Introduction: Tranexamic acid (TXA) is routinely used during cardiac surgical procedures involving cardiopulmonary bypass (CPB) in order to reduce blood loss [1]. Although the optimum dose of TXA has been a subject of debate, a dosing regimen also sometimes referred to as the BART dose remains a popular choice for high-risk cardiac surgery [2]. The pharmacokinetics of TXA during the perioperative period with this antifibrinolytic dose has not been studied. The primary objective of this study was to measure the TXA plasma concentrations following infusion of the BART dose during cardiac surgery with the use of CPB. The secondary objectives of this study were to ascertain if observed TXA concentrations were within the suggested target range to allow optimal inhibition of tissue plasminogen activator (TPA) and to evaluate elimination kinetics of TXA in the postoperative period following discontinuation of the infusion.

Methods: Following REB approval, we recruited and obtained written, informed consent from five patients undergoing elective cardiac surgery with the use of CPB. An initial TXA bolus of 30 mg.kg\(^{-1}\) was infused over 15 minutes followed by a 16 mg.kg\(^{-1}\).hr\(^{-1}\) infusion until chest closure with a 2 mg.kg\(^{-1}\) load within the pump prime [2]. Blood samples were taken at baseline, 5 min after the bolus, post-sternotomy, 5 min after commencing CPB and at 30 minute intervals whilst on CPB. Postoperative samples were taken in the ICU at 5 minutes and 1, 2, 3, 4, 6, 8, 10, 12 and 24 hours after discontinuation of the infusion. TXA was extracted from plasma samples using solid phase microextraction (SPME) and concentrations were measured using tandem liquid chromatography-mass spectrometry as previously described [3].

Results: Plasma concentration of TXA when compared with simulated TXA levels using a two-compartment pharmacokinetic model previously described by Dowd at al [4] are illustrated in figure 1.

Discussion: This is the first study that describes pharmacokinetics of the BART dose of TXA including elimination kinetics up to 24 hours after discontinuation of the infusion.

The results of our study show that infusion of the BART dose of TXA results in plasma TXA concentrations higher than the suggested therapeutic levels (100 µg/ml) at all time points during the intraoperative period. Furthermore plasma TXA concentrations allowing 80% inhibition of TPA activity were demonstrated in majority of our patients up to six hours after discontinuation of infusion. Plasma TXA concentrations were below the limit of detection 12 hours (corresponding to six elimination half-lives) after discontinuation of the infusion in all patients.

Recently several investigators have associated high-dose TXA as a probable etiology of postoperative seizures following cardiac surgery [5]. Our results suggest that further work on TXA pharmacokinetics is required to establish a balance between effective yet safe dose in patients undergoing high-risk cardiac surgery.

3 Can J Anesth 2012; 59: 14-20
4 Anesthesiology 2002; 97: 390-99
5 Anesth Analg 2010; 110: 350-3