Epistaxis in Anticoagulated Patients with Atrial Fibrillation in the ENGAGE AF-TIMI 48 Trial

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Background

Epistaxis is common with anticoagulant therapy yet under-investigated in cardiovascular clinical trials and observational studies. These bleeding events are often troublesome to patients and may lead to anticoagulant discontinuation.

Purpose

To describe the frequency and severity of epistaxis and subsequent study drug discontinuation in patients with atrial fibrillation (AF) randomized to edoxaban vs warfarin.

Methods

21,105 participants with AF and CHADS2≥2 were randomized to a higher-dose edoxaban regimen (HDER; 60 mg daily), a lower-dose edoxaban regimen (LDER; 30 mg daily), or warfarin. Patients meeting predefined dose-reduction criteria received half the typical dose (i.e., 30 mg or 15 mg daily).

Participants with any epistaxis events were compared to those with exclusively non-epistaxis bleeding. Participants with more than one bleeding event were categorized according to the most severe event. Participants with intracranial hemorrhage were excluded.

Proportions were compared using a Pearson’s chi-squared test and treatment arms were compared using a Cox proportional hazards model.

Results

5,247 participants had a bleeding event, of whom 1,008 (19.2%) had epistaxis and 4329 (80.8%) had exclusively non-epistaxis bleeding.

**Fig 1. ISTH severity for epistaxis vs non-epistaxis bleeding**

- **Major/CRNM/Minor**
  - LDER
    - 0.73 (0.62-0.86)
    - 0.70 (0.58-0.85)
    - 0.65 (0.29-1.45)
  - HDER
    - 1.09 (0.95-1.26)
    - 1.00 (0.84-1.19)
    - 0.47 (0.19-1.15)

**Fig 2. Permanent study drug discontinuation following epistaxis vs non-epistaxis bleeding**

- **Major/CRNM/Minor**
  - LDER
    - 59.4% (32.5%)
    - 53.6% (33.3%)
    - 32.5% (33.3%)
  - HDER
    - 33.3% (23.9%)

Limitations

Participants were categorized according to their most severe bleeding event, which may obscure the relationship between bleeding episodes and drug discontinuation among participants with more than one event.

Conclusions

Epistaxis is frequent in patients with atrial fibrillation on anticoagulation, is symptomatically important, and is associated with a high rate of study drug discontinuation. Epistaxis deserves increased attention in cardiovascular research as well as in the development of clinical strategies to avoid disruption of anticoagulant therapy.

Declaration of interest:
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