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ABSTRACT N. PO70

CLINICAL SAFETY AND MONITORING OF APIXABAN COMBINED WITH TACROLIMUS AND EVEROLIMUS IN KIDNEY TRANSPLANT PATIENTS: A PROSPECTIVE STUDY.

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Background and Aims

The use of direct oral anticoagulants (DOACs) in kidney transplant recipients presents a clinical challenge due to potential drug–drug interactions with immunosuppressive agents, particularly tacrolimus and everolimus. Data on the safety and efficacy of DOACs in this population are limited. This study aims to describe our clinical experience with anticoagulant therapy in kidney transplant recipients treated with tacrolimus, with or without everolimus, focusing on drug levels, safety, and outcomes.

Methods

We conducted a prospective analysis of five kidney transplant recipients receiving apixaban for atrial fibrillation (AF) or venous thromboembolism (VTE). These patients were treated with tacrolimus alone or in combination with everolimus and were followed at our center between November 2020 and April 2025, with a median follow-up of 20 months (IQR 12 – 40 months). Apixaban levels (measured via anti-Xa calibrated assay) were assessed at trough (12 hours after drug administration) and peak (4 hours after drug administration). In one patient (Pt.1), measurements were taken during both 5 mg and 2.5 mg treatment periods. Data collected also included demographic and clinical information, indications for anticoagulation, tacrolimus and everolimus plasma concentrations, average tacrolimus and everolimus plasma concentrations over the last year, hemoglobin levels, renal function, and the safety profile (major/minor bleeding, cardioembolism, or VTE).

Results

We included 5 patients (F/M: 2/3) with a median age of 77 years (IQR 72 – 79 years). All patients were receiving tacrolimus treatment, with one patient also receiving everolimus, in combination with other immunosuppressive drugs (Table 1). Creatinine and hemoglobin levels remained stable throughout the follow-up. The average tacrolimus levels were within the target range in 4 out of 5 patients (median 5.5 ug/L, IQR 4.6 – 6.2 ug/L), and slightly reduced in one (without renal complications) - see Table 1. The average everolimus level was within the therapeutic range in the only patient receiving this drug. Apixaban plasma levels were within the therapeutic range at both peak and trough for Pt.2 and Pt.5, and for Pt.1 (only during treatment with apixaban 5 mg). In Pt.3, Pt.4, and during apixaban 2.5 mg treatment in Pt.1, the levels were elevated compared to the reference range (see Table 1). Pt.4 experienced a thrombotic complication (ischemic injury to the toe), but no patient has had minor or major bleedings according to ISTH criteria.

Conclusions

In our cohort of kidney transplant recipients, the combination of apixaban with tacrolimus (with or without everolimus) appeared to be safe and effective, with no increased risk of thrombosis, bleeding or renal complications. Apixaban levels were predominantly within the therapeutic range, suggesting that, when carefully monitored, apixaban may be a viable anticoagulant option in this complex clinical setting. Larger prospective studies are needed to confirm these preliminary findings.

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	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Median (IQR)
Age (years)	72	77	54	85	79	77 (72–79)
Sex (M/F)	M	F	F	M	M	-
Years since transplant	6	6	8	8	7	7 (6–8)
Immunosuppressant	TAC + MMF + steroid	TAC + MMF	TAC + EVE	TAC + MMF + steroid	TAC + MMF + steroid	-
VTE/AF	TEV	AF	TEV	TEV	AF	
Months FU in DOAC	54	20	12	6	40	20 (12–40)
Comorbidities	Atrophic gastritis	Hypertension, dyslipidemia	LES, breast cancer	Hypertension, dyslipidemia	Hypertension, MGUS	-
Smoker	Former	Never	Never	Former	Former	-
Hb (g/dL)	13.6	11.7	12.8	11.9	11.1	11.9 (11.7–12.8)
Creatinine (mg/dL)	1.1	1.3	1	1.2	3	1.2 (1.1-1.3)
eGFR (ml/min)	60	40	70	40	25	-
Baseline tacrolimus (ug/L)	4	8.7	1.8	7.1	3	4 (3-7.1)
Average tacrolimus level (ug/L)	5.5	6.2	2.9	5.7	4.6	5.5 (4.6-6.2)
Target tacrolimus level (ug/L)	4 - 6	6 – 6.5	3 – 3.5	5 - 6	4 - 6	-
Baseline everolimus (ug/L)	-	-	3.4	-	-	-
Average everolimus level (ug/L)	-	-	3.1	-	-	-
Target everolimus level (ug/L)	-	-	3 - 3.5	-	-	-
No. of dose changes/year	2	2	1	0	3	-
Apixaban 5 mg trough (ng/mL)	135	132.6	-	283.7	-	135 (132.6-283.7)
Apixaban 5 mg peak (ng/mL)	211	284.1	-	399	-	284.1 (211-399)
Apixaban 2.5 mg trough (ng/mL)	125	-	135	-	114	125 (114-135)
Apixaban 2.5 mg peak (ng/mL)	189	-	-	-	144	166.5 (n.a.)
VTE/cardioembolism	0	0	0	1	0	-
Minor bleeding	0	0	0	0	0	-
Major bleeding	0	0	0	0	0	-

Patients' characteristics, anticoagulant and immunosuppressant treatment, and outcomes