TITLE: Statin Therapy in Adults with Diabetes: Clinical Efficacy

DATE: 13 September 2011

RESEARCH QUESTION(S)

1. What is the clinical efficacy of statin therapy versus placebo or standard care in adults with diabetes and without a history of cardiovascular diseases?

2. What is the clinical efficacy of statin therapy versus placebo or standard care in adults with diabetes and with a history of cardiovascular diseases?

KEY MESSAGE

Evidence suggests that statin therapy is an efficient therapy when compared with placebo or standard of care in adults with diabetes with or without a history of cardiovascular diseases.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2011, Issue 8), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and abbreviated list of major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials. The search was also limited to English language documents published between Jan 1, 2006 and Sep 1, 2011. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.
RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

One systematic review, one meta-analysis, and sixteen randomized controlled trials were identified regarding the clinical efficacy of statin therapy versus placebo or standard of care in adults with diabetes with or without a history of cardiovascular disease. Additional references of potential interest can be found in the appendix.

OVERALL SUMMARY OF FINDINGS

One systematic review\(^1\) found that statin therapy reduced mortality and morbidity in those at higher risk of coronary heart disease (CHD) events such as patients with Type 2 diabetes mellitus. Similarly, a meta-analysis\(^2\) found a reduction in vascular mortality in diabetes patients when their LDL cholesterol was lowered with statin therapy.

Sixteen randomized controlled trials\(^3-18\) studying the clinical efficacy of statin therapy versus placebo or standard of care in adults with diabetes with or without a history of cardiovascular disease are summarized in Table 1.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study population, length and size</th>
<th>Intervention and comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gumprecht et al.(^3)</td>
<td>Type 2 diabetes and combined dyslipidemia 12 weeks N=418</td>
<td>Atorvastatin Pitavastatin</td>
<td>- No significantly different reduction in LDL-C between statins Pitavastatin favourable effect on glycemic status</td>
</tr>
<tr>
<td>Koksal et al.(^4)</td>
<td>Diabetes with hyperlipidemia 3 months N=62</td>
<td>Atorvastatin Rosuvastatin</td>
<td>- No significantly different reduction in LDL-C between statins Both statins reduced increased oxidative stress</td>
</tr>
<tr>
<td>Su et al.(^5)</td>
<td>Type 2 diabetes 12 weeks N=151</td>
<td>Atorvastatin Simvastatin</td>
<td>- Atorvastatin reduced oxidative stress more effectively than simvastatin</td>
</tr>
<tr>
<td>Adsule et al.(^6)</td>
<td>Type 2 diabetes with dyslipidemia 12 weeks N=60</td>
<td>Atorvastatin Rosuvastatin Simvastatin</td>
<td>- Rosuvastatin more efficacious than simvastatin and comparable to atorvastatin</td>
</tr>
</tbody>
</table>
### Table 1: Randomized controlled trials of statin therapy versus placebo or standard of care in adults with diabetes with or without a history of cardiovascular disease

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study population, length and size</th>
<th>Intervention and comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ukinc et al.⁷</td>
<td>Type 2 diabetes One year N=50</td>
<td>Atorvastatin Simvastatin</td>
<td>- Both treatments effective at controlling hypercholesterolemia</td>
</tr>
<tr>
<td>Betteridge et al.⁸</td>
<td>Type 2 diabetes N=509</td>
<td>Atorvastatin Rosuvastatin</td>
<td>- Both treatments effectively decreased CRP levels</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Rosuvastatin decreases LDL-C significantly more than atorvastatin</td>
</tr>
<tr>
<td>Shepherd et al.⁹</td>
<td>Diabetes patients with CHD 4.9 years median follow-up N=1501</td>
<td>Atorvastatin 80 mg/day Atorvastatin 10 mg/day</td>
<td>- Intensive therapy with atorvastatin significantly reduced rate of major cardiovascular events compared with regular atorvastatin therapy</td>
</tr>
<tr>
<td><strong>Statin versus placebo</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adel et al.¹⁰</td>
<td>Type 2 diabetes with normal serum cholesterol 4 weeks N=60</td>
<td>Atorvastatin Placebo</td>
<td>- Atorvastatin improves endothelial function compared with placebo</td>
</tr>
<tr>
<td>Heljic et al.¹¹</td>
<td>Type 2 diabetes without pre-existing CHD One year N=95</td>
<td>Simvastatin Placebo</td>
<td>- Simvastatin reduced the risk of CHD</td>
</tr>
<tr>
<td>Holmann et al.¹²</td>
<td>Type 2 diabetes without known CVD 4 months N=800</td>
<td>Atorvastatin Omega-3-acid ethyl esters 90 Placebo</td>
<td>- Atorvastatin significantly decreased LDL-C and 10-year CVD risks; compared with placebo</td>
</tr>
<tr>
<td>Verges et al.¹³</td>
<td>Type 2 diabetes 6 weeks N=8</td>
<td>Rosuvastatin Placebo</td>
<td>- Rosuvastatin significantly reduced plasma LDL-C, triglycerides, and HDL-TG</td>
</tr>
<tr>
<td>Hitman et al.¹⁴</td>
<td>Type 2 diabetes without known macrovascular disease 3.9 years median follow-up</td>
<td>Atorvastatin Placebo</td>
<td>- Atorvastatin reduced incidence of non-hemorrhagic strokes by 50% compared to placebo</td>
</tr>
</tbody>
</table>
Table 1: Randomized controlled trials of statin therapy versus placebo or standard of care in adults with diabetes with or without a history of cardiovascular disease

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study population, length and size</th>
<th>Intervention and comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knopp et al.</td>
<td>Type 2 diabetes 4 years N=2410</td>
<td>Atorvastatin Placebo</td>
<td>Atorvastatin did not significantly reduce cardiovascular events compared with placebo</td>
</tr>
<tr>
<td>Miller et al.</td>
<td>Type 2 diabetes and low HDL-C 6 weeks N=151</td>
<td>Simvastatin 80 mg/day Simvastatin 40 mg/day Placebo</td>
<td>Simvastatin effectively reduced elevated levels of TG-rich lipoproteins</td>
</tr>
</tbody>
</table>

Statin versus other treatments

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study population, length and size</th>
<th>Intervention and comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kato et al.</td>
<td>Diabetes patients with metabolic syndrome 24 weeks</td>
<td>Pitavastatin Colestimide</td>
<td>Pitavastatin reduced LDL-C levels more effectively than colestimide</td>
</tr>
<tr>
<td>Kojima et al.</td>
<td>Diabetic patients with normal cholesterol and CHD 2 years N=1016</td>
<td>Statin Non-statin</td>
<td>Statin therapy improved prognosis in diabetic patients</td>
</tr>
</tbody>
</table>

CHD=coronary heart disease; CRP=C-reactive protein; CVD=cardiovascular disease; HDL-C=high density lipoprotein cholesterol; HDL-TG=high density lipoprotein triglycerides; LDL-C=low density lipoprotein cholesterol

Statin therapy appears to be an effective therapy for reducing LDL-C levels and the risk of cardiovascular diseases in patients with Type 2 diabetes with or without a history of cardiovascular disease when compared to placebo. Different statins may vary slightly in efficacy. Overall, statin therapy seems to reduce the elevated risk for cardiovascular disease that accompanies diabetic patients.
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses


Randomized Controlled Trials

Statin therapy versus statin therapy


8. Betteridge DJ, Gibson JM, Sager PT. Comparison of effectiveness of rosvuastatin versus atorvastatin on the achievement of combined C-reactive protein (<2 mg/L) and low-density lipoprotein cholesterol (< 70 mg/dl) targets in patients with type 2 diabetes mellitus (from the ANDROMEDA study). Am J Cardiol. 2007 Oct 15;100(8):1245-8. PubMed: PM17920365


**Statin versus placebo**


Statin versus other treatments


PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca
APPENDIX – FURTHER INFORMATION:

Review articles

   PubMed: PM20171948

   PubMed: PM20544054

   PubMed: PM19322080

   PubMed: PM18316949

   PubMed: PM18316955

   PubMed: PM18669808

   PubMed: PM17910520

   PubMed: PM17646562

   PubMed: PM16755211

Additional references

Randomized controlled trials (surrogate outcome)

Post-hoc analysis


Other articles
