行政院國家科學委員會補助專題研究計畫成果報告

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※ 糖尿病患紅血球的鉀離子及myo-inositol ※
※ 運輸之研究 ※

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計畫主持人：黃建寧

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中文摘要

糖尿病的致病原因至今尚未清楚，但似乎與長期的高血糖作用下導致病人體內細胞的正常功能遭受破壞有關。在本計劃中，我們以紅血球為模型，測量病人紅血球在長期高血糖作用下，其肌醇與牛膽質運輸的變化。我們發現糖尿病人紅血球在長期的高糖(high glucose)作用下，其肌醇的運輸顯著地遭受抑制。此一受抑制的肌醇運輸在正常人的紅血球在高糖下較不明顯。而病人紅血球肌醇運輸的抑制在低血鉀中則並無變化。另一方面，病人紅血球在長期的高糖作用下，其牛膽質運輸則受到促進。此一促進的幅度則較正常人紅血球要小。而病人紅血球牛膽質運輸的促進在低血鉀中幅度減小。此結果顯示糖尿病人紅血球上之肌醇與牛膽質的運輸可能會受到高血糖的影響。

關鍵詞：糖尿病、紅血球、肌醇

Abstract

Although pathological manifestations of diabetes mellitus have been characterized in many tissues, the mechanism of tissue damage remains unclear. In the current study, we investigate the effects of high glucose on the transport of myo-inositol and taurine in red blood cells (RBC) of diabetic patients. Treating diabetic RBC with high glucose resulted in significant inhibition of myo-inositol transport. Comparing with normal RBC, the inhibition of myo-inositol transport in diabetic RBC was significantly increased. Low extracellular potassium did not affect this inhibition of myo-inositol transport in diabetic RBC. Treating diabetic RBC with high glucose also resulted in enhanced taurine transport. Comparing with normal RBC, the enhancement of taurine transport in diabetic RBC was significantly increased. Low extracellular potassium also decreased this enhancement of taurine transport in diabetic RBC. These results suggest that the transport of myo-inositol and taurine in diabetic RBC are affected by high glucose condition.

Keywords: Diabetes mellitus, Red blood cells, myo-inositol

緣由與目的

Diabetes mellitus is a heterogeneous disorder in which normal glucose homeostasis is impaired because of varying degrees of insulin resistance and inadequate insulin secretion. Chronic hyperglycemia, which is one of the major characteristics of diabetes, could subsequently lead to various implications. Although the pathological manifestations of this disorder have been well characterized in many tissues, the mechanism of tissue damage still remains unclear.

The myo-inositol transport under hyperglycemia was intensively studied in various cell types of diabetes. The detailed mechanisms of regulating the myo-inositol transport by high glucose are unclear. Thus, in the current study, we choose to measure the transport of myo-inositol under high

glucose in diabetic cell types. This may further clarify the mechanism of myo-inositol depletion by high glucose in diabetes.

Taurine is present abundantly as a free amino acid in various cell types, including red blood cells, leukemia cells and platelets. Recent studies have suggested that taurine is involved with diabetes by affecting glucose utilization and interacting with insulin receptors. Under hyperglycemia, taurine uptake has been demonstrated to be enhanced in brain cells and in retinal pigment epithelium of streptozocin-induced diabetes rats.

In the current study, we have investigated the effect of high glucose on myo-inositol and taurine transport in normal and diabetic human red blood cells (RBC). In addition, we further examine the effect of low extracellular potassium on high glucose-induced myo-inositol and taurine transport in normal and diabetic human RBC.

結果與討論

Adding high glucose resulted in a slower myo-inositol transport in normal RBC. After 2 hours incubation, high glucose significantly inhibited the myo-inositol release in normal RBC. In normal RBC incubated with low extracellular potassium solution did not cause significantly change in myo-inositol transport comparing in control solution. These results suggest that low extracellular potassium did not affect the inhibition of myo-inositol transport under high glucose in normal RBC. We further measure the effects of low extracellular potassium on myo-inositol transport in diabetic RBC under high glucose condition. The diabetic RBC under high glucose plus low extracellular potassium conditions significant inhibited the myo-inositol transport under control plus low extracellular potassium condition. The inhibition rate of high glucose with low extracellular potassium is higher in diabetic RBC (18.67% and 27%, respectively) than in normal RBC (7.21% and 10.17%, respectively).

Although the myo-inositol transport under high glucose was suggested to be inhibited in normal and diabetic cell types, however, several laboratories reported controversial results. In the current study, we show that high glucose induces significant inhibition of myo-inositol release in normal and diabetic RBC. The scale of inhibition is not significantly different between normal and diabetic subjects, suggesting the control mechanism of myo-inositol transport may not be abnormal in diabetic RBC. Our results also show that low extracellular potassium does not significantly affect the high glucose induced myo-inositol release in normal or diabetic RBC. These results imply that in diabetic patients with complication of hypokalemia, low serum potassium may not further enhance tissue damage.

Normal RBC incubated in control solution resulted in gradually efflux of taurine in normal RBC. The addition of high glucose increased the taurine transport from normal RBC. In contrast, high glucose was showed to significantly inhibit taurine transport in diabetic RBC. In normal RBC, low extracellular potassium condition did not significantly affect the taurine transport. However, treating diabetic RBC in high glucose with low extracellular potassium also increased the taurine transport.

Recently, the role of taurine played in the development of complications in diabetes mellitus has been investigated intensively. Under high glucose condition, taurine uptake was shown to be enhanced in brain and retinal pigment epithelium of normal and diabetic rats. Our results show that under high glucose condition, taurine transport in human erythrocytes is enhanced in normal subjects but not in diabetic subjects. These observations provide evidence to confirm that the transport of taurine in cell types of diabetic patients is significantly affected by high glucose. Under low extracellular

potassium, the enhanced taurine transport in normal RBC by high glucose treatment was not observed in diabetic RBC. This may imply the effect of low extracellular potassium on diabetic RBC to increase taurine transport may be compensated by high glucose treatment. Since the uncommon occurrence of hyperglycemia complexicated with hypokalemia, the physiological significance of these observations needs to explore further.

計劃成果自評

本計劃之研究結果與計劃內容相符，而且達成預期目標。此計劃之研究結果在學術上頗具價值，具備在學術期刊上發表的價值。尤其一些令人意外的結果如病人紅血球上之肌醇運輸遭到高糖之狀態抑制等，應可加強此一計劃學術上的應用價值。

參考文獻

1. Saransaari P, Oja SS (1998) Release of endogenous glutamate, aspartate, GABA, and taurine from hippocampal slices from adult and developing mice under cell-damaging conditions. Neurochem Res 23:563-570
2. Raccah D, Coste T, Cameron NE, Dufayet D, Vague P, Hohman TC (1998) Effect of the aldose reductase inhibitor tolrestat on nerve conduction velocity Na/K ATPase activity, and polyols in red blood cells, sciatic nerve, kidney cortex, and kidney medulla of diabetic rats, J Diabet Comp 12:154-162
3. Reddy VN (1992) Study of the polyol pathway and cell permeability in human lens and retinal pigment epithelium in tissue culture. Invest Ophthalmol Vis Sci 33:2334-2339