Efficacy and safety of celecoxib on the incidence of recurrent colorectal adenomas: a systematic review and meta-analysis

ABSTRACT

Background: Celecoxib has previously been shown to be effective in reducing recurrent colorectal adenomas, but its long-term effects are unknown. In addition, safety issues are of major concern. Therefore, we examined the efficacy and safety of celecoxib as a chemopreventive agent along with its posttreatment effect. Methods: We performed a meta-analysis based on a systematic review of randomized controlled trials (RCTs) comparing celecoxib at various doses (400 mg once daily, 200 mg twice daily, and 400 mg twice daily) vs placebo in persons with history of colorectal adenomas. Several databases were searched from inception up to April 2018. Long-term follow-ups of RCTs were also included to evaluate posttreatment effect. Primary outcome was the incidence of recurrent colorectal adenomas. Various safety outcomes were evaluated, especially cardiovascular (CV) events. Risk-benefit integrated analyses were also performed. Results: A total of three RCTs (4,420 patients) and three post-trial studies (2,159 patients) were included in the analysis. Use of celecoxib at any dose for 1-3 years significantly reduced the incidence of recurrent advanced adenomas (risk ratio, 0.42 [95% CI, 0.34-0.53]) and any adenomas (0.67 [95% CI, 0.62-0.72]) compared with placebo. Subgroup analysis on different dosing suggested a greater effect with 400 mg twice daily. However, celecoxib 400 mg twice daily significantly increased the risk of serious adverse (1.2 [95% CI, 1.0-1.5]) and CV events (3.42 [95% CI, 1.56-7.46]), while celecoxib at 400 mg/day, especially with once daily dosing, did not increase CV risk (1.01 [95% CI, 0.70-1.46]). Analysis of post-trial studies indicated that the treatment effect disappeared (1.15 [95% CI, 0.88-1.49]) after discontinuing celecoxib for >2 years. Conclusion: Celecoxib 400 mg once daily dosing could potentially be considered as a viable chemopreventive option in patients with high risk of adenomas but with low CV risk. Long-term trials on celecoxib at a dose of ≤400 mg either once or twice daily are warranted.

Keyword: Celecoxib; Chemoprevention; Colorectal adenomas; Colorectal cancer; Meta-analysis; Randomized controlled trials; Risk–benefit integrated analyses