

Abstract Submission No.: A-1209**Alleviating Restless Legs Syndrome (RLS) in Hemodialysis Patients: Unveiling the Therapeutic Impact of Palm Tocotrienol-Rich Fraction (TRF)**

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Objectives : Restless legs syndrome (RLS) poses a persistent challenge for maintenance hemodialysis (MHD) patients, significantly impacting their quality of life. In the absence of effective non-pharmacologic interventions, our study aims to investigate the potential of daily supplementation with 300mg of palm tocotrienol-rich-fraction (TRF) over 12 months in improving RLS among MHD patients.

Methods : RLS was examined as a secondary outcome in the PATCH (Palm Tocotrienols in Chronic Hemodialysis) study—a randomized, double-blind, placebo-controlled trial involving Malaysian MHD patients (ClinicalTrials.gov ID: NCT02913690). Participants received daily supplementation of 300mg TRF (n=170) or placebo (n=166) over 12 months, with compliance monitored through capsule counting. RLS severity was assessed at quarterly intervals (baseline, 3, 6, 9, and 12 months) using the International RLS Study Group rating scale (IRLS). Generalized estimating equations gauged changes in RLS severity over time between TRF and placebo groups. Intention-to-treat (ITT) analysis was implemented for all patients, while a sensitivity analysis focused on MHD patients with RLS at baseline for robustness assessment.

Results : Comparable socio-demographic and clinical variables were noted between the TRF and placebo groups (Table 1). The prevalence of RLS at baseline was 14% (47/336), with IRLS scores ranging from 2 (mild) to 33 (very severe). A significant main effect of the group was observed ($P_{\text{Group}}=0.003$) after adjusting for confounding factors. The mean IRLS score in the TRF group was significantly lower than the placebo group, with sustained benefits manifesting notably after 6-12 months of intervention (Figure 1). The sensitivity analysis further underscored the greater reduction in RLS severity within the TRF group.

Conclusions : Daily 300mg TRF supplementation effectively mitigates RLS severity in MHD patients, with a notable and sustained benefit emerging after 6 months. This study signifies a promising avenue for addressing RLS in MHD patients and calls for further exploration into the mechanistic underpinnings of tocotrienol-mediated relief.

Variables	Intervention (n=170) n (%) or Mean ± SEM	Control (n=166) n (%) or Mean ± SEM	p
Socio-demographic Variables			
Age (years)	54.0 ± 0.9	53.4 ± 0.9	0.652 ^a
Gender (male)	97 (57.1)	97 (58.4)	0.799
Ethnicity			0.424
Malays	78 (45.9)	80 (48.2)	
Chinese	67 (39.4)	53 (31.9)	
Indians	23 (13.5)	31 (18.7)	
Education			0.859
None	6 (3.5)	7 (4.2)	
Primary	39 (22.9)	44 (26.5)	
Secondary	84 (49.4)	78 (47.0)	
College/University	41 (24.1)	37 (22.3)	
Marital Status			0.723
Married	142 (83.5)	141 (84.9)	
Single	28 (16.5)	25 (15.1)	
Employment Status			0.154
Working	115 (67.6)	124 (74.7)	
Not Working	55 (2.4)	42 (25.3)	
Monthly Income (RM)			0.959
<500	65 (38.2)	64 (38.6)	
501-1000	28 (16.5)	28 (16.9)	
1001-2000	37 (21.8)	35 (21.1)	
2001-3000	14 (8.2)	17 (10.2)	
>3000	26 (15.3)	22 (13.3)	
Clinical Variables			
Presence of Diabetes	84 (49.4)	77 (46.4)	0.579
Dialysis Vintage (months)	68.8 ± 4.3	70.8 ± 4.2	0.583 ^a
Dialysis Adequacy (Kt/V)	1.57 ± 0.02	1.56 ± 0.03	0.735 ^b
Primary Outcome Variables			
Lipid Profile			
Total Cholesterol, TC (mmol/L)	4.09 ± 0.07	4.23 ± 0.07	0.156 ^b
HDL Cholesterol, HDL-C (mmol/L)	1.10 ± 0.03	1.03 ± 0.02	0.214 ^a
LDL Cholesterol, LDL-C (mmol/L)	2.52 ± 0.06	2.63 ± 0.07	0.231 ^b
Triacylglyceride TAG (mmol/L)	1.52 ± 0.06	1.66 ± 0.07	0.144 ^a
TC/HDL-C ratio	4.03 ± 0.10	4.32 ± 0.12	0.113 ^a
Inflammation			
hsCRP	6.00 ± 0.39	6.82 ± 0.48	0.399 ^a
Secondary Outcome Variable			
IRLS Score for ITT ^c	2.12 ± 0.46	2.23 ± 0.48	0.822 ^a
IRLS Score for sensitivity analysis ^d	15.65 ± 1.49	15.42 ± 1.58	0.914 ^b

Categorical data were analyzed by Pearson χ^2 test whilst continuous data were analyzed by Mann Whitney U test (skewed)^a and independent t-test (normally distributed)^b; ^c Mean IRLS scores for all PATCH subjects with and without RLS at baseline; ^d Mean IRLS scores for PATCH subjects with RLS at baseline

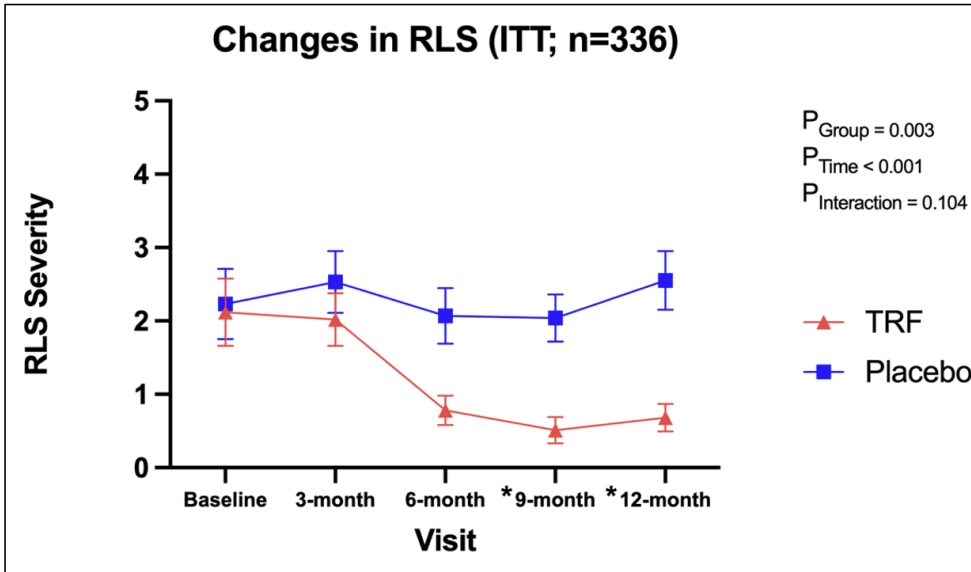


Figure 1: Changes in RLS Severity per ITT analysis

Note: *Significant Difference ($P < 0.05$) compared with placebo

Abbreviations: ITT, Intention-to-treat; TRF, tocotrienol-rich fraction