Tranexamic acid (TXA) can reduce blood loss in total knee arthroplasty (TKA), but the safest and most effective administration route is unclear.

In a double blind randomized controlled study:

- **Intravenous (IV) TXA**
  - 1.0 g TXA
  - • before tourniquet inflation
  - • 3 hours later

- **Topical TXA**
  - 3.0 g TXA
  - • 5 min before final tourniquet release

Wound and blood tests:
- • Degree of fibrinolysis (plasmin-anti-plasmin (PAP))
- • Thrombin generation (prothrombin fragment (PF) 1.2)
  - • TXA
  - • Interleukin-6

1 h after tourniquet release:
- (1 IV dose)
- Degree of fibrinolysis comparable between both groups
- Therapeutic systemic TXA levels seen in topical group

4 h after tourniquet release:
- • IV group had lower degree of fibrinolysis than topical group
- • No difference in thrombin generation between both groups

Given that therapeutic systemic TXA levels were achieved with topical TXA, and that mechanisms of action, coagulation, and fibrinolytic profiles were similar between topical and single dose IV TXA, it may be simpler to use a single IV TXA dose when safety is a concern.