Review Article and Clinical Experience: Insulin Glargine Combined with Oral Agent in T2DM (Clinical Uses of Formulas: 1/3, 5-5, 2-2, 1-1, and 1-2)

Abstrak:

A map of oral agents for diabetes (OADS), either at present or in the future should be well recognized. Four of such OADS (glimepiride, glinides, gliclazide, metformin) have claimed showing atheroprotective properties beyond its hypoglycemic or anti-hypoglycemic effects. On the basis of clinical experiences and molecular mechanisms, glimepiride (GLIM) can be summarized having 3B - 3A - 9D properties: 3-fold higher rate of Binding to receptor (3B), 3-fold lower Affinity to receptor (3A), and 9-fold faster rate of Dissociation from receptor (9D). These effects (3B-3A-9D) may result in potential therapeutical benefits, including: rapid onset (due to 3-fold higher rate of Binding = 3B) and less hypoglycemic events due to lower Affinity (3A) and faster Dissociation (9D). By using therapeutic concentration (in contrast to glibenclamide), GLIM (via PI3-Kinase Pathway) increases insulin-stimulated glycogen synthesis (GS) in human muscle cells (GS effect). In addition, GLIM inhibits platelet aggregation which may in turn have a preventive effect on the development of diabetic vascular complications (more pronounced effect than gliclazide). The ideal basal insulin should ideally have the following six characteristics: 1. mimics normal pancreatic basal insulin secretion, 2. long-lasting 24-hour effect, 3. smooth, peakless profile, 4. reproducible and predictable effects, 5. reduces risk of nocturnal hypoglycemia, and 6. once-daily administration. Insulin Glargine (GLAR) is a novel peakless long-acting insulin analogue that is available for clinical use and it has a smooth profile and long, 24-hour duration of action. Thus, GLAR is an improved basal component for combination regimens (Method A, B, and C) with OADS in the treatment of type 2 diabetes mellitus (T2DM). The most frequent indication of CTOI is, patients with T2DM who failed to be treated with a maximal dose of OHA, although medical nutrition therapy (MNT) and programmed regular exercise have been perfectly adhered to. Based on clinical experiences another 6 (six) indications of CTOI are listed in this manuscript. For the clinical practice point of view, Formulas: 1/3, 5-5, 2-2, 1-1 and Formula 1-2 are provided for the CTOI in the management of patients with T2DM. GLIM can be combined with insulin therapy (f.e. with GLAR) in the treatment of T2DM. Based on the clinical experiences, such a combination can be performed by 3 Methods such as Method- A : both GLIM-GLAR administered in the Morning, Method- B : GLAR-Morning and GLIM-Evening, and Method- C : GLIM-Morning and GLAR-Evening. Conclusions: GLIM is 3 gen. sulphonylurea which shows quintuple pleiotropic cardioprotective properties beyond its hypoglycemic effect. GLAR is a human peakless insulin analogue that exhibits a 24-hours action profile (as a basal insulin) with fewer episodes of nocturnal hypoglycemia. Thus, the CTOI: GLIM and GLAR combination, may provide for cardioprotective properties. On the basis of clinical experiences, Method-A (by using a prebreakfast injection of insulin GLAR coincides with GLIM) has been proven to be most effective and well tolerated.

Keyword:
sulphonylurea, insulin glargine, glimepiride, oral agents T2DM, atheroprotective effects

Daftar Pustaka:

Bijlstra PJ, Lutterman JA, Russel FGM et al Interaction of Sulphonylurea derivatives with vascular ATP-sensitive potassium channels in humans Diabetologia 1996 -