Abstract

Regulation of glucagon secretion in porcine pancreatic islets

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Background & Aims: The potential use of porcine islets for transplantation in humans has triggered interest in understanding porcine islet physiology. However, the number of studies dedicated to this topic has remained limited, as most islet physiologists prefer to use the less time-consuming rodent model or the more clinically relevant human islet. Overall, in vitro glucose stimulation of porcine islets is known to increase islet insulin output by a deceiving 1.5 to 3-fold compared to a 12 to 16-fold increase when human or rodent islets are stimulated. This particularity of porcine islets is also confirmed in vivo by insulinemia measurements during IVGTT. An often-overlooked aspect of pig islet physiology is its alpha cell activity and regulation of its glucagon secretion. In vitro islet perifusion is a reliable method to study the dynamics of hormone secretion in response to different stimuli. We thus used this method to quantify and study glucagon secretion from pig islets.
Material & Methods: Pancreatic islets were isolated from 20 neonatal (14 to 21-day old) and 5 adult (>2 years) pigs and then cultured in appropriate media. Islet perifusion experiments were performed 8 to 10 days post-isolation for neonatal islets and 1 to 2 days post-isolation for adult islets. Insulin and glucagon were quantified in perifusion effluent fractions as well as in islet extracts by RIA.
Results: Glucagon content averaged 817 pg/IEQ in neonatal islets and decreased to 471 pg/IEQ in adult islets as confirmed by glucagon immunostaining on pancreatic sections. Increasing glucose concentration from 1 mM to 15 mM markedly inhibited glucagon secretion independently of animal age. Interestingly, the effect of high glucose was more drastic on glucagon secretion (G1/G15 ratio = 5.9) compared to its effect on insulin secretion (G15/G1 ratio = 2.2). In vivo, glucose injection during IVGTT initiated a quick (2-10 minutes) 3-fold decrease of plasmatic glucagon whereas the increase of plasmatic insulin took 20-60 minutes to become significant. Interestingly, in transgenic InsGLP1M3R pigs, the greater insulin response was compensated by higher glucagon secretion.
Conclusion & Perspectives: Porcine islets are known for their low and slow response to glucose stimulation when it comes to insulin secretion. Here, we show that glucagon secretion is markedly affected by the increase of glucose concentration both in vitro and in vivo. These results suggest that regulation of glucagon secretion significantly contributes to glucose homeostasis in pigs and probably compensates for the mild changes in insulin secretion in response to changes in glucose concentration.

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