

How safe is acetaminophen use in patients treated with vitamin K antagonists? A systematic review and meta-analysis

Thromb Res, Volume 135, issue 1, p58-61, january 01, 2015

Authors

Daniel Caldeira, João Costa, Márcio Barra, Fausto J. Pinto, Joaquim J. Ferreira

Abstract

Introduction

Acetaminophen is a commonly prescribed and over-the-counter used drug, and is considered to be the preferred treatment choice for anticoagulated patients requiring analgesic drug therapy. However, observational data have suggested that this drug combination may increase the International Normalized Ratio (INR) values and bleeding events in patients taking Vitamin K antagonists (VKAs). Still, the clinical impact of this putative effect remains unknown. Therefore, we performed a systematic review of randomized controlled trials (RCTs) to estimate the impact of concomitant use of acetaminophen and VKA in the INR measurements.

Methods

Systematic review and meta-analysis of RCTs comparing acetaminophen versus placebo or no treatment, in VKA-treated patients and reporting INR estimates. Medline and Cochrane Library were searched up to April 2014. Primary outcome was the mean difference (MD) between the greatest INR elevations in each treatment arm. Random-effects meta-analysis was performed to derive pooled estimates and 95% Confidence Interval (CI). Heterogeneity was evaluated with I² test.

Results

Seven RCTs (n = 225 patients) were included. Acetaminophen was associated with a mean 0.62 INR increase (95%CI: 0.46 to 0.78; I² = 25%) compared to placebo in VKA-treated patients. Studies did not report any major bleeding event. Meta-regression showed a significant 0.17 mean increase of the INR per each daily gram of acetaminophen (95%CI: 0.004 to 0.33).

Conclusion

Acetaminophen is associated with a statistically significant and possible clinically relevant increase in the INR, with a dose dependent relationship. Patients treated concomitantly with VKA and acetaminophen should be monitored more regularly for possible VKA dosage adjustment.

Keywords

Acetaminophen, Warfarin, Coumarins, International Normalized Ratio, Anticoagulants