Risk of Substantial Intraocular Bleeding With Novel Oral Anticoagulants - Systematic Review and Meta-analysis

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Abstract

Importance

In noninferiority trials, novel oral anticoagulants (NOACs), also known as non–vitamin K oral anticoagulants, were at least noninferior to standard care in the prevention of most prothrombotic conditions. However, differences exist in the safety profile of antithrombotic drugs, and little is known about their intraocular bleeding risk.

Objective

To evaluate the risk of substantial intraocular bleeding associated with NOACs.

Data Sources

MEDLINE, Cochrane Library, SciELO collection, and Web of Science databases were searched from inception to November 2014, as well as other systematic reviews and regulatory agencies documentation.

Study Selection

All phase 3 randomized clinical trials (RCTs) comparing NOACs with any other control that reported intraocular bleeding events.

Data Extraction and Synthesis

Data were extracted independently by 2 of the authors and pooled using random-effects meta-analysis. Heterogeneity was assessed with the I2 test.

Main Outcomes and Measures

Substantial intraocular bleeding was evaluated with pooled risk ratios (RRs) and 95% CIs.

Results

Seventeen RCTs were included. In patients with atrial fibrillation, no difference was identified between NOACs and vitamin K antagonists (RR, 0.84; 95% CI, 0.59-1.19; I2 = 35%; 5 RCTs), and no increased risk was identified compared with acetylsalicylic acid (RR, 14.96; 95% CI, 0.85-262.00; 1 RCT). In patients with venous thromboembolism, no increased risk of substantial intraocular bleeding compared with sequential treatment with low-molecular-weight heparin and a vitamin K antagonist (RR, 0.67; 95% CI, 0.37-1.20; I2 = 0%; 5 RCTs) was identified.

Regarding patients who underwent orthopedic surgery, the risk was not different between NOACs and low-molecular-weight heparin (RR, 2.13; 95% CI, 0.22-20.50; I2 = 0%; 5 RCTs).

Conclusions and Relevance

Randomized data suggest that no differences exist in the risk of substantial intraocular bleeding between NOACs and other antithrombotic drugs. However, the number of events was scarce so that additional studies from larger databases that monitor patients under conditions of ophthalmologic routine clinical practice should be performed to better characterize the safety profile of NOACs.