Effects of Pomegranate Polyphenols on Cognitive and Functional Recovery Following Ischemic Stroke: A Randomized, Placebo-controlled, Double-blinded Trial

Paolo Jorge MD, John Bellone PhD, Jeffrey Murray MA, Mary Kim MD, Travis Fogel PhD, Desiree Wallace PharmD, Rich Hartman PhD
Loma Linda University Health, Department of Physical Medicine & Rehabilitation, Department of Psychology

LOMA LINDA UNIVERSITY HEALTH

OBJECTIVES

Cognitive impairment after stroke is associated with poor long-term survival, higher disability, and greater institutionalization rates. Pathophysiology leading to injury includes oxidative stress and inflammation causing cell apoptosis. Studies involving pomegranate polyphenols (PPs) targeting these pro-apoptotic mechanisms showed improved memory function following cardiac surgery. Furthermore, rodent models have shown improved balance, sensorimotor coordination, and locomotion after PP consumption. The study objective is to determine if pomegranate polyphenol supplementation enhances cognitive recovery and functional mobility status-post ischemic stroke.

DESIGN

183 patients were screened at an acute rehabilitation facility from June 2015-March 2016. 16 adults met inclusion criteria and consented to participate. Half of the subjects received PP (n=8), half received placebo (n=8). Permuted-block randomization (block size 4, allocation 1:1) ensured balanced groups. Allocation was concealed through pharmacy-controlled randomization. After baseline neuropsychological and functional mobility testing, participants received PP or placebo BID for 7 days, followed by post-treatment testing. One participant from each group was excluded from final cognitive analyses after failing to complete post-treatment cognitive testing.

Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) and FIM score were the primary outcome measures for cognitive recovery and functional mobility since their validity and reliability in the stroke population have been established. Fisher's exact test was used to assess differences in treatment group for categorical demographic and stroke characteristic variables. Independent samples t tests were used for continuous demographic and baseline data. Change scores were calculated by subtracting each subject's pre-treatment score from their post-treatment score. Independent samples t-tests were used with these change scores to assess group differences in change from pre- to post-treatment testing. Pearson product-moment correlation was used to compare the primary cognitive and functional measures: RBANS total scale index score change and FIM score change.

Table 1. Demographics & stroke data by group.

	POM	Placebo	P-value
Age in years (Mean ± SD) [range]	58.13 (13.62) [39-73]	59.63 (13.48) [40-77]	.83[a]
Years of education	13.57 (1.81) [12-16]	14.14 (2.33) [12-18]	.70[a]
Male/female	6/2	5/3	1.00[b]
Race (frequency)			.55[c]
White	4	5	
Black	3	1	
Hispanic	1	1	
Asian	0	1	
IQ estimate*	84.38 (7.39) [76-100]	96.63 (11.77) [85-115]	.03[a]
Lesion laterality, right/left	8/0	5/3	.20[b]
Lesion location (frequency)			.13[c]
Cortical	3	0	
Subcortical	4	5	
Mix	1	3	
Time from stroke onset to treatment initiation in days	12.50 (2.45) [9-16]	13.88 (5.84) [8-27]	.53[a]
Length of rehabilitation stay in days	16.50 (2.45) [11-25]	22.13 (6.47) [16-32]	.08[a]
Diabetes (%)	25	50	.61[b]
Dyslipidemia (%)	63	75	1.00[b]
Hypertension (%)	100	100	1.00[b]
Baseline RBANS Scores	67.71	78.00	.04[a]
Baseline FIM Scores	62.00	69.50	.33[a]

[a] Independent samples *t* test
[b] Fisher's exact test
[c] Chi-squared test
* IQ estimate based on Test of Premorbid Functioning (TOPF) score. It is compared to normative data and is a standard score (mean = 100, SD = 15)

Figure 1. RBANS change scores.

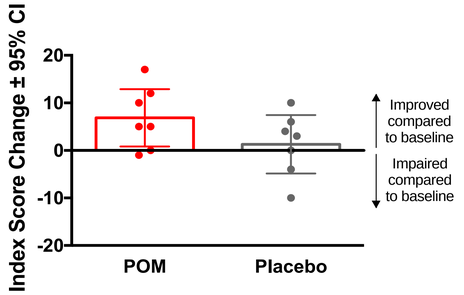


Figure 2. RBANS cognitive domains.

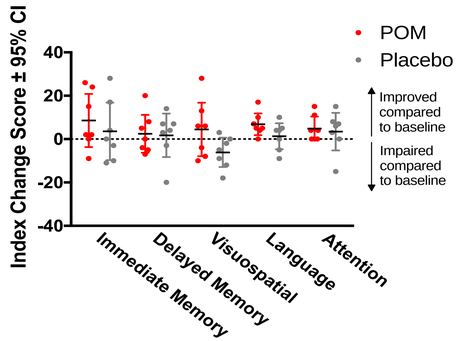


Figure 3. FIM change scores.

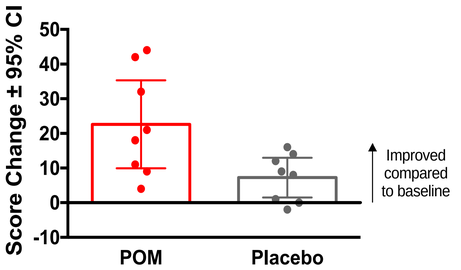
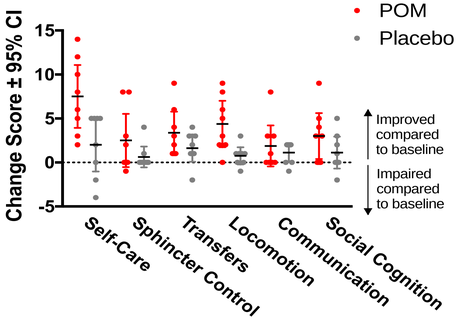
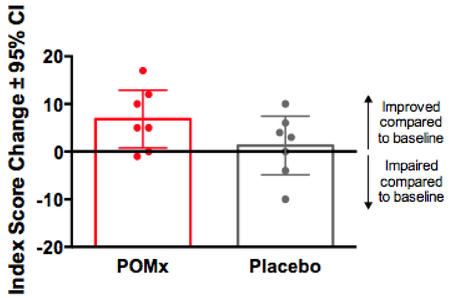


Figure 4. FIM score sub-measures.



CONCLUSION

Pomegranate polyphenols enhance cognitive and functional recovery after ischemic stroke relative to placebo controls. These effects were driven by trends in visuospatial/constructional and language domains as well as significant improvement in self-care and locomotion sub-measures. Additionally, these cognitive and functional improvements associated with pomegranate polyphenol administration may lead to shortened length of acute rehabilitation stay.


Index Score Change ± 95% CI
20
10
0
-10
-20
POMx
Placebo
Improved compared to baseline
Impaired compared to baseline