

Effect of a culturally appropriate lifestyle intervention on biomarkers for diabetes among Mexican immigrants

Abstract

The prevalence of Type 2 diabetes is greatest among Hispanics of Mexican descent. In this project, a culturally appropriate lifestyle intervention targeting diet, exercise and psychosocial factors was delivered to Mexican immigrants living in Iowa. Participants were randomly assigned to a 6-week intervention or a control group. Blood was collected prior to (PRE) and at six months after the intervention (POST) to measure biomarkers associated with Type 2 diabetes and examine cellular pathways that may contribute to the disease process. The results showed a significant decrease from PRE to POST in glycated hemoglobin (HbA1c), a measure that reflects blood glucose level over the prior 2-3 months. The reduction of HbA1c was found in both intervention and control participants. In a subset of individuals, inflammatory proteins were measured in blood monocytes, as inflammatory pathways have been associated with the diabetes disease process. After the intervention, a reduction in the inflammatory cytokine IL-1 β was observed, and the ratio of pro-inflammatory to anti-inflammatory proteins was skewed towards less inflammation. Greater IL-1 β was significantly correlated with HbA1c. These findings demonstrate a relationship between inflammation and blood glucose level in Mexican immigrants, and show some promise for a culturally appropriate intervention in reducing risk of diabetes.

Introduction

- As of 2015, an estimated 84.1 million people (33.1%) had pre-diabetes with 90% unaware of this condition. Mexicans were identified as having the highest prevalence of diabetes (13.8%) compared to other Hispanic ethnic groups (1).
- The success of diabetes prevention programs in Hispanics has been mixed (2-McCurley), and therefore, a new program, Abriendo Caminos, designed to be culturally appropriate, was tested for efficacy in improving glucose regulation.
- Inflammation has been recognized as a contributing factor to the pathogenesis of diabetes (Cefalu, Dixit). For that reason, the association between glucose regulation and inflammatory responses were measured, and the effect of the Abriendo Caminos intervention on inflammatory response was assessed.
- It was hypothesized that glucose control and inflammation would improve in participants who completed the Abriendo Caminos intervention, and that inflammatory factors would be associated with a marker of glucose control, HbA1c.

Methods

Participants were recruited from a larger study that sought to evaluate the efficacy of a culturally appropriate lifestyle-modification education program in reducing the risk of developing Type 2 diabetes in Mexican immigrants. Blood was collected at study onset to assess HbA1c.

Methods, cont.

- HbA1c was measured using an HbA1c now kit by PTS diagnostics.
- Peripheral blood mononuclear cells were isolated by density centrifugation with Ficoll Paque Plus (GE Healthcare).
- Monocytes were separated by negative selection using Miltenyi pan-monocyte isolation kit and separation on an autoMACS column to isolate CD14⁺ and CD16⁺ monocyte populations.
- Isolated monocytes were adjusted to 1 x 10⁶ cells/ml, and cultured for 24h at 37^oC, 5%CO₂ with lipopolysaccharide (LPS) or monosodium urate (MSU), activators of inflammatory pathways.
- Cell culture supernatants were collected and assessed for cytokine or chemokine concentration by multiplex (Millipore 41 plex kit).
- Statistical analyses were performed with SPSS, t-test to compare differences in cytokines pre and post-intervention, and a mixed ANOVA with repeated measures (treatment*time) to compare HbA1c. Pearson correlations were performed to assess the association between HbA1c and cytokines or chemokines.

Results

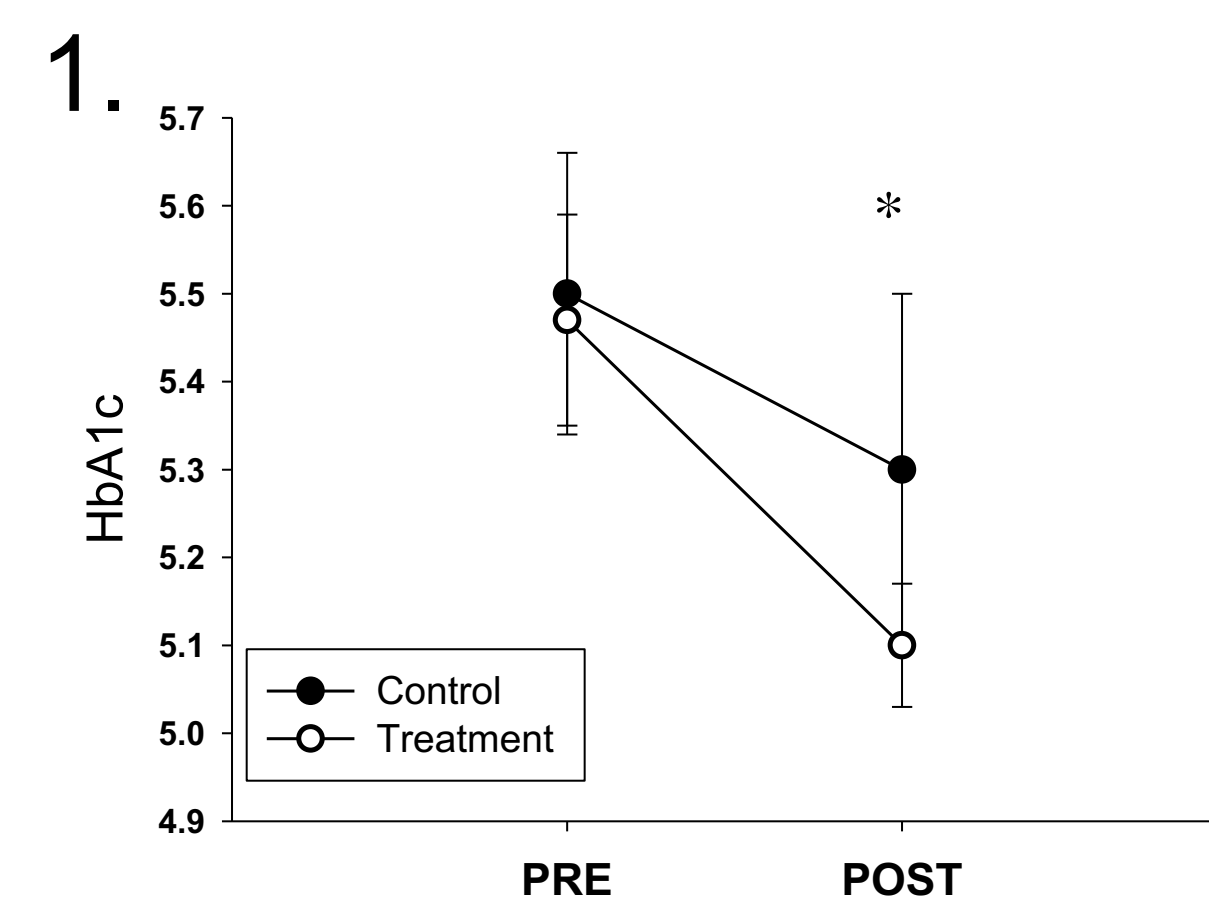


Figure 1. HbA1c was measured prior to the intervention (PRE) and 6 months later (POST). A significant decrease in HbA1c was observed at the POST compared to PRE for both groups, with no significant difference between groups or treatment by time interaction (n=13 control, n=29 treatment)

Table 1. Correlation between HbA1c and cytokines/chemokines

Cytokine / Chemokine	IL-1B	TNF α	IL-6	IL-17	IP10 (CXCL10)	MCP3 (CCL7)
Pearson correlation	0.419	0.308	0.409	-0.472	-0.251	-0.332
Significance	0.001*	0.021*	0.002*	0.001*	0.063*	0.012*

Table 1. A correlation between HbA1c level and MSU or LPS-stimulated monocyte cytokine or chemokine production was assessed in participants prior to the intervention. The pro-inflammatory cytokines IL-1 β , IL-6, and TNF α were significantly positively correlated with HbA1c level whereas IL-17 and the chemokines IP-10 and MCP were negatively correlated with HbA1c level.

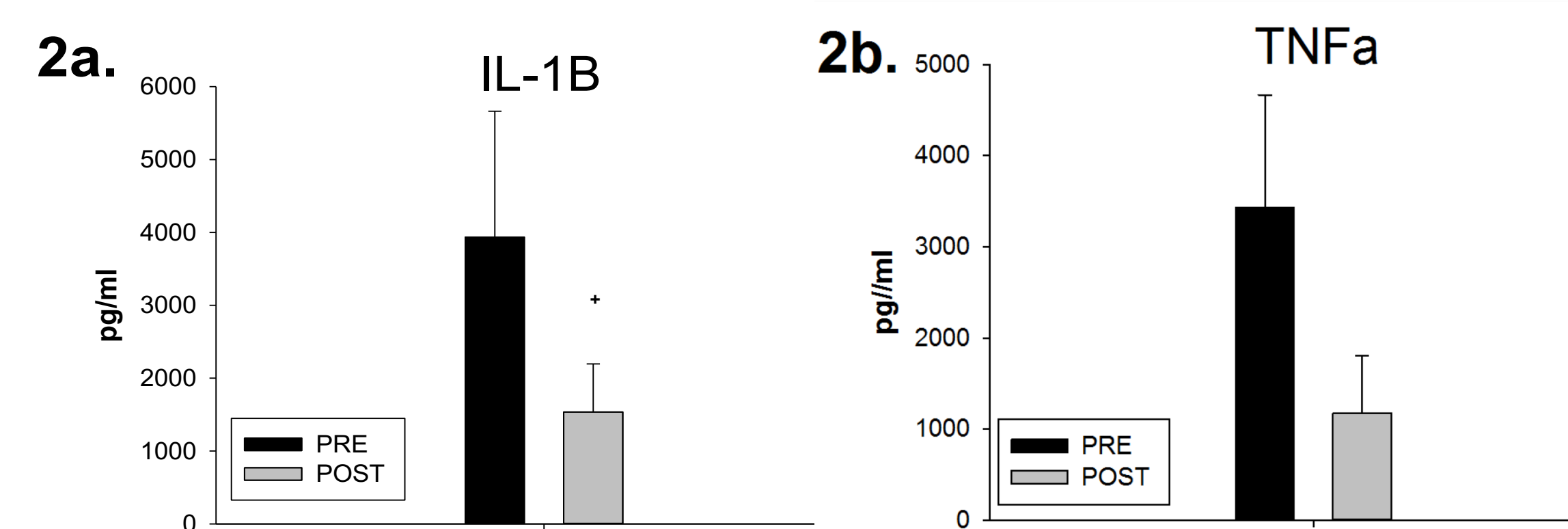


Figure 2. LPS-induced monocyte production of proinflammatory cytokines showed a trend towards a decrease after the intervention (+ indicates p < 0.10, n=9)

Results

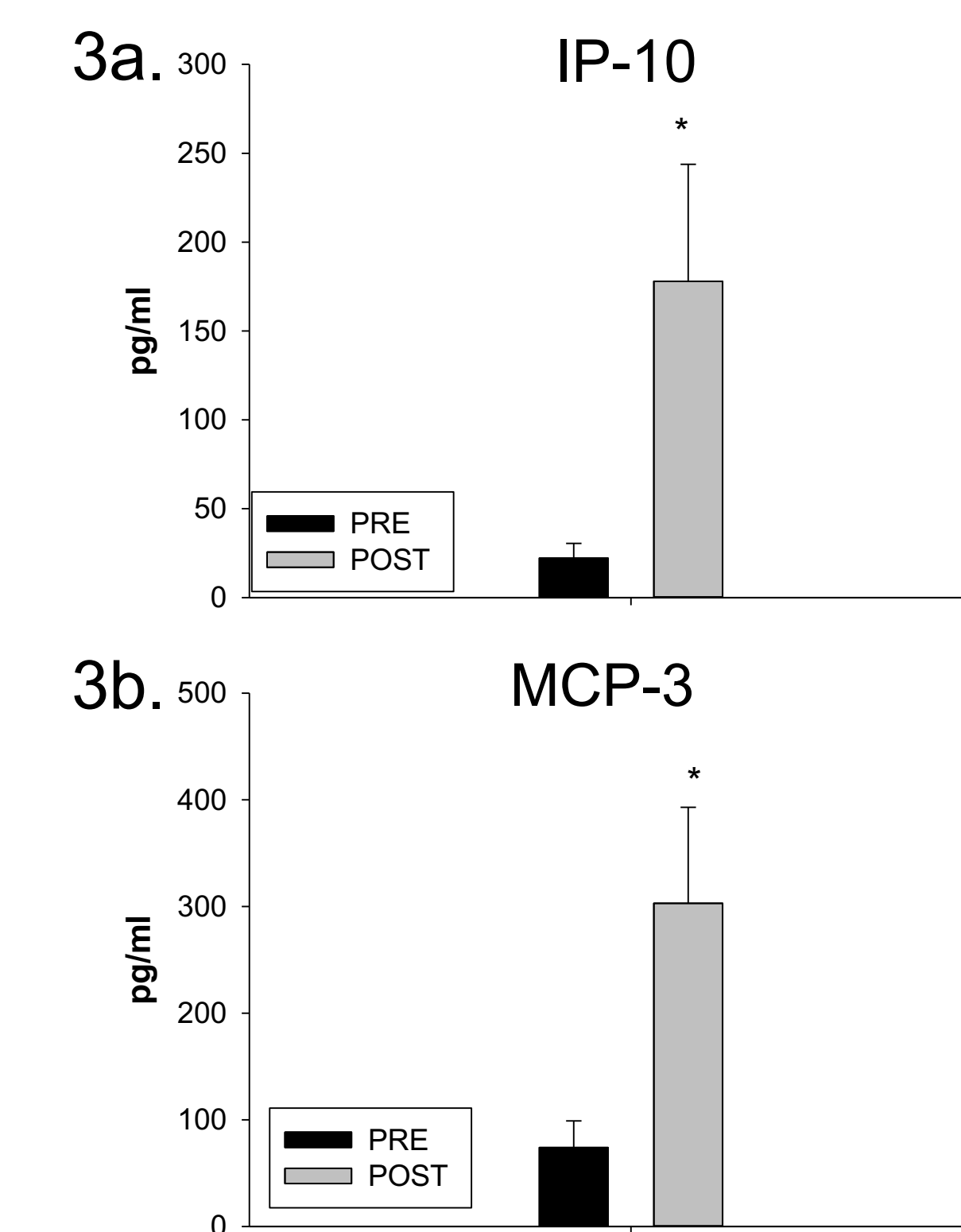


Figure 3. LPS-induced monocyte production of chemokines IP-10 and MCP3 was significantly greater after the intervention. * p < 0.05 (n=9)

Table 2. Ratio of inflammatory to anti-inflammatory cytokines

Inflammatory / Anti-inflammatory Ratio	PRE	POST
IL-1B/IL10 LPS-stimulated	172.9	29.8*
IL-1B/IL10 MSU-stimulated	156.7	15.9*

Table 2. The calculated ratio of pro-inflammatory cytokine IL-1B to anti-inflammatory cytokine IL-10 shows a decrease from the pre to post-time point (p < 0.05). This finding occurred when monocytes were stimulated with either LPS or MSU.

Conclusions

- HbA1c was significantly correlated with greater monocyte-stimulated pro-inflammatory cytokine production, providing additional support to existing studies showing an association between inflammation and HbA1c. To our knowledge, this study is the first to demonstrate this association in monocytes obtained from a Mexican immigrant population.
- Following the Abriendo Caminos intervention, HbA1c decreased significantly. However, a decline was also observed in the control group. It is possible that control participants also modified lifestyle practices as they were aware of their participation in the research study. Additional analysis will be needed to evaluate the extent to which the control group may have changed exercise and/or diet.
- Although a control comparison group is needed, the finding from this study suggest that the Abriendo Caminos intervention may reduce activation of inflammatory pathways in monocytes, potentially resulting in reduced risk of diabetes as demonstrated by reduced HbA1c.
- To our knowledge, there have not been previous reports of a negative correlation between chemokines IP-10, MCP3 and HbA1c level. These findings warrant further investigation as it is possible that these chemokines have a protective role.

References

- ¹National Center for Chronic Disease Prevention and Health Promotion, Division of Diabetes Translation (2017). *National Diabetes Statistics Report, 2017*. [online] National Center for Chronic Disease Prevention and Health Promotion, Division of Diabetes Translation, pp.2-7.
- ²Cefalu WT. Inflammation, insulin resistance, and type 2 diabetes: back to the future? *Diabetes*. 2009, 58 (2):307-08.
- ³Dixit VD. Nlrp3 inflammasome activation in type 2 diabetes: is it clinically relevant? *Diabetes*. 2013, 62 (1):22-24.
- ⁴McCurley JL, Gutierrez AP, Gallo LC. Diabetes prevention in U.S. Hispanic adults: a systematic review of culturally tailored interventions. *Am J Prev Med*. 2017, 52 (4):519-29.