Control/Tracking Number: A-10-417-EASD
Activity: Abstract
Current Date/Time: 3/30/2010 9:17:28 AM

Abnormal regulation of pancreatic β-cell Na,K-ATPase on glucose intolerant rats

Author Block: A.R. Costa[1,2], C.M. Antunes[1,3], J. Cruz-Morais[1,2];
[1]Chemistry, University of Évora, Évora, Portugal, [2]ICAAM - Institute of Mediterranean Agricultural and Environmental Sciences, Évora, Portugal, [3]CNC - Centre for Neurosciences and Cell Biology, Coimbra, Portugal.

Abstract:
Background and aims: Glucose (G) is the most important physiological insulin secretagogue. It is widely accepted that, in pancreatic -cell, G evoked early ionic events such as membrane depolarization and Ca^{2+} influx through voltage dependent Ca^{2+} channels triggers insulin exocytosis. However, the role of other electrogenic systems, namely ionic pumps, to these events remains essentially uninvestigated. It is known that the activity of Na,K-ATPase is modified in type 2 diabetes (T2D). The pump is responsible for maintaining Na^+ and K^+ gradients across the plasma membrane and generates a net outward current as a result of $3Na^+/2K^+$ exchange. It remains elusive whether Na,K-ATPase activity is regulated by G in pancreatic β-cell and/or this current contributes to the ionic events regulating insulin secretion.
The aim of this work was to assess G evoked regulation of Na,K-ATPase activity in intact -cells of normal and G intolerant rats.
Materials and methods: Pancreatic -cells, from normal (controls) or glucose-intolerant Wistar rats (GIR), were isolated and cultured (48h). Cell batches were pre-incubated (30min) with 2.1mM G to reach basal. Afterwards cells were challenged with [G] in the interval 0-11.1mM for 60min, for dose-dependence evaluation, or with 8.4mM G for 5-120min, for time-dependence evaluation. ATPase activity was assessed in intact cells by colorimetric quantification of Pi formed in 30min. Na,K-ATPase activity was calculated by the difference between the activities obtained in the absence and in presence the of 1mM ouabain.
Results: G evoked both time- and dose-dependent regulation of Na,K-ATPase. In β-cells from controls, G induced a bimodal regulation of Na,K-ATPase. In the absence of G, Na,K-ATPase activity was 0.056±0.015U/mg. Raising [G] to 2.1mM induced a ≈3 fold increase of Na,K-ATPase activity whereas a further increase in [G] in the interval of 5.6-11.1mM evoked a significant reduction of Na,K-ATPase activity to the levels observed in the absence of the secretagogue. Compared to 2mM G, the activity was reduced in 68%, 55% and 66% when [G] was increased to 5.6, 8.4 and 11.1mM, respectively (n=3-12). GIR β-cells exhibit an altered profile of response to the secretagogue; In the absence of G, Na,K-ATPase activity was ≈4 fold the activity observed in the controls (0.202±0.036U/mg; n=3). The pump activity remained unchanged for 2.1-5.6mM G and similar to maximal activity observed in the controls (0.188±0.035 U/mg, for 2.1mM G; n=4). A significant reduction of the pump activity in GIR β-cells was induced by 8.4mM G (0.118±0.018 U/mg).
G (8mM) induced a time-dependent inhibition of Na,K-ATPase with a biphasic profile. Pump activity decreased to a minimum value (32%) after 20min exposure to G, showing a partial recovery to 45%, 46% and 47% for 30, 60 and 120min, respectively (n=5-12). GIR β-cells showed an attenuated response to G (59% activity after 20min) without any recovery (n=5-11).
Conclusions: This work demonstrates that Na,K-ATPase is finely regulated by G in pancreatic β-cell from normal subjects. This regulation is impaired in GIR where desensitization and an attenuation of the inhibitory action of G were observed. In summary, Na,K-ATPase contribution to G-induced ionic events and insulin secretion might be relevant in T2D development.

:

Keyword (Complete): 12 Beta cell signal transduction
Study information (Complete):
No human / animal studies : True

Grant Acknowledgement (Complete):
Was grant/support received for this study?: Yes
Supported By: : This work was supported by ICAAM, CNC and a PhD grant from FEA

Status: Complete

European Association for the Study of Diabetes (EASD)
Rheindorfer Weg 3
D-40591 Düsseldorf - Germany
Tel: +49-211-758 469 0 - Fax: +49-211-758 469 29
Web: http://www.easd.org
E-mail: abstracts@easd.org

Leave OASIS Feedback!