Do statins adversely affect the HbA_{1c} of diabetic patients?

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Abstract

This paper discusses the adverse effect of statins on the HbA_{1c} levels of diabetic patients. Studies have shown that statins may slightly worsen the HbA_{1c} level. The effects vary depending on the type of statins, the dosage and the duration of therapy. However, it has been confirmed that statin use has benefits that outweigh its harms. Therefore, a diabetic patient should be given advice on the need for appropriate lifestyle changes and the importance of continuing the statins.

Assess

Mdm P is a 38-year-old Malay woman who has been diabetic for the past 2 years. She is taking metformin 500 mg BD and simvastatin 40 mg ON. Metformin was started 1 year ago, whilst simvastatin was started 6 months ago. Her previous HbA_{1c} values were all below 6.5%. However, her latest HbA_{1c} is 6.9% and fasting blood glucose is 6.5 mmol/L. She has not changed her dietary habit in the past 3 months.

Ask

Do statins adversely affect the HbA_{1c} level of diabetes patients?

In PICO format

Population	Adult with well-controlled diabetes and dyslipidaemia
Intervention	Statins
Control	No treatment
Outcome	Increased HbA_{1c}

Acquire

To answer the above clinical question, we searched PubMed using a combination of the following Medical Subject Headings terms: diabetes mellitus, type 2; hydroxymethylglutaryl-CoA reductase inhibitors; haemoglobin A, glycosylated and meta-analysis. We also supplemented the above search by replacing 'meta-analysis' with 'randomised controlled trials' to look for clinical trials published between 2011 and 2015.

Discussion

Statins use is associated with a small but statistically significant increase risk in new-onset diabetes.[1] This observation has raised concerns whether this adverse effect of statins extends to the worsening of glycaemic control among patients with pre-existing diabetes mellitus.

We found two meta-analyses that address our evidence-based medicine question:

1. Erqou et al[2] conducted a meta-analysis of nine randomised controlled trials (number of study participants = 9696, statins = 4980, control = 4716). With an average follow-up of 3.6 years, the mean HbA_{1c} was statistically significantly higher in study participants randomised to statins vs control groups: 0.12% (95% confidence interval [CI]: 0.04–0.20) or 1.3 mmol/mol (95% CI: 0.4–2.2).
2. Zhou et al[3] conducted a meta-analysis of 26 randomised controlled trials (number of study participants = 3232). They found that statins did not have statistically significant effect on HbA_{1c} (weight mean difference 0.04%, 95% CI: –0.08–0.16). Notably, a detrimental effect was significant in atorvastatin therapy whereas the ameliorative effect was seen in simvastatin therapy.

The above two meta-analyses came to differing conclusions primarily because they included different sets of randomised controlled trials. Of note, Zhou et al[3] failed to include the American Society for Parenteral and Enteral Nutrition (ASPEN) study (n = 2410) in which the atorvastatin group had worse HbA_{1c} at follow-up (0.1 mmol/L).

Further, we found two randomised controlled trials published between 2012 and 2015:

1. Ogawa et al[4] randomised 1049 diabetes patients to receive rosuvastatin 5 mg or atorvastatin 10 mg. There were no significant differences between the two groups in the effect on HbA_{1c} at 12 months, but both groups showed an increase of HbA_{1c} of between 0.11% and 0.12% as compared to the HbA_{1c} recorded prior to the research. However, this was not statistically significant.
2. Simsek et al[5] randomised 263 diabetes patients to rosuvastatin 40 mg or atorvastatin 80 mg. At 24 weeks, both groups showed a statistically significant increase in HbA_{1c} (average of 0.3% or 4 mmol/mol).

Answer

The above-cited studies showed that statins most likely lead to a slight worsening of HbA_{1c}, although the magnitude of effect may vary depending on the type of statins, the dosage as well as duration of therapy. There is no prospective data showing that this detrimental effect of statins would result in an increase in diabetes-related end-organ damage or cardiovascular events. However, it has been confirmed that statins use can reduce the the number of major cardiovascular and and cerebrovascular events in diabetes patients without pre-existing cardiovascular diseases (0.79, 95% CI: 0.66–0.95).[6] It is our view that statins use has benefits that outweigh its harms.

Apply

In the case of Mdm P, repeated HbA_{1c} testing is needed to verify the adverse change. Thereafter, appropriate lifestyle changes need to be re-emphasised. She will be counselled regarding the importance of continuing the statins to prevent cardiovascular and cerebrovascular events.

Conflict of interest: None

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