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Acute pancreatitis associated with GLP-1 Agonists (Exenatide and Liraglutide) exposure: a meta-analysis of published randomized controlled clinical trials

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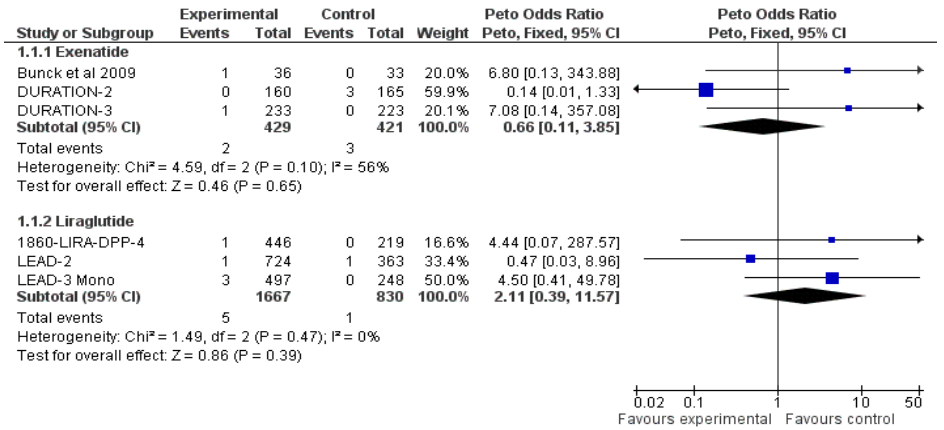
Introduction: Post-marketing surveillance – spontaneous reports - of exenatide (Byetta), a GLP-1 agonist approved for type 2 diabetes mellitus, raised the possibility for its association with acute pancreatitis (AP). Latter, in 2010, another new GLP-1 agonist, liraglutide (Victoza), was approved by the FDA. This study was aimed at identifying the risk of developing AP in patients exposed to exenatide or liraglutide, according to published data from randomized clinical trials (RCT).

Methods: A meta-analysis was carried out pooling data from studies identified on a Medline and on a Cochrane Library search. Abstracts from scientific meetings were also searched. Studies were included if they were randomized controlled clinical trials (RCT), evaluating exenatide or liraglutide in type 2 diabetes mellitus, using active or placebo as control. Peto's odds ratio (OR) was estimated. Results obtained were compared with both fixed and random-effects models.

Results: Of the 219 retrieved publications, 8 met the inclusion criteria. 5 AP were identified in the exenatide RCTs, 2 of which in exenatide-treated patients. Peto's OR for exenatide exposure and AP risk was 0.66 [0.11, 3.85]. Of the 6 AP identified for liraglutide RCT's, 5 were found in liraglutide-treated patients. Peto's OR for liraglutide exposure and AP risk was 2.11 [0.39, 11.57]. Both fixed and random-effects models didn't reveal different results.

Figure 1 - Meta-analysis of the incidence of acute pancreatitis events in type 2 diabetic patients treated with Exenatide or Liraglutide



Conclusions: These findings don't provide evidence for increased AP risk and GLP-1 agonists exposure. However further experimental and observational studies are needed to confirm such findings due to the limitations of currently available data: number of patients exposed, length of exposure and lack of effectiveness outcomes under real clinical practice conditions.

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