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## INTRODUCTION

The selective muscle relaxant binding agent sugammadex (Bridion®) is associated with transient and limited prolongation of activated partial thromboplastin time (APTT) and prothrombin time (PT) in humans, likely caused by inhibition of the formation of factor Xa and factor Xa activity. As sugammadex is used in surgical patients who are often anticoagulated, evaluation of potential interactions on clotting of sugammadex with commonly used anticoagulants is indicated.

## AIM

To investigate the potential interaction between sugammadex and various anticoagulants.

## METHODS

- Plasma from healthy male volunteers spiked *in vitro* with anticoagulants in therapeutic concentration range:
  - Fondaparinux / Dabigatran / Rivaroxaban / Enoxaparin / UFH;
  - Addition of sugammadex to anticoagulant-spiked plasma in concentrations corresponding with the mean peak plasma concentrations for the highest clinical doses of 4 and 16 mg/kg sugammadex (50 and 200 µg/mL respectively);
- Readout: absolute and relative increase in APTT.

## RESULTS

- Sugammadex (50 µg/mL) prolonged APTT by an additional 5-6 seconds in the presence of the highest concentrations of fondaparinux, dabigatran, enoxaparin and UFH and by 9 seconds for rivaroxaban (Table 1);
- Dose-dependent sugammadex-effect on APTT independently of the anticoagulant concentration (fondaparinux, dabigatran, enoxaparin and UFH), with the exception of rivaroxaban, for which the sugammadex-effect relationship increased with increasing rivaroxaban concentration (Table 1).

Table 1: Effect of sugammadex on APTT in anticoagulant-spiked plasma

Anticoagulant	[Anticoagulant]	[Sugammadex] (µg/mL)		
		0	50	200
		APTT (s)	APTT increase in s (relative)	
Fondaparinux	0.3 µg/mL	41.9	+8 (18.5%)	+18 (43.6%)
	0.6 µg/mL	43.7	+5 (11.8%)	+9 (21.2%)
Dabigatran	106 ng/mL	52.4	+9 (16.9%)	+24 (45.7%)
	212 ng/mL	62.4	+6 (10.0%)	+18 (29.2%)
Rivaroxaban	100 ng/mL	51.3	+7 (13.3%)	+18 (34.4%)
	200 ng/mL	56.7	+9 (15.5%)	+30 (51.9%)
Enoxaparin	5 µg/mL	62.5	+9 (12.5%)	+13 (21.0%)
	10 µg/mL	84.6	+6 (7.5%)	+19 (22.1%)
UFH	0.15 U/mL	45.6	+6 (14%)	+12 (27%)

## CONCLUSIONS

Sugammadex prolonged APTT *in vitro* in the presence of UFH, enoxaparin, fondaparinux, dabigatran and rivaroxaban, with the strongest effect observed for the latter. The limited prolongation in APTT when combining sugammadex and UFH/LMWH appear to be in accordance with clinical data showing no increase in bleeding events in surgical patients treated with UFH/LMWH<sup>1</sup>; clinical data on other anticoagulants are currently lacking.

<sup>1</sup>Anesthesiology, 2014;121(5):969-77