Laboratory Assessment of Dabigatran Levels and Anti-Xa Anticoagulant Levels

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INTRODUCTION

Direct oral anticoagulants (DOACs) show inter- and intra - individual variability in plasma concentrations. Assessment of the individual response to drug treatment and risk balance could require laboratory measurement.

AIM

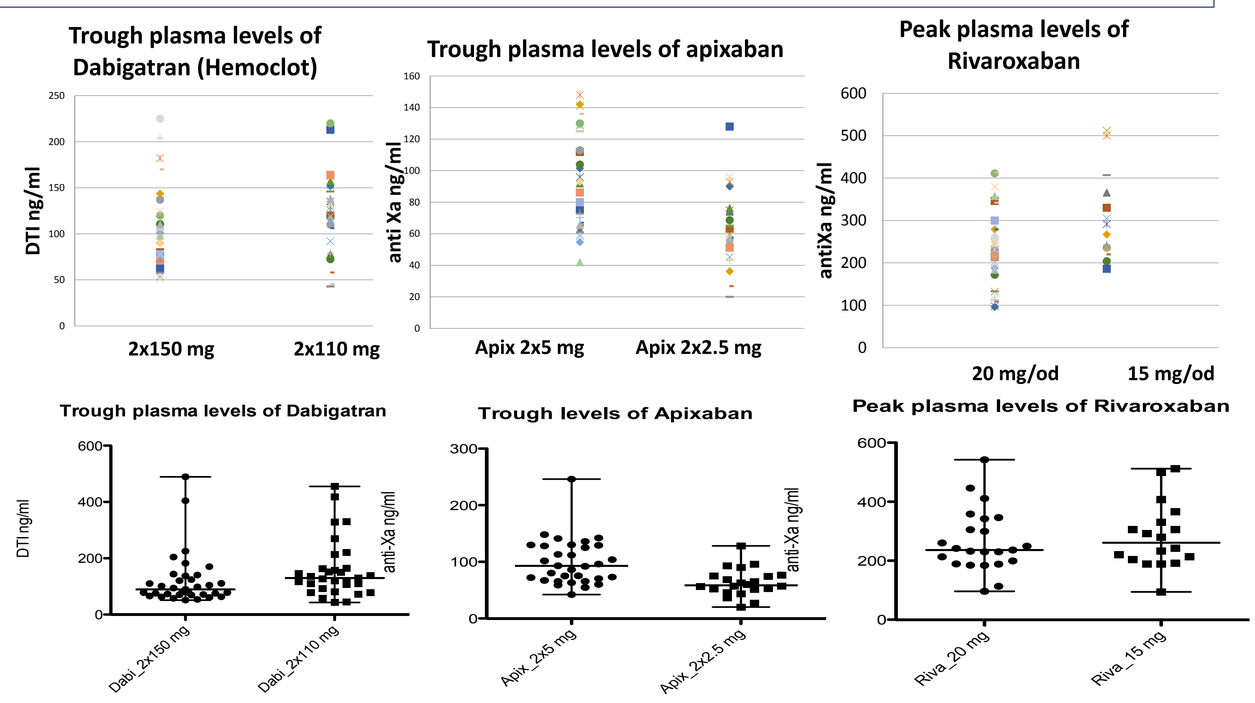
To evaluate the variation in DOAC drug levels among individual outpatients.

METHOD

A total of 165 patients with non-valvular atrial fibrillation were enrolled, 60 of them were on dabigatran (150 mg or 110 mg twice daily), 65 patients on apixaban (5 mg or 2.5 mg twice daily), and 40 patients on rivaroxaban (20 mg or 15 mg once daily). Blood was taken at trough level for dabigatran or apixaban and at peak level for rivaroxaban. Diluted-thrombin-time (DTI) was performed with Hemoclot (Hyphen BioMed) for dabigatran and anti-FXa measurments for apixaban and rivaroxaban was calibrated with Hyphen DiXaI on CS 2500 (Sysmex).

RESULTS

Dabigatran given at a dose 150 mg twice daily produced plasma trough level of 85 ng/ml (52 – 182 ng/ml) and at 110 mg twice daily of 117 ng/ml (43 – 195 ng/ml), expressed as median (5-95th%tile). Four patients with reduced GFR (35-38 ml/min) had values above the upper limit with the highest value - 455 ng/ml and three had values below 30 ng/ml. The median trough level for apixaban 5 mg twice daily was 86 ng/ml (55 – 141 ng/ml) and for 2.5 mg twice daily 58 ng/ml (21 – 141 ng/ml. Two patients had values above the upper limit (*up to 680 ng/ml)* and three with obesity had values below 50 ng/ml. Rivaroxaban administered at a dose 20 mg daily or 15 mg daily produced peak of 215 ng/ml (98 – 403 ng/ml) and 267 ng/ml (188 – 450 ng/ml), respectively with three values above the 95^{-th} %tile. Five patients with rivaroxaban experienced mucosal bleeding. We observed haematuria in patients on dabigatran treatment.



	Dabigatran 2 x 150 mg	Dabigatran 2 x 110 mg	Apixaban 2 x 5 mg	Apixaban 2 x 2.5 mg	Rivaroxaban 20 mg/d	Rivaroxaban 15 mg/d
Median	85 ng/ml	117 ng/ml	86 ng/ml	58 ng/ml	215	267
5th %tile	52 ng/ml	43 ng/ml	55 ng/ml	28 ng/ml	98	188
95th %tile	182 ng/ml	195 ng/ml	141 ng/ml	96 ng/ml	403	502
VC %	44%	37%	32%	38%	40%	34%
N	33	27	40	25	23	17
Age (yrs)	66 (55-79)	75 (57-85)	68 (45-85)	79 (69 – 84)	66 (45-80)	71 (58 – 83)
Weight (kg)	84 (61-135)	84 (55-101)	90 (60-118)	77 (62-97)	80 (64-113)	78 (53 – 92)
GFR ml/min	77 (59-150)	63 (36-79)	66 (52-120)	67 (40-92)	80 (40 – 120)	67 (37 – 88)

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CONCLUSIONS

Fifteen out of 165 measured levels (9%) were beyond the expected limits in our outpatient groups, which allows for better assessment of risk balance in such patients.

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