

Patients who develop oedema on initiating thiazolidinedione therapy have an improved glycaemic response: a MASTERMIND study

JM Dennis, AT Hattersley, M Weedon, C. Angwin, L Rodgers, ER Pearson, WE Henley, BM Shields for the MASTERMIND consortium

Background/Aim: Oedema is a common and serious side effect of thiazolidinedione therapy. A stratified medicine approach would aim to give thiazolidinediones to patients likely to have a good glycaemic response but to not develop oedema. We investigated whether oedema was associated with glycaemic response to thiazolidinedione therapy.

Methods: We studied 10,486 patients initiating a thiazolidinedione from Clinical Practice Research Datalink (CPRD), and identified medical records of oedema in the subsequent twelve months. Response was defined as change in HbA1c at twelve months and was adjusted for baseline HbA1c, baseline BMI, gender and adherence (medication possession ratio). In secondary analyses we restricted oedema classification to patients with concomitant weight gain. As a comparison the same analysis was performed in 13,089 patients initiating a sulfonylurea.

Results: The 3% of patients with recorded oedema on thiazolidinediones had a mean (CI) 3 (1.7-4.3)mmol/mol greater fall in HbA1c ($p<0.001$) compared to those without oedema. This improved response increased when oedema was associated with weight gain, with a 4.1 (1.9-6.2)mmol/mol greater HbA1c fall when weight gain >3 kg ($p<0.001$) and a 5.2 (2.1-8.4)mmol/mol greater fall when weight gain >8 kg ($p<0.001$). In sulfonylurea patients oedema was not associated with response (HbA1c fall difference 1 (-0.5-2.5)mmol/mol, $p=0.2$), even when associated with weight gain >3 kg ($p=0.19$).

Conclusion: Patients with Type 2 diabetes who develop oedema on initiating thiazolidinediones have an improved glycaemic response, and more severe oedema is associated with greater HbA1c reduction. This supports glycaemic lowering and fluid retention being mediated by a common pathway of thiazolidinedione drug action.