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Review Article and Clinical Experience: New Insights Into Oral Agents in the Treatment of T2DM (The Roles of Fixed-Dose Oral Agents Combination)

Abstrak :

Recent advances in the development of strategies for the treatment of type 2 diabetes mellitus (T2DM) including a map of oral agents for diabetes (OADS) should be recognized. It has been widely reported that metformin, glimepiride, glinides, and gliclazide were 4(four) OADS which showed atheroprotective properties. Importantly, as reported by the landmark UKPDS in 1998, metformin has proven to be more than an OAD beyond its antihyperglycemia effects. Its pleiotropic effects, such as antiatherogenic properties, inhibitor of glyclation processes, and reducer of microvascular dysfunction may result in cardiovascular benefits. Moreover, 21 metabolic and endocrine effects of metformin are summarized in this paper. Type 2 diabetes mellitus (T2DM) may range from predominantly insulin resistance (IR) with relative insulin deficiency to predominantly secretory defect (impaired acute insulin response = impaired AIR or impaired first phase of insulin secretion) with insulin resistance. Thus, the dual endocrine defects are involved in T2DM. Rationally, metformin and glibenclamide address directly such dual endocrine defects (IR and impaired AIR). As reported in UKPDS-1998, both metformin and glibenclamide decreased significantly the risk of diabetic vascular complications: diabetes-related death 42%, all cause mortality 36%, all diabetes-related end point 32 %, myocardial infarction 39%, and stroke 41%. Glucovance is the ideal combination of metformin and glibenclamide formulated and engineered for optimal drug delivery. Earlier absorption of glibenclamide from a freely-soluble metformin matrix in glucovance taken with meals may help to deal with the postprandial hyperglycemia. Glucovance is therefore optimized to cope with both fasting and postprandial hyperglycemia. Many reports (2001-2003) are in favour of glucovance showing metabolic and potential cardiovascular benefits. One of them (2003) showed that one year treatment with this new drug was associated with durable improvement in AIC (-1.7%), fasting plasma glucose = FPG (-55 mg/dl), improvement in lipid profiles (Total Cholesterol, LDL-Cholesterol, Slightly HDL-Cholesterol) but TG was unaffected, and no increase in body weight. These changes imply a modest improvement in cardiovascular risk profile. Conclusions: The pathophysiology of T2DM and the dual endocrine defects of T2DM (IR and impaired AIR) should be well recognized. The first strong indication of a potentially beneficial effect of fixed combination of metformin and glibenclamide on the cardiovascular system comes from the landmark UKPDS. Such a fixed combination engineered for optimal release called glucovance, therefore, can be used as new strategy for the treatment of T2DM if no contraindications (especially for metformin) exist.

Keyword :

oral agents, type 2 diabetes mellitus, metformin, glibenclamide, UKPDS, glucovance

Daftar Pustaka :

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