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EFFECTS OF RANKL ON LOWER DEPRESSIVE SYMPTOMS IN HEMODIALYSIS PATIENTS

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Objectives : Depression and osteoporosis are common diseases in dialysis patients. In addition, patients with osteoporosis are more susceptible to depression. Contrary to previous anti-osteoporosis agents, denosumab and romosozumab could be used in dialysis patients and have similar action mechanisms for blocking RANKL. RANKL causes bone resorption after binding RANKL, but binding with OPG leads to suppress of bone resorption. In recent mice study, inhibition of RANKL with denosumab improved depressive-like phenotype. Besides, it was found that OPG was associated with depression. Therefore, this study aimed to investigate the association of depressive symptoms with RANKL and OPG in hemodialysis patients.

Methods : We conducted a cross-sectional study with a total of 172 hemodialysis patients. The participants were measured for plasma RANKL, OPG, MMP-2, and MMP-9 levels. Logistic regression analysis was performed to evaluate the effect of RANKL and OPG on the presence of depressive symptoms.

Results : The depressive symptoms were observed in 90 (52.3%) subjects. RANKL tertile 3 had negative association with BDI score (β -4.527, 95% CI -8.310 – -0.743) in univariate analysis, and this association persisted even after multivariate adjustments (β -5.603, 95% CI -9.715 – -1.491) in linear regression. In logistic regression between RANKL tertiles and depressive symptoms, RANKL tertile 3 had significantly lower unadjusted OR (0.40, 95% CI 0.19-0.86), and multivariate-adjusted OR (0.31, 95% CI 0.12-0.82) for depressive symptoms. OPG was not significantly associated with depressive symptoms.

Conclusions : Higher plasma RANKL concentrations were significantly associated with lower depressive symptoms in HD patients.

Table1..png

BDI score [†]	β (95% CI) [‡]		P [‡]	
	Univariate [‡]	value [‡]	Multivariate [‡]	value [‡]
Charlson comorbidity index [‡]	1.837 (0.814 – 2.860) [‡]	<0.001 [‡]	1.176 (-0.446 – 2.799) [‡]	0.154 [‡]
Pre-HD SBP [‡]	0.016 (0.098 – 0.066) [‡]	0.699 [‡]	-0.017 (-0.115 – 0.081) [‡]	0.734 [‡]
Presence of RRF [‡]	-2.163 (-6.022 – 1.696) [‡]	0.269 [‡]	-5.024 (-10.198 – 0.150) [‡]	0.056 [‡]
Hemoglobin [‡]	-1.218 (-2.499 – 0.064) [‡]	0.062 [‡]	-0.183 (-1.730 – 1.364) [‡]	0.815 [‡]
Albumin [‡]	-7.187 (-12.344 – -2.029) [‡]	0.007 [‡]	-2.210 (-8.7106 – 4.286) [‡]	0.502 [‡]
Ca [‡]	0.407 (-1.570 – 2.385) [‡]	0.685 [‡]	0.593 (-1.592 – 2.779) [‡]	0.592 [‡]
Phosphorus [‡]	-1.400 (-2.630 – -0.170) [‡]	0.026 [‡]	-0.183 (-1.633 – 1.271) [‡]	0.805 [‡]
Bone specific ALP [‡]	-0.098 (-0.260 – 0.064) [‡]	0.233 [‡]	-0.128 (-0.317 – 0.060) [‡]	0.180 [‡]
Parathyroid hormone [‡]	-0.004 (-0.011 – 0.002) [‡]	0.208 [‡]	-0.005 (-0.013 – 0.003) [‡]	0.251 [‡]
25(OH) Vitamin D [‡]	-0.058 (-0.213 – 0.098) [‡]	0.463 [‡]	-0.068 (-0.237 – 0.100) [‡]	0.424 [‡]
RANKL tertile 1 [‡]	Reference [‡]	[‡]	[‡]	[‡]
RANKL tertile 2 [‡]	-3.092 (-6.860 – 0.676) [‡]	0.107 [‡]	-3.475 (-7.557 – 0.606) [‡]	0.094 [‡]
RANKL tertile 3 [‡]	-4.527 (-8.310 – -0.743) [‡]	0.019 [‡]	-5.603 (-9.715 – -1.491) [‡]	0.008 [‡]
OPG tertile 1 [‡]	Reference [‡]	[‡]	[‡]	[‡]
OPG tertile 2 [‡]	1.737 (-2.083 – 5.556) [‡]	0.037 [‡]	-1.456 (-5.975 – 3.064) [‡]	0.525 [‡]
OPG tertile 3 [‡]	1.323 (-2.480 – 5.126) [‡]	0.493 [‡]	-3.183 (-8.474 – 2.108) [‡]	0.236 [‡]
RANKL/OPG tertile 1 [‡]	Reference [‡]	[‡]	[‡]	[‡]
RANKL/OPG tertile 2 [‡]	-5.035 (-8.733 – -1.337) [‡]	0.008 [‡]	-5.152 (-9.280 – -1.025) [‡]	0.015 [‡]
RANKL/OPG tertile 3 [‡]	-6.121 (-9.803 – -2.438) [‡]	0.001 [‡]	-4.422 (-8.617 – 0.226) [‡]	0.039 [‡]

BDI Beck's Depression Inventory, SBP Systolic Blood Pressure, RRF Residual Renal Function, ALP Alkaline Phosphate, RANKL receptor activator of nuclear factor-κB ligand, OPG Osteoprotegerin [‡]

Multivariate, adjusted for age, sex, BMI, Diabetes mellitus, cardiovascular diseases, HD vintage, spKt/V, hsCRP[‡]

Table1..png

	OR (95% CI) [‡]		P [‡]	
	Unadjusted [‡]	value [‡]	Adjusted [‡]	Value [‡]
RANKL tertile 1 [‡]	Reference [‡]	[‡]	Reference [‡]	[‡]
RANKL tertile 2 [‡]	0.51 (0.24-1.09) [‡]	0.080 [‡]	0.42 (0.16-1.09) [‡]	0.074 [‡]
RANKL tertile 3 [‡]	0.40 (0.19-0.86) [‡]	0.018 [‡]	0.31 (0.12-0.82) [‡]	0.018 [‡]
OPG tertile 1 [‡]	Reference [‡]	[‡]	Reference [‡]	[‡]
OPG tertile 2 [‡]	1.64 (0.78-3.44) [‡]	0.191 [‡]	0.59 (0.20-1.69) [‡]	0.326 [‡]
OPG tertile 3 [‡]	1.37 (0.66-2.85) [‡]	0.401 [‡]	0.29 (0.08-1.02) [‡]	0.165 [‡]
RANKL/OPG tertile 1 [‡]	Reference [‡]	[‡]	Reference [‡]	[‡]
RANKL/OPG tertile 2 [‡]	0.48 (0.23-1.03) [‡]	0.059 [‡]	0.51 (0.20-1.32) [‡]	0.041 [‡]
RANKL/OPG tertile 3 [‡]	0.35 (0.17-0.75) [‡]	0.007 [‡]	0.55 (0.21-1.42) [‡]	0.256 [‡]

RANKL receptor activator of nuclear factor-κB ligand, OPG Osteoprotegerin, OR Odds Ratio, CI Confidential Interval[‡]

Multivariate, adjusted for age, sex, BMI, Diabetes mellitus, cardiovascular diseases, HD vintage, spKt/V, hsCRP[‡]