CONCLUSIÓN

Los factores nutricionales genéticos y el estilo de vida (sedentarismo, stress) contribuyen al desarrollo de una serie de anormalidades metabólicas muy comunes en la población en general, tales como: dislipemias (incremento de los niveles de triglicéridos, y/o colesterol plasmático), intolerancia a la glucosa, Diabetes Mellitus no insulino dependiente (Tipo II), hipertensión, obesidad, etc. La morbimortalidad asociada a estas patologías representa un considerable problema socio económico. Diferentes investigaciones también han demostrado que un sostenido incremento de triglicéridos plasmáticos puede constituir un riesgo adicional de enfermedad cardiovascular independiente de otros factores de riesgo tales como: niveles plasmáticos de colesterol, LDL colesterol, hipertensión, obesidad, etc..

La presencia simultánea de dislipemias, hipertensión, resistencia insulínica e intolerancia a la glucosa en un mismo individuo constituye el llamado "Síndrome X" que al presente es un tema aún no resuelto desde el punto de vista de su patogenicidad y consecuentemente de su posible prevención y tratamiento.

El modelo experimental de hipertrigliceridemia, intolerancia a la glucosa, y resistencia insulínica acompañado de hipertensión (73,139) inducido nutricionalmente en ratas normales por una ingesta prolongada de dieta rica en sacarosa utilizado en el desarrollo de esta Tesis presenta aspectos bioquímicos-metabólicos que se asemejan a los observados en el mencionado Síndrome "X".

Utilizando el diseño experimental del corazón aislado perfundido, este modelo nos permitió abordar algunos aspectos relacionados con la captación, y destino metabólico de la glucosa, así como la movilización de lípidos en el músculo cardíaco.

En los corazones aislados perfundidos la selección del combustible energético se encuentra en parte regulada por la disponibilidad de sustratos exógenos; cuando los corazones de ratas alimentadas con dieta rica en sacarosa son perfundidos en un entorno metabólico -glucosa, lípidos (ácido palmítico)- en concentraciones semejantes a las observadas en el plasma de los animales "in vivo", nuestros resultados muestran:

1) *Menor captación y utilización de la glucosa* .

2) *Menor oxidación de glucosa* (estimada como la actividad del complejo PDH).

La alterada captación, destino y oxidación de la glucosa no se normaliza cuando los corazones son perfundidos en presencia de glucosa como única fuente de energía exógena.

En estas condiciones experimentales, la acelerada velocidad de lipólisis del pool accesible de triglicéridos endógenos y la subsecuente oxidación de ácidos grasos es la fuente energética preferencial del miocardio. La hormona insulina adicionada "in vitro", al medio de perfusión, aunque mejora la captación y oxidación de glucosa (incrementa la actividad del complejo PDH y disminuye la actividad PDH-Quinasa), no logra normalizar estos parámetros.

Estos hallazgos sugieren que al menos dos mecanismos podrían contribuir al alterado metabolismo de la glucosa en el músculo cardíaco de los animales alimentados con dieta rica en sacarosa:

a- la menor captación y utilización de glucosa (basal) y bajo el estímulo de la insulina podría ser el resultado de una disminuída capacidad de los transportadores de glucosa y/o podría reflejar un defecto en el proceso acoplado insulina-receptor en la generación de señales intracelulares

b- una incrementada disponibilidad y oxidación de lípidos (baja actividad del complejo PDH y alta actividad de la enzima PDH-Quinasa) que a su turno disminuirían la captación de la glucosa y su utilización.

Sin restar importancia al primer mecanismo mencionado que debería ser analizado en futuros trabajos, hemos comprobado que inhibiendo la entrada de los ácidos grasos a la mitocondria y su subsecuente oxidación por la adición de un inhibidor específico de la CPT-I, se normaliza la actividad del complejo enzimático PDH y sus metabolitos reguladores.

En los animales alimentados con dieta rica en sacarosa se observa una transición en función del tiempo de ingesta, desde normoglucemia e hiperinsulinemia a normoinsulinemia y anormal homeostasis de la glucosa que tal vez podría asemejarse a la progresión en el desarrollo de la Diabetes Mellitus no insulino dependiente del humano; por lo que este modelo nutricional experimental podría ser de mucha utilidad para el estudio de algunos de los mecanismos fisiopatológicos relacionados con este síndrome en general y en el tejido cardíaco en particular. Al respecto trabajos de

Gotzche(140) y Ruddy y col.(141), destacan las anormalidades observadas en el desempeño cardíaco en pacientes diabéticos descompensados, con corto tiempo de desarrollo de la enfermedad y sin causas de cardiopatía diabética conocida.

Un tema interesante por resolver en un futuro inmediato, es si los cambios bioquímicos demostrados a lo largo de esta tesis, pueden constituir manifestaciones tempranas de las anomalías mecánicas presentes en el corazón diabético.

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