Post-prandial Hyperglycemia in Type 2 Diabetes Mellitus, Diabetic Cornea Neuropathy and Beta Hydroxyl Butyrate in Diabetic Ketoacidosis

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INTRODUCTION

Type 2 Diabetes Mellitus is one of metabolic disorder, which is characterized by elevation of blood glucose level as consequences of insulin resistance and insulin deficiency. By the history of illness, Diabetic patients because of various condition will experience various complications, either as acute (hypoglycemia, ketoacidosis, and Non-ketotic hyperosmolarity) or chronic complication (macro and microangiopathy, including neuropathy).

Post-prandial Hyperglycemia

Various studies has convinced the correlation between diabetes mellitus and the incidence of cardiovascular disease. This is due to beside hyperglycemia itself has been a risk factor for cardiovascular disease the diabetic patients often have other cardiovascular risk factor, such as hypertension, obesity, coagulation factor defect and dislipidemia.[1] We estimates that 75% cause of death in Diabetes Mellitus are Cardiovascular Disease, and 30% of it are caused by acute miocardium infark. Considering the so closed correlation, Adult Treatment Panel (ATP) III of National Cholesterol Education Program (NCEP) has placed diabetes mellitus as a risk factor that has equal risk level with cardiovascular disease in promoting the next cardiovascular disease.[2]

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Various studies that comparing the role of fasting hyperglycemia with post prandial, demonstrate that post prandial hyperglycemia has increased the risk of vascular complication. One year observation in diabetes Intervention Study (DIS)[3] 1996 has proven that elevation in post prandial blood glucose is a risk factor of miocardium infark incidence and vascular mortality of type 2 diabetes mellitus patient. In 1997 Haller[4] suggests that elevation of post-prandial blood glucose has very important role in initial development process of micro and macro-vascular complication.

While in DECODE[5] (diabetes epidemiology: collaborative analysis of diagnostic criteria in Europe) 1999, they demonstrate that the relative risk of cardiovascular incidence neither in fasting blood glucose ≥126mg/dl nor <110mg/dl group has no significant elevation. In contrast, the mortality risk of cardiovascular disease increase significantly in the group with blood glucose of 2 hour oral glucose tolerance test (OGTT) ≥200mg/dl or more, compared to <140mg/dl level.

Therefore the goal treatment of type 2 diabetes mellitus are to restore blood glucose level as normal as possible or resemble to normal level, that is by correcting the peak level of post prandial blood glucose. Nowdays, there are various kind of drugs to solve this problem, i.e. methylglinide group: derivate of phenil-alanine (nateglinide) and derivate of benzoic acid (repaglinide); alpha-gluco-oxydase inhibitor group; lispro insuline and aspart insulin.

Blood glucose control itself is not enough to prevent the development of cardiovascular disease. *United Kingdom Prospective Diabetes Study* (UKPDS)[6] has proven that tight blood glucose control by oral diabetics drugs compare to the group with diet planning and exercise for type 2 diabetes mellitus, has decreased the incidence of microangiopathy successfully, but it is not

satisfying to decrease the macrovascular complication. Indeed, there was decrease of acute miocardium infark incidence, but it was only 16%, while mortality rate as consequences of cardiovascular disease and stroke statistically is not significant enough. It seems that treatment for hyperglycemia itself is not enough to prevent the complication of cardiovascular disease. Gaede et al[7] demonstrates that prevention of cardiovascular complication in type 2 diabetes mellitus must be intensive and multi-factor prevention. This means that beside intensive treatment to the hyperglycemia, there should be any treatment for other risk factor such as hypertension, microalbuminuria and dyslipidemia.

Diabetic Cornea Neuropathy

Diabetic neuropathy is one of chronic complication that usualy found in diabetes mellitus, and depends on the method of observation – the incidence of diabetic neuropathy is vary from 8–62%. Various studies in Cipto Mangunkusumo Hospital demonstrates that even the neuropathy symptoms has not found yet in type 2 diabetes Mellitus patients, but on electromyography examination, the neuropathy cases was found of 82,3%.[8]

Some theories may explain the pathogenesis of diabetic neuropathy such as theory of metabolic, vascular, auto immune and deficit of nerve growth factor. The process of diabetic neuropathy initially develop from prolong hyperglycemia. As consequences there is incresing of poliol pathway activity, advance glycosilation end products (AGEs) synthesis, free radikal formation and activation of protein kinase C (PKC), which will end in decrease of vasodilatation, so that the nerve blood supply is decreased, and together with low level of intracellular myoinocitol, the diabetic neuropathy will be occured.[9]

The nerve defect as consequences of hyperglycemia also occur in optic nerve. It will cause lower corneal sensitivity and lacrimal secretion , so that the blinking reflex is decreasing. Decreasing of blinking reflex will increse the risk of corneal ulcer incidence.[10] The problem is, the most found nerve defect in diabetic patient is symetric distal sensoric polyneuropathy, so that attention of management is more focused on that defect instead of corneal neuropathy. Moreover, the amount of corneal nerve fiber is 400 times more compared to lower extremities nerve fiber, so that if there is only lower nerve conduction speed in lower extremities, the defect in cornea may not occur yet.

Considering complication risk of eye that may occur, studies about corneal neuropathy in diabetic patient especially about diagnostic procedure is extremely required, with the aim to increase alertness of that complication risk. Hence, beside standard neurologic examination start from history, comprehensive physicall examination, and peripheral neuropathy examination using Semmes-Weinstein monofilament, bio-esthesiometer, electromyography, autonomic neuropathy determination. Studies about corneal sensitivity using Cohcet-Bonet and examination of lacrimal gland secretion using Schirmer test has become very important.

Ketoacidosis Diabetic

Ketoacidosis diabetic (KAD) is one of seriously acute complication with high mortality rate. Even in experienced health centres, the mortality rate of KAD is still about 5%, and the characteristic metabolic alteration process in diabetic patient was occurred rapidly.[11] Meanwhile, last data in Ciptomangunkusumo Hospital demonstrates that every year the value of KAD patients administration was increasing. In this condition, we need high quality doctor in establishing diagnosis and giving adequate KAD treatment, so that it will suppress the mortality rate.

The ongoing KAD management is based on standard protocol, i.e. fluid resuscitation; insulin and antibiotic; and correction of acid base and electrolyte balance. During KAD treatment, monitoring was strictly done, such as hemodynamic monitoring, hydration status, blood glucose examination every one hour, electrolyte examination q 6 hour, blood gas analysis q 6 hour. Strict monitoring should be continuously done until the parameters and patient condition have recovered, then the lax monitoring will be conducted.[12]

In fact, protocol of KAD management like this has given good result. But some studies about KAD, which evaluate beta hydroxil-Butyrate or which is called as 3 HB (keton bodies except aceton and acetoacetate) as monitoring parameter, has given more information in KAD management. Aceton and acetoacetate has more volatile in nature and has lower concentration compared to 3 HB. There is different chemical properties, then using 3 HB as parameter of KAD development monitoring is expected to have better management result.[13]

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