A RANDOMIZED CONTROLLED TRIAL OF BERBERINE EFFICACY ON METABOLIC SYNDROME PLUS HIV

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BACKGROUND

Antiretroviral therapy has increased the life expectancy of people living with HIV (PLWH). Nevertheless, this increase is not free of comorbidities, and metabolic syndrome is among the most prevalent[1]. Berberine is an alkaloid that has been shown to ameliorate metabolic syndrome components like glucose tolerance and insulin resistance, but it had not been tested in PLWH[2,3].

Our aims were to evaluate the efficacy of berberine for improving clinical features, insulin resistance, metabolic profile, and inflammatory markers.

METHODS

A randomized, double-blind, placebo-controlled trial was performed in adults living with HIV under virological suppression and with metabolic syndrome diagnosis who were assigned to receive either berberine 500 mg TID or placebo for 20 weeks. The primary outcomes were a composite of weight reduction, insulin resistance decrease, and lipid profile improvement. In dependent variable paired t-test or Wilcoxon's test, and independent variable unpaired t-test or Mann–Whitney U test were used.

RESULTS

Forty-three participants were randomized (22 in the berberine group (BBR) and 21 in the placebo group (CTR)); at the end, 19 in the BBR and 17 in the CTR group completed the intervention period and were analyzed. At 20 weeks, the BBR group showed the following improvements: reduction in weight and body mass index (2.8 kg, p=0.001; 0.99, p=0.003, respectively), lower insulin resistance revealed by a TyG*BMI decrease of 8 points (p=0.01); additionally, a reduction in TNF-alpha of 1 pg/mL was found (p=0.023), and a tendency toward benefit was shown in HOMA-IR and HOMA-%beta (Decrease 0.59, p=0.085; increase 3.5%, p=0.065, respectively). Conversely, the CTR group had higher total cholesterol and c-LDL (Increase 22 mg/dL, p=0.005; increase 20 mg/dL, p=0.024, respectively), and worse IL-6 concentration (Increase 0.69 pg/mL, p=0.018).

Table 1. Cardiometabolic, surrogate indexes for the evaluation of insulin resistance, and glycemia control enzymes

Variables	Group A (BBR) n=19	Intragroup *p*-value	Group B (CTR) n=17	Intragroup *p*-value	Intergroup *p*-value
Age, years, (Media ±SD)	46±9.2	-	47±9.1	-	0.854
Gender: n(%) Male Female	9 (47) 10 (53)	-	13 (76) 4 (23)	-	-
Weight, Kg (Median, IQR) Baseline Week 20	83 (77-97) 82 (73-95)	↓2.8 **0.001**	87 (77-91) 86 (76-91)	↓0.9 0.463	0.931 0.943
BMI (kg/m^2) (Media ±SD) Baseline Week 20	32 ±6.4 31 ±6.2	↓0.99 **0.003**	31 ±4.7 31 ±4.4	↓0.25 0.338	0.284 0.448
TC, mg/dL (Median, IQR) Baseline Week 20	174 (141-201) 172 (133-206)	↓2.3 0.464	163 (146-186) 186 (167-194)	↑22 **0.005**	0.278 0.076
LDL-c, mg/dL (Median, IQR) Baseline Week 20	103 (79-123) 90 (68-121)	↓5 0.163	94 (70-118) 109 (96-127)	↑20 **0.024**	0.419 0.072
TyG index*BMI (Median, IQR) Baseline Week 20	272 (250-309) 264 (231-298)	↓8 **0.010**	282 (236-305) 280 (241-304)	↓2 0.517	0.817 0.893
HOMA-IR (Media ±SD) Baseline Week 20	2.4 ±1.7 1.8 ±0.92	↓0.59 0.085	2.2 ±1.1 2.4 ±1.5	↑0.23 **0.041**	0.317 0.083
HOMA-%β (Median, IQR) Baseline Week 20	151 (133-181) 154 (119-164)	↑3.5% 0.065	159 (115-186) 158 (128-191)	↓1% **0.041**	0.866 0.393
HOMA-%S (Media ±SD) Baseline Week 20	59 ±36 61 ±26	↑1.8% 0.859	61 ±36 55 ±29	↓5.9% 0.153	0.442 0.267
C-Peptide, pg/mL (Median, IQR) Baseline Week 20	501 (71-801) 554 (63-887)	↑37 0.209	431 (199-879) 917 (548-1298)	↑174 **0.039**	0.526 **0.035**
TNF-α (Media ±SD) Baseline Week 20	2.3 ±2.1 1.3 ±0.64	↓1.0 **0.023**	1.4 ±0.47 1.0 ±0.62	↓0.3 0.078	0.092 0.185
IL-6 (Media ±SD) Baseline Week 20	1.4 ±0.42 4.6±2.1	↑0.32 0.16	0.89 ±0.3 1.6 ± 0.3	↑0.69 **0.018**	0.315 0.187

BBR: Berberine group, CTR: Control group, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance, HOMA-%β: Homeostasis Model Assessment estimates % pancreatic beta cell function (in steady state), HOMA-%S: Homeostasis Model Assessment estimates % insulin sensitivity, IL: Interleukin, TNF-α: Tumor Necrosis Factor alpha, SD: Standard deviation, IQR: Interquartile range. In dependent variable paired t-test or Wilcoxon's test, and independent variable unpaired t-test or Mann–Whitney U test were used.

Furthermore, an increase in HOMA-IR (Increase 0.23, p=0.041) was concurrent with a decrease in beta-cell function (HOMA-%beta decreased 1%, p=0.041) and higher C-peptide levels (Increase 174 pg/mL, p=0.039). See table 1. There were no serious adverse effects in both groups.

CONCLUSIONS

In PLWH under virological suppression, berberine improves metabolic syndrome by reducing weight and body mass index, insulin resistance, and proinflammatory profile, among a tendency to increase beta-cell function, while the control group showed worsening in total cholesterol, c-LDL, IL-6 levels, insulin resistance, and beta-cell function, at the end of the follow-up. Further studies with more people and longer intervention periods need to be explored.

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ADDITIONAL KEY INFORMATION

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Conflict of interest:
There are no conflicts of interest declared in relation to this research from any author.