine, University of Hawaii

Copyright ©2018 by the authors. *Journal of Health Disparities Research and Practice* is produced by The Berkeley Electronic Press (bepress). https://digitalscholarship.unlv.edu/jhdrp

Protective Effects of Insulin in Cardiomyocytes Against Iron-mediated Cell Death*

Carina Tanaka and Takashi Matsui, M.D., Ph.D., FAHA

Abstract

When an acute myocardial infarction (MI) occurs, the heart becomes ischemic. Medical treatments such as stents have improved the recovery process after a MI, but there is still a high risk for heart failure. Due to the resulting intramyocardial hemorrhage, residual hemoglobin with excess iron compromises cardiomyocyte (CM) survival. Previous studies suggest that the magnitude of CM cell death is directly proportional to the level of adverse left ventricular (LV) remodeling. Mechanistic target of rapamycin (mTOR) is a key downstream signaling pathway that is sufficient for CM cell survival against iron and responds to insulin, a cardioprotective growth factor. However, the effect of insulin in excess iron-induced cell death in CMs is not well characterized. Using H9c2 cardiomyoblasts, originally derived from embryonic rat ventricle cells, the effects of insulin in CM cell survival against excess iron were examined. The cells were pre-treated with varying dosages of insulin before applying iron (III) citrate. Cell viability was assessed by Live/Dead Assay, in which live cells stain with calcein AM (green) and nuclei of dead cells stain with ethidium homodimer-1 (red). In comparison to the amount of cell death caused by iron alone, insulin decreased dead cell count substantially. The greatest concentration of 1μM of insulin with iron resulted in a statistical significance of $p<0.02$ (n=3-4). The results indicate that insulin has the potential to mediate iron-induced CM death. Understanding the effect of insulin as a combatant of iron-induced cell death with an intramyocardial approach would lead to better therapeutic preventions of heart failure.

KEYWORDS: Myocardial infarction; LV remodeling; Intramyocardial hemorrhage; Cardiomyocyte; mTOR; Insulin

---

*The STEP-UP HS program is supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, Grant number: R25DK78386-12.

Journal of Health Disparities Research and Practice
Volume 12, STEP-UP Special Issue, Summer 2019, pp. 42
© 2011 Center for Health Disparities Research
School of Public Health
University of Nevada, Las Vegas

Protective Effects of Insulin in Cardiomyocytes Against Iron-mediated Cell Death

Carina Tanaka
Takashi Matsui, M.D., Ph.D., FAHA, Department of Anatomy, Biochemistry & Physiology, John A. Burns School of Medicine, University of Hawaii
Coordinating Center: University of Hawai'i Manoa

ABSTRACT

When an acute myocardial infarction (MI) occurs, the heart becomes ischemic. Medical treatments such as stents have improved the recovery process after a MI, but there is still a high risk for heart failure. Due to the resulting intramyocardial hemorrhage, residual hemoglobin with excess iron compromises cardiomyocyte (CM) survival. Previous studies suggest that the magnitude of CM cell death is directly proportional to the level of adverse left ventricular (LV) remodeling. Mechanistic target of rapamycin (mTOR) is a key downstream signaling pathway that is sufficient for CM cell survival against iron and responds to insulin, a cardioprotective growth factor. However, the effect of insulin in excess iron-induced cell death in CMs is not well characterized. Using H9c2 cardiomyoblasts, originally derived from embryonic rat ventricle cells, the effects of insulin in CM cell survival against excess iron were examined. The cells were pre-treated with varying dosages of insulin before applying iron (III) citrate. Cell viability was assessed by Live/Dead Assay, in which live cells stain with calcein AM (green) and nuclei of dead cells stain with ethidium homodimer-1 (red). In comparison to the amount of cell death caused by iron alone, insulin decreased dead cell count substantially. The greatest concentration of 1μM of insulin with iron resulted in a statistical significance of $p<0.02$ ($n=3-4$). The results indicate that insulin has the potential to mediate iron-induced CM death. Understanding the effect of insulin as a combatant of iron-induced cell death with an intramyocardial approach would lead to better therapeutic preventions of heart failure.

Keywords: Myocardial infarction, LV remodeling, Intramyocardial hemorrhage, Cardiomyocyte, mTOR, Insulin

ACKNOWLEDGEMENTS

The STEP-UP HS program is supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, Grant number: R25DK78386-12.