Research Article

Cerebrospinal Fluid Glucose and Protein Glycosylation Process in Poorly Controlled Diabetes

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Abstract

Diabetes mellitus (DM) is a common disorder affecting individuals of all age groups in human beings. In this work, the author calculated for the required energy for glycated cerebrospinal albumin per unit in poor controlled DM. According to this work, the required energy is positive implying that there could be a consumption of energy from surrounding during the process. It is concluded that the required energy might have some pathophysiological effects on diabetic brain.

Keywords: Glycated protein, cerebrospinal fluid, diabetes

INTRODUCTION

Diabetes mellitus (DM) is a common disorder affecting individuals of all age groups in human beings. This disease is associated with significant morbidity and mortality and increasing costs, and its prevalent rate is statistically increasing to a significant epidemic proportion. Neurological complication in DM is a serious complication. McLean et al. noted that part of this effect might be caused by the presence of glycosylated albumin and this phenomenon might underlie some important complications related to DM.

Hyperglycemia can bring increased formation and accumulation of advanced glycation end products, and these quoted problematic molecules can play a significant role in the development of macro- and microvascular complications in blood of diabetic patients. This process can be seen in the cerebrospinal fluid as
Both glucose and albumin can be detected in cerebrospinal fluid (CSF) and the glycosylation process can be seen. In addition, glycosylated albumin transcellular transport across brain capillary endothelial cells is confirmed in a previous report. In this work, the author calculated for the required energy for glycated CSF albumin per unit in poor controlled DM and found that the required energy might have some effects on the pathophysiology process of diabetic brain complication.

**METHODS**

Pathways for glycosylation reaction

Concerning the glycosylation in formation of glycated protein, the reaction starts at a specific site between N terminal of protein and glucose. In biochemistry, the two major important pathways in formation of a glycated protein are a) formation of a specific protein-glucose Schiff base (alidimine) and b) linkage rearrangement to result in finalized ketoamine. These biochemical processes for formation of a glycated protein is not reversible. This is a general pathway for all biological systems in human beings. In this paper, the specific system is the “CSF” and studied protein is “albumin”.

**RESULTS**

The calculated molecular weight and required energy for complex formation for a glycated protein molecule in CSF is calculated and presented in Table 1.

<table>
<thead>
<tr>
<th>Step of formation</th>
<th>alidimine formation</th>
<th>ketoamine formation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bond breaking*</td>
<td>1 C-H, 1 C=O, 2 N-H</td>
<td>1 C=N, 1 C-O, 1 O-H</td>
</tr>
<tr>
<td>Bond forming**</td>
<td>1 C-H, 1 C-N, 2 O-H</td>
<td>1 C-N, 1 N-H, 1 C-H, 1 C=O</td>
</tr>
<tr>
<td>Required energy***</td>
<td>432 kCal/mol</td>
<td>-362 kCal/mol</td>
</tr>
</tbody>
</table>

*Bond breaking will get in energy.
**Bond forming will give out energy.
***required energy = getting in energy - giving out energy

**DISCUSSION**

The actual mechanisms of hyperglycemia in the pathogenesis of diabetic complications remain not clarified although have been widely mentioned in the literature. Of several theories, the advanced glycated protein development due to hyperglycemia is widely mentioned. Chronic hyperglycemia can facilitate the biochemical reaction between glucose and proteins and brings the formation of advanced glycated proteins, which lead to non reversible cross-links with many macromolecules such as collagen.
In DM, CSF glucose level is reported to be significantly higher than that of non-DM\(^{(4-5)}\). The glycosylation of the protein especially for albumin in the CSF can be expected. For an evidence to confirm this expectation, Sihlbom et al.\(^{(15)}\) recently reported the measurement of glycosylated proteins in CSF. In this work, the author calculated the required energy per unit of the glycated albumin formation reaction in CSF. According to this study, the required energy is positive implying that there could be a consumption of energy from surrounding during the process. To support this result, there are scientific evidences that advanced glycation end product formation and accumulation in brain could contribute to neuronal death\(^{(12)}\). Mastrocola et al.\(^{(9)}\) mentioned that diabetic encephalopathy, characterized by impaired cognitive functions and neurochemical and structural abnormalities, might involve direct neuronal damage caused by intracellular glucose. Mastrocola et al.\(^{(9)}\) also proposed that oxidative and nitrosative stress, by reducing the activity of complexes III, IV and V of the respiratory chain and decreasing ATP levels, which confirmed the nature of energy consumption in this work might lead to mitochondrial dysfunction. Indeed, this phenomenon is the same as that previously described in blood\(^{(17)}\).

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REFERENCES

