"Clinical Study to evaluate aspirin usage as adjuvant therapy in diabetic patient treated with Glimepiride."

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Non-insulin dependent diabetes mellitus is associated with reduced insulin sensitivity and/or defects in insulin secretion. However, it is still not clear which defect produces the development of the clinical manifestations; insulin resistance or insulin deficiency. Insulin resistance, insulin secretion, glucose effectiveness and hepatic glucose production, all are causes for the development of NIDDM. Sulfonylurea drugs are hypoglycemic agents recommended for treatment of NIDDM patients, together with diet control. Glimepiride is a second generation sulfonylurea which has advantages over conventional sulfonylurea, including lower dosage, rapid onset, longer duration of action and lower insulin level with a strong extra pancreatic activity. Aspirin is used in NIDDM patients to prevent the development of diabetic complications through the inhibition of thromboxane A2 and the inhibition of glycated hemoglobin.

The objectives of this study is to evaluate the efficacy of Glimepiride in treating diabetic patients, and also the role of Aspirin in hyperglycemic control and the effect of Aspirin-Glimepiride as combined therapy in treating diabetic patients. Also, to evaluate the

effect of aspirin on Glimepiride disposition", in healthy human volunteers by monitoring the serum concentration of Glimepiride before and following Aspirin administration.

This study included 40 subjects classified into four groups from A to D, treated, with Glimepride 3mg once daily for group (A), Aspirin 650mg once daily for group (B), glimepride and aspirin for group (C), and control group (D). received no treatment.

The results indicated that all treatments exhibited a reduction in blood glucose in diabetic patients. However, the highest %reduction of blood glucose was found in group C who received both Glimepiride and Aspirin. This may be attributed to a combined effect of Glimepiride and Aspirin. Glimepiride acts both pancreatically and extrapancreatically through increasing cell insulin secretion, reducing the rate of hepatic glucose production, increasing insulin receptor sensitivity and/or number, and potentiating post receptor effects, while Aspirin would affect glucose homeostasis through inhibition of PGE2, activation of calcium-calmodulin complex, increasing β-cell sensitivity to glucose load, and/or inhibition of insulin clearance.

On the other hand group B who received Aspirin alone showed the least % reduction in blood glucose which may be due to the possible mechanism of action of arachidonic acid accumulation which stimulates insulin release in a time-concentration-dependent way.

The present data revealed that the investigated diabetic patients receiving Glimepiride and/or Aspirin showed a significant reduction in HbAlc% after one month treatment as a result of the significant reduction of blood glucose. Moreover, Aspirin decreases %HbAIc through acetylation of body proteins thus modifying its ligand binding properties as well as acetylation of hemoglobin which blocks glycation.

Serum insulin level was elevated as a result of treatment with Glimpiride and also with Aspirin. The highest %elevation in fasting serum insulin was found in group C who received both Glimepiride and Aspirin. This effect can be attributed to the insulinotropic effect of Glimepiride through the stimulation of Na^+-K^+ ATP pump resulting in insulin release. In addition, Aspirin, through inhibition of PGE2, leads to continuous production of arachidonic acid which would stimulate insulin release suggesting that Aspirin may enhance cell sensitivity to glucose load rather than inhibiting insulin clearance or reducing hepatic glucose production.

More detailed explanation for the effect of the combined therapy of Glimepiride and Aspirin would be clearly understood by monitoring serum Glimepiride concentration before and following Aspirin administration.

Aspirin affected some Glimepiride plasma profile such as: (1) AUC, a significant higher serum concentration of Glimepiride in early stage was observed at four hours, reduction in half-life, and increase in absorption rate of glimepiride.

The change in Glimepiride profile by the use of Aspirin could be refered to; (1) the change in gastric lumen pH by Aspirin which may affect Glimepiride absorption, (2) the possible protein binding competition between Aspirin and Glimepiride, which may be responsible for the higher Glimepiride concentration after Aspirin ingestion, and finally Glimepiride would be more pharmacologically active.

This is consistent with, and confirmed by, the clinical results obtained by this study where Aspirin-Glimepiride combined therapy showed the best glycemic control than the use of either drug alone.

Abstract

Clinical Study on Parenteral Nutrition and Critically III Patients

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Nutritional support for the critically ill patients is today an integral part of the treatment concept in intensive care medicine.

The objective of the present work was to study and evaluate the outcomes of nutritional support (PN or mixed PN+EN) taking place in five Egyptian hospitals and one Saudi Arabian hospital. Our evaluation was based on assessing different criterias as: Body weight variations before and after nutritional support, status of patients after ending the nutritional support (alive or dead), immune status suspected, complications as the result of nutritional support provided for patients, duration of nutritional support, clinical improvement and recovery by investigating different laboratory tests as: CBC, liver function tests, kidney functions tests, electrolytes, random blood glucose, T.prot and the extent of applying practical guidelines for calculating, preparing, administering and monitoring of nutritional support.

By evaluating these outcomes we can recognize the risk factors that lead to high % of sepsis, morbidity and mortality among patients and to emphasize the role of the clinical pharmacist in the preparation, calculation and administration of nutritional requirements.

A total of 62 patients included in our study, 14 patients were excluded during the work due to different uncontrollable reasons as sudden death, incomplete laboratory data or insufficient patient information. The rest 48 patients were divided into three groups. The first group involved 9 neonates, the second group involved 9 infants and children, while the third group was divided into two subgroups (A and B), each subgroup involved 15 adult patients. Patients of subgroup IIIA received small volumes of EN besides PN while patients of subgroup IIIB received PN only. This division is directed towards investigating the effect of receiving small volumes of EN beside PN on the patients outcomes (sepsis, morbidity, mortality)

our study showed that sepsis was the most relevant complication that leaded to death in our patients specially in patients in whom the PN guidelines was not achieved where the % of patients who developed sepsis was (70.3) and death was (59.6)while the % of sepsis was (9.1) and percentage % of death was (8.l) in the patients whom the guidelines of PN was achieved as creating specialized nutrition support team, implementing clinical pharmacy unit, designing PN order form, periodic monitoring of PN and applying aseptic techniques during preparing and administering of PN.

So, PN support can be dangerous if not monitored by skilled and knowledgeable health care professionals which emphasize the importance of the clinical pharmacist involvement in the nutrition support team.