Insulin Therapy- An Update on Insulin Analogues

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Insulin has been used to treat diabetes since the early 1920s. In the past, insulin was obtained from animal sources (i.e. pigs and cows). With the advances in recombinant DNA technology, human insulin was commercially available in the 1980s. Recently, it is possible to modify the amino acid sequence to produce insulin analogues with desirable pharmacodynamic properties. The various formulations of insulin analogues have different properties in the time from injection to peak action and duration of action.

Insulin lispro is a insulin analogue created by reversal of the amino acids at positions 28 and 29 on the human insulin B chain. Insulin aspart differs from human insulin by substitution of aspartic acid for proline in position B28. Insulin glulisine involves substitution of lysine for the asparagine at position B3 and of glutamic acid for the lysine in position B29. Treatment with these monomeric insulin analogues (lispro, aspart, and glulisine) might improve glycemic control in the postprandial state, and patients may inject these insulin analogues immediately before meals. It also may be associated with a lower risk of hypoglycemis in the post-absorbed phase.

Insulin glargine is a recombinant insulin analogue in that asparagine at position A21 is replaced by glycine and two arginines are added to the carboxyl-terminus of the B chain. Insulin detemir differs from human insulin in which a C14 fatty acid chain has been attached to amino acid B29 and the threonine in position B30 has been eliminated. Insulin glargine is completely soluble in the vial at pH4 but precipitates when neutralized in tissues on injection, producing 24 hour duration of action in most patients. Insulin detemir has been covalently bound to the insulin molecule, which may cause of more

consistent absorption after subcutaneous injection.