HMG CoA reductase inhibitors and the risk of colorectal cancer

This article discusses non-FDA approved uses of simvastatin and pravastatin Presenter: J. N. Poynter
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Background
In vitro data have shown that 3-hydroxy-2-methylglutaryl coenzyme A (HMG CoA) reductase is overexpressed in colorectal cancer (CRC) cell lines and statins induce apoptosis these cell lines. Additionally, statins reduce tumor formation in animal models. Statins have been noted to be associated with a reduced risk of colorectal cancer (CRC) in a randomized clinical trial of patients with myocardial infarction. This study investigated the association between HMG CoA reductase inhibitors and CRC in a population-based case-control study.

Materials and Methods

- Molecular Epidemiology of Colorectal Cancer Study (MECC)
- Cases and controls are matched for age, gender, Jewish vs non-Jewish ethnicity
- CRC diagnosis was confirmed by standardized pathology review
- Subjects were interviewed for personal and family history of cancer, screening practices, other medical conditions, medication use, physical activity, and nutritional data including a food frequency questionnaire
- Use of HMG CoA reductase inhibitors was measured by self report with a minimum duration of five years of use
- Use of statins was confirmed by prescription records
- Statistical analysis was performed using odds ratio to estimate RR and logistic regression with adjustment for other factors

Results

- 1814 CRC patients (median age 69.9, 1248 Jewish, 566 non-Jewish, 383 with high cholesterol) and 1959 controls (median age 71.1, 1248 Jewish, 711 non-Jewish, 515 with high cholesterol)
- 106 cases and 222 controls reported >5 years statin use; 1708 cases and 1737 controls did not report statin use (Odds Ratio 0.49; 95% CI 0.38-0.62). The use of statins was confirmed in 96.5% of patients
- There was a strong association between statin use and decreased risk of CRC ( OR 0.54; p<0.001) and this effect was not modified by the use of ASA or NSAIDs
● Among statin users 44% used pravastatin and 52% simvastatin
● There was no significant association between use of benzafibrate and risk of CRC
● The protective effect of statins was not explained by other factors such as a general cholesterol lowering property, use of different statins, use of ASA or NSAIDs, ethnicity, family history, physical activity, diet or high cholesterol

Author’s Conclusions

● HMG CoA reductase inhibitors are associated with a 46% reduction in the risk of colorectal cancer
● This protective effect is specific to this class of lipid-lowering agents
● Further investigation in chemoprevention and therapeutic clinical trials are needed

Clinical/Scientific Implications
This is a large retrospective case-control study investigating the association between HMG CoA reductase inhibitors and the risk of developing CRC. Statins are associated with a reduction in the risk of colorectal cancer based on this study. However, this is indeed a retrospective, non-randomized study with limited information on the dose and duration of statin use. Although promising, these data are still limited and need confirmation in prospective randomized trials. It is not recommended statins be used as a preventive for CRC at this time.