Venue: PYRAMID 2
22nd August 2007
1515-1630 hr

Symposium 4A: Diabetes Mellitus

S4A-1. Studies on medicinal plants useful in diabetes mellitus and diseases associated with elevated lipids

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Earlier studies by our group resulted in the isolation of one active compound from fenugreek seeds, two compounds from banyan tree bark, three compounds from bitter gourd fruits and one from garlic bulbs. Fenugreek and banyan compounds were found to be useful in improving elevated glucose, HbA1c, lipids and other parameters of blood in alloxan induced diabetes mellitus of rabbits and also bringing down the elevated blood lipids in cholesterol fed rabbits. Bitter gourd compound improved only the elevated blood glucose and HbA1c but not the lipid parameters. Their mechanism of action was both pancreatic and extra pancreatic. In cholesterol fed rabbits, the garlic compound not only brought down all the elevated lipids but also increased HDL cholesterol, which is an advantage. In addition studies carried out with, Terminalia chebula and Brassica nigra indicated that the water extracts of these two plants showed good anti hyperglycemic activity in streptozotocin induced diabetes in rats. Active compounds are being isolated. In order to pursue clinical trials, we initially carried out acute, sub acute and chronic toxicity studies with the fenugreek, banyan and garlic compounds in two species of animals- one rodents (mice) and one non rodents (guinea pigs). There were no deaths and side effects even with 15 times effective dose. With fenugreek compound there were no deaths and side effects even with 3gm/kg body weight. Attempts are currently under way to initiate clinical trials to demonstrate the efficacy of these drugs in patients suffering from diabetes.

S4A-2. Global standardisation of HBA_{1C}: What can we expect?

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Glycated hemoglobin (Hb) is formed by nonenzymatic binding of glucose to Hb during red blood cell lifespan, in an irreversible and cumulative way. HbA_{1c}, the major glycated Hb species, is characterized by the binding of glucose to one or two N-terminal valine residues of chains [N-(1 dexoxyfructos-1-yl)haemoglobin beta chain, DOF-Hb]. HbA_{1c} is the gold standard of glycemic evaluation during diabetic patient monitoring. Its value reflects the variations of glycaemia during the 4 to 6 weeks before sampling. Besides, HbA_{1c} level is strongly related to long term complications in type 1 and type 2 diabetes, as demonstrated by large scale clinical studies (DCCT and UKPDS). The diversity of methods used to measure HbA_{1c}, was responsible for discrepancy of results among laboratories. Several standardization schemes have been run in various countries, such as the NGSP-DCCT (National Glycohemoglobin Standardization Progam – Diabetes Control and Complications Trial) in USA. This widely accepted system provided HbA_{1c} reference values of 4 to 6% of total Hb, and therapeutic targets of 6.5% or 7.0%, according to the type of diabetes. However, no worldwide agreement existed on the reference method. The IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) international standardization program has recently described reference method (liquid chromatography / mass spectrometry or capillary electrophoresis) and materials (-N-terminal glycated hexapeptide).

This new, more specific, reference method provided HbA_{1c} values 1 to 2% lower. Although both systems of values are strongly correlated, the implementation in clinical practice necessitates wide-scale information and education strategies. Alternative solutions such as the expression of HbA_{1c} as mmol/mol Hb, or as equivalents of mean blood glucose, are currently under consideration by clinical and biological societies.

S4A-3. Autoimmunity in diabetes mellitus

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Type 1 diabetes mellitus results from a destruction of insulin producing pancreatic islet -cells. Specific autoantibodies against pancreatic islet cell antigens are frequently detected in sera of the patients with type 1 diabetes mellitus. Islet cell antibodies (ICAs) and autoantibodies against glutamic acid decarboxylase (GAD), insulinoma-associated tyrosine phosphatase-like protein 2 (IA-2) and insulin are useful markers for autoimmune pathogenesis of type 1 diabetes mellitus. ICAs were first identified more than 30 years ago by indirect immunofluorescence on cryostatic sections of human pancreas. In 70 to 90% of the newly diagnosed patients with type 1 diabetes mellitus, islet cell autoantibodies have been reported to be positive. ICAs possibly recognize GAD, IA-2, or antigens not yet identified. The test requires high-quality human pancreas samples, provides semi-quantitative results, and requires an investigator of extensive experience. Autoantibodies against an isoenzyme of GAD with a molecular weight of 65 kDa (GAD65) are shown to be positive in 60 to 80% of the patients with type 1 diabetes mellitus. GAD65 antibodies can be detected by RIA and ELISA, with the highest sensitivity for RIA using human recombinant GAD65. Autoantibodies against IA-2 are detected in 50 to 70% of children and adolescents, and in 30 to 50% of adults with type 1 diabetes mellitus. The most sensitive detection can be achieved by RIA using human recombinant IA-2. Autoantibodies against insulin are detected in 50 to 70% of the children with type 1 diabetes mellitus, and in 20 to 30% of the older patients with type 1 diabetes mellitus. Insulin autoantibodies are detected using RIA. Once insulin therapy is started, antibodies are produced against exogenous insulin that cannot be distinguished from insulin autoantibodies. Significance of autoantibodies against islet cell antigens in prediction, differential diagnosis, and intervention strategies of type 1 diabetes mellitus will be reviewed and discussed.