

EDITORIAL

HUMAN INSULINS – UPDATE

Use of human insulins in diabetes care has come of age; these are now available in India against a price.

In this context, one needs to examine various issues that provide information regarding

- a. Physiological aspects
- b. Efficacy in diabetes control and
- c. Practical problems in application of these newer insulin's

In India, there are estimated 10-12 million diabetics and of these approximately 10% require insulin for their glycaemic control. Sales in India indicate purchase of insulin by a few thousand patients only. What happens to the remaining is anybody's guess! The possible reasons for low usage are lack of health awareness, non-availability of proper medical care or perhaps a resource constraint.

An attempt is made here to present relevant information on the merits and demerits of human insulins. Basically two preparations are now available, Semisynthetic Human Insulin (SHI) (B₃₀ alanine from pork insulin replaced by threonine) or Biosynthetic Human Insulin (BHI). The BHI version of human insulin seems to have an edge of consumer preference.

Physiological Aspects

Absorption: Following subcutaneous injection, BHI is absorbed slightly faster than the corresponding pork insulin because of its greater hydrophilic nature [1, 2].

Thus in practice, time interval between administration of BHI and food intake should be shorter than with pork insulin. Again for the same reason, BHI may perhaps cause less effective overnight control.

Immunogenicity: There is evidence for less antibody formation (IgG) with human insulin on long term basis [3]. Again antibodies as a result of use of less purified or mixed species insulin may alter insulin pharmacokinetics leading to higher

post-prandial blood glucose levels and to an increased risk for delayed hypoglycaemia [4]. The reduced propensity of antibody formation with human insulin suggests that these insulins are likely to have a more predictable pharmacokinetic profile.

Intermediary Metabolism: BHI has greater effect on ketone body metabolism and lowers the level of beta-hydroxybutyrate as compared to SHI. The glycerol concentration has been reported to be relatively higher and HDL concentration lower with BHI as compared to the SHI [5].

Efficacy of Diabetes Control

A modest reduction in dosage of BHI may be necessary in-patients currently stabilised on high doses of mixed species or less purified animal insulin. For patients receiving > 40 units daily, a 20% reduction is recommended.

Schedules of twice, thrice daily injection, or the ratio of mixtures of soluble-intermediate type need not be varied; objective being to achieve round-the-clock euglycaemia.

Much controversy has appeared on hypoglycaemia unawareness and this is considered to be related to effect on the counter-regulatory hormones. It has been suggested that pork insulin elicit larger increments of epinephrine, cortisol, glucagon and growth hormone, than BHI [6]. Recently, in a double blind multi crossover study in 50 patients, no difference in hypoglycaemic awareness between human and porcine insulin was observed (0.25 vs. 0.27). The mean percentage of hypoglycaemic episodes associated with reduced or absent awareness was 64% (SD 30%) for human insulin and 69% (SD 31%) for porcine insulin [7]. As published in this number, a multicentric clinical trial on 90 insulin requiring diabetics (71% IDDM, 39% NIDDM), comparing SHI and BHI is reported. The two insulins were indistinguishable as regards to the clinical efficacy [8].

Practical Application

The question being addressed is, as to when does one need to prescribe human insulin? It would be considered the treatment of choice for newly diagnosed diabetics, in diabetes occurring during pregnancy and in-patients being treated

intermittently with insulin. In cases of immunological insulin resistance in-patients with allergic reaction against animal insulin, human insulin is the only option.

There is no compelling reason to change patients on purified pork insulin over to human insulin if their diabetes is presently well controlled. In our country, where cost factors weigh heavily, if human insulin were to be available at the same cost as purified pork insulin, it would be worthy of preference.

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