Effects of rocuronium and sugammadex on human platelet functions *in vitro*

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Background

Rocuronium (RN), an aminosteroidal non-depolarizing neuromuscular agent, and sugammadex (SG), a selective relaxant binding agent for RN, have been widely used in general anesthesia. In this study, we examined the effects of RN and SG on platelet aggregation, and expression of P-selectin (PS), an adhesion molecule on the surface of activated platelets.

Methods

Informed consent was given and the protocol was approved by the ethical committee. Venous blood was taken with 10 % volume of 3.8% tri-sodium citrate from healthy volunteers. Platelet-rich plasma (PRP) was prepared by centrifugation at 160 g for 10 min.

(1) Aggregation Study by Light Transmission Method

Aggregometer
Hema Tracer 712

PRP containing RN, SG, or RN + equimolar SG was incubated at 37°C for 3 min. Adenosine diphosphate (ADP)-induced aggregation was measured for 7 min as a change in light transmission using aggregometer.

(2) Flow cytometry analysis for P-selectin expression

Gating
by FSC & SSC

Gating
by CD61 expression
(PerCP-labeled)

Measurement of
PS expression
(PE-labeled)

Identification of Platelet

PRP was stimulated by ADP with RN or RN + equimolar SG at room temperature for 30 min. PerCP-labeled anti-CD61 antibody and PE-labeled anti-CD62P (PS) antibody were co-incubated. PS expression levels on activated platelet surface membranes were recorded as the mean fluorescent intensity (MFI) by Flow cytometry.

Results

Fig. 1

All data were compared with ANOVA, followed by the Dunnett's test.

Fig. 2

n=5 each. The data are expressed as mean ± S.D. *p<0.05

RN suppressed ADP-induced platelet aggregation (>310 μg/ml) and PS expression (>3.1 μg/ml), but this effect was not abolished by equimolar SG (Fig. 1A, 1B and 2). SG (100 mg/ml) suppressed ADP-induced platelet aggregation (Fig. 1B).

Discussion

Morpholine ring → Suppressive effect?

SG forms tight complexes at a 1:1 ratio with RN by encapsulating. Our results demonstrate that RN and RN-SG complex suppressed platelet functions within the usual therapeutic concentration range (< 10 μg/ml). Therefore, it might be possible that RN and RN-SG complex affect platelet functions in the clinical setting. SG does not completely encapsulate RN. Morpholine ring in RN molecule is outside SG molecule and known to have suppressive effect on platelet functions by P2Y12 receptor blocking. Therefore, Morpholine ring may contribute to this suppressive effect.

Conclusion

RN and RN-SG complex suppressed platelet functions. SG did not abolish this suppressive effects of RN.