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Editorial OMICS International

The Liver – A Victim at the Middle – due to Association of Oral Antidiabetics Drugs with Statin

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Editorial

The most important objectives of this presentation are to attract attention that the associations between oral anti-diabetics drugs and statin at the categories of patients with type 2 obese diabetes mellitus and dyslipidaemia, is dangerous. We know that diabetic patient's type 2 obese needs diet and oral antidiabetics drugs (biguanide or combination between biguanide and sulfonylurea) to maintain the value of glycaemia in normal range. But, in all most of cases, because they are obese persons, dyslipidemic with increased level of cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides, they need in same time administration of statin with oral anti-diabetic drugs or sometimes receive combination between statins, fibrates and oral anti-diabetics drugs.

Because the both medications present the side effects increase level of transaminases, we must to avoid the association between these two drugs. However, this combination is routinely use in the medical practice daily. This situation is valuable for a patient with normal (intact function of the liver before administration), but we must to consider that some person drinks alcohol and the association between HCV infection and type 2 diabetes mellitus is very often and for this reason, in this situation exist many risk factors, which increase the level of transaminases and damaged the liver: alcohol consumption, viral hepatitis with C virus or B virus and drugs as well. For this important reason, the combination between these categories of drugs must to be avoided in the medical practice. The association between the oral anti diabetic drugs and statin must to be avoiding at maximum in the medical practice to protect the liver. For dyslipidaemia, the patients must to follow only diet and the oral anti-diabetic drugs must to be prescribed together with hepato-protector drugs.

A review of 35 randomized clinical statin trials reported from 1966 to 2005, involving 74,102 patients, reported an absolute risk of transaminase (also referred to as aminotransferase) elevations from statin therapy of only about 4 per 1000 patients (risk difference [RD]=4.2; 95% confidence interval [CI], 1.5-6.9) [1].

A retrospective review over a 5-year period of 23,000 patients receiving statins in a large health maintenance organization found that only 17 (0.1%) patients had severe elevations of ALT (defined as >10 times the ULN). Of those 17 patients, 13 cases were associated with drug-drug interactions, and all but 1 resolved with discontinuation of the statin [2].

The issue isn't very easy, because the truth is that this pathology-combination between obesity, dyslipidaemia, diabetes mellitus type 2 obese is very common and we see frequent therapeutic schemes with oral antidiabetic drugs and hypolipemiante drugs-statin or fibrates or the both. Often, daily, we can confront with the clinical cases with this combination of diseases and honestly they needs together with diet, change their life style also the drugs: oral antidiabetics drugs: biguanide as Metformin, Meguan, Metfogama, Maninil) or combination between biguanide and sulfonylurea as Siofor, Diaprel or drugs which contain the both combination biguanide and sulfonylurea in same pill as Glibomet, for therapy of type 2 obese diabetes mellitus, to maintain in normal range the value of glycaemia.

Recently, a large prospective cohort study was performed to examine whether patients with type 2 diabetes are at an increased risk of developing acute liver failure [3]. This study suggested that diabetic patients are twice as likely to suffer hepatic failure compared to normal patients. Another study of the same prospective cohort population indicated that diabetes is associated with increased risk of hepatocellular carcinoma and chronic liver diseases [4].

First-generation sulfonylureas include tolbutamide (Orinase), tolazamide (Tolinase), and chlorpropamide (Diabinese). Chlorpropamide and tolbutamide are well recognized as causes of hepatotoxicity [5].

Second-generation sulfonylureas include glipizide (Glucotrol), glyburide (DiaBeta, Micronase, Glynase), and glimepiride (Amaryl). Drug-induced hepatotoxicity has been reported infrequently with second-generation sulfonylureas. For glimepiride, a second-generation sulfonylurea, there have been no reports of hepatotoxicity in English literature; however, hepatotoxicity has been reported in French literature [6,7].

A well-documented case of acute hepatitis caused by an idiosyncratic adverse reaction to metformin or to one of its metabolites, has also been reported [8].

In other case of an elderly woman with DM-2 who presented with symptoms of hepatotoxicity after 3 weeks of metformin treatment, metformin appeared to have caused a mixed-type (hepatocellular and cholestatic) hepatic damage [9].

In same time because they are patients with dyslipidaemia needs also together with diet low in fatty hypolipemiant drugs (statin or statin with fibrates) for become in normal range the values of cholesterol and triglycerides, to prevent the risk of ischemic heart disease and heart attack. More than that is very common that these categories of patients have liver steatosis and some physicians use the therapy with statin also for this diagnosis. For this reason, very frequent we will see therapeutic schemes with associations of oral antidiabetics drugs and statin or with fibrates in same time also for therapy of liver steatosis. So, is very common to see in the medical practice a therapeutic scheme with oral anti-diabetics drugs and statin in same time and sometime with fibrate also at the categories of patients obese, dyslipidemia and with type 2 diabetes mellitus. The

most important issue is that the both drugs pass the liver and are eliminate by the liver and are hepatotoxic.

The liver is at middle like a victim in this equation. So, the oral anti-diabetics drugs (biguanide or biguanide with sulfonylurea) present side effect on the liver with increased level of transaminases and the statin present the same side effects on the liver with increased level of transaminases. The most important issue is that the both medications pass the liver and are eliminate by the liver and for this reason, the liver is at the middle and become easy a victim in combination of these drugs developing an important side effect -the increase level of transaminases consecutive of cytolysis of the liver cells. Sometimes the level of increase transaminases could be significant and determine confusions with liver diseases as: acute viral hepatitis or chronic viral hepatitis activates but the viral markers are negative (AgHbs and Atc anti HCV negative) and they are non-alcoholic persons as well. This combination of drugs must to be avoided at maximum in the medical practice to protect the liver regarding the dangerous side effects – increase level of transaminases. Also, we must to take into account the presence of other risk factors which can increase the level of transaminases such as alcohol consumption, viral hepatitis with B or C or D virus or consume of other drugs in same time for other reasons which pass the liver as well. We must to use only diet and change of life style for therapy with dyslipidemia, when we start a therapeutic scheme with oral antidiabetic drugs for therapy of obese type 2 diabetes mellitus to protect the liver. More than that, when we start the oral antidiabetic drugs therapeutic scheme the protocol must to be with hepatoprotector drugs in same time from the first instance to protect the liver regarding the side effects of drugs.

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