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Risk of anaemia with metformin use in type 2 diabetes: A MASTERMIND study

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Objective: To evaluate the association between metformin use and anaemia risk in type 2 diabetes, and the time-course for this, in randomised controlled trial (RCT) and real-world population data.

Research design and methods: Anaemia was defined as a haemoglobin measure less than 11g/dL. In RCTs (ADOPT (n=3,967), UKPDS (n=1,473)), logistic regression was used to model anaemia risk and non-linear mixed models for change in haematological parameters. In the observational GoDARTS population (n=3,485), discrete-time failure analysis was used to model the effect of cumulative metformin exposure on anaemia risk.

Results: In ADOPT, compared with sulfonylureas, the odds ratio(OR)(95%CI) for anaemia was 1.93(1.10,3.38) for metformin and 4.18(2.50,7.00) for thiazolidinediones. In UKPDS, compared with diet, the OR(95%CI) was 3.40(1.98,5.83) for metformin, 0.96(0.57,1.62) for sulfonylureas and 1.08(0.62,1.87) for insulin.

In ADOPT, haemoglobin and haematocrit dropped following metformin initiation by six months, with no further decrease after three years. In UKPDS, haemoglobin fell by three years in the metformin group compared to other treatments. At years six and nine, haemoglobin was reduced in all treatment groups, with no greater difference seen in the metformin group. In GoDARTS, each 1g/day of metformin use was associated with a 2% higher annual risk of anaemia.

Conclusions: Metformin use is associated with early risk of anaemia in individuals with type 2 diabetes, a finding consistent across two RCTs and replicated in one real-world study. The mechanism for this early fall in haemoglobin is uncertain, but given the time course is unlikely to be due to vitamin B12 deficiency alone.



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