

Association Between Hypoglycaemia And Serious Adverse Events In Older Patients Treated With Glucose Lowering Agents: Systematic Review And Meta-analysis

Recent research suggests that hypoglycaemia may be an important risk factor for cardiovascular events, death and falls and fractures. We evaluated the risk of complications associated with hypoglycaemic episodes in older patients receiving glucose lowering agents for diabetes mellitus. We searched MEDLINE and EMBASE over a ten year span 2005 to 2015 for observational studies of the association between hypoglycaemia and adverse events in participants aged >55 years. Assessment of study validity was based on ascertainment of hypoglycaemia, adverse events and risk of confounding. We conducted random effects inverse variance meta-analyses, and assessed heterogeneity using the I^2 statistic. Meta-analysis of six studies demonstrated a significantly increased risk of cardiovascular events in patients who had hypoglycaemic episodes, pooled odds ratio of 1.88 (95% Confidence Interval [CI] 1.64, 2.16, $I^2=57%$). Three studies demonstrated a significantly increased risk of falls in patients with hypoglycaemic episodes; pooled odds ratio 1.80 (95% CI 1.50, 2.16, $I^2=32%$). Five studies demonstrated a significantly increased risk of overall mortality in association with hypoglycaemia; pooled odds ratio 2.14 (95% CI 1.67, 2.74, $I^2=87%$). In addition, there is some suggestion (based on smaller datasets) of significantly increased risk of fractures in patients with hypoglycaemia; pooled odds ratio from two studies 2.19 (95% CI 1.79, 2.68, $I^2=0%$), and a significantly increased risk of microvascular complications; pooled odds ratio from two studies 1.77 (95% CI 1.49, 2.10, $I^2=0%$). Limitations are heterogeneity in the meta-analysis, and temporal relationships. Publication bias may favour reporting of more significant findings. Our meta-analysis demonstrates significantly increased risks of adverse events in older patients with hypoglycaemic events. Glucose lowering therapy should be carefully tailored and monitored to optimize benefit: harm in older patients who are susceptible to serious adverse events.

