

Thiazolidinediones and Salivary Gland Enlargement

M.H. Monster-Simons, J. Labadie, A.C. van Grootheest

Netherlands Pharmacovigilance Centre Lareb, 's-Hertogenbosch, The Netherlands

Introduction: Thiazolidine derivatives, i.e pioglitazone and rosiglitazone are used in type 2 diabetes mellitus treatment. Thiazolidinediones are selective agonists at the peroxisome proliferator activated receptor gamma (PPAR γ) which is present in adipose tissue, skeletal muscle and liver. Stimulation of PPAR γ reduces insulin resistance. In addition thiazolidine derivatives preserve β cell function in the pancreas. Due to PPAR γ 's wide tissue distribution thiazolidinediones do not only improve insulin resistance but also can cause a variety of adverse drug reactions related to its mechanism of action. The pharmacological effects of thiazolidinediones include weight gain due to increased adiposity, hypoglycaemia, fluid retention and as result of this, congestive heart failure.

Aim of the study: Description of 3 case reports concerning the use of thiazolidinediones and salivary gland enlargement

Methods: Spontaneous reports received by the Netherlands Pharmacovigilance Centre Lareb between July 2000 and May 2007.

Results: Lareb received 3 reports of salivary gland enlargement. *Patient A:* A 65-year old male developed a bilateral parotitis 5 weeks after he started using pioglitazone, which subsided after withdrawal of the drug. Concomitant medication used was acenocoumarol, fluticasone/salmeterol and hydrochlorothiazide. *Patient B:* A 65 year-old female who experienced bilateral parotid enlargement with accompanying sialosis 7 months after starting rosiglitazone treatment. She recovered after cessation of the drug. Concomitant medication was gliclazide, simvastatin and metformin. *Patient C:* A 73 year-old female with bilateral parotid enlargement 2 months after starting rosiglitazone. She also used calciumcarbonate, glimepiride and risedronate. Other causes could not be excluded. In 2006 Health Canada published a case series of 5 reports in which an association between parotid gland enlargement and rosiglitazone was reported. The WHO database contains 21 reports of salivary gland enlargement on rosiglitazone and 3 on pioglitazone supporting this association. In addition, sialoadenitis was reported 5 times on rosiglitazone and once on pioglitazone.

Conclusion: These case reports illustrate that administration of thiazolidinediones may cause salivary gland enlargement. PPAR γ is present in salivary gland tissue and has a role in resolution of inflammation. Activation would promote salivary mucin synthesis.

For more information about this publication, please contact info@lareb.nl