Brazilian Journal of

OTORHINOLARYNGOLOGY

www.bjorl.org

ORIGINAL ARTICLE

Glucose metabolism disorders and vestibular manifestations: evaluation through computerized dynamic posturography ☆

Roseli Saraiva Moreira Bittar [a,*], Maruska D'Aparecida Santos [a], Raquel Mezzalira [b]

[a] *Department of Otoneurology, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (FM-USP), São Paulo, SP, Brazil*
[b] *Department of Otorhinolaryngology, Head and Neck Surgery, Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil*

Abstract

Introduction: Global sugar consumption has increased in the past 50 years; its abusive intake is responsible for peripheral insulin resistance, which causes the metabolic syndrome – obesity, diabetes mellitus, hypertension, and coronary heart disease.

Objective: To evaluate the effect of a fractionated diet without glucose as treatment for labyrinthine disorders associated with glucose–insulin index.

Methods: The study design was a prospective randomized controlled trial. Fifty-one patients were divided into two groups: the diet group (DG), which comprised subjects treated with a fractionated diet with glucose restriction, and the control group (CG), in which individuals were not counseled regarding diet. Patients underwent computerized dynamic posturography (CDP) and visual analog scale (VAS) on the first and 30th days of the study.

Results: There was improvement in the assessed posturographic conditions and VAS self-assessment in the DG group after 30 days when compared to the control group.

Conclusion: The fractionated diet with glucose restriction was effective for the treatment of vestibular dysfunction associated with glucose metabolism disorders.

© 2015 Associação Brasileira de Otorrinolaringologia e Cirurgia Cérvico-Facial. Published by Elsevier Editora Ltda. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Distúrbios do metabolismo da glicose e manifestações vestibulares: avaliação pela posturografia dinâmica computadorizada

Resumo

Introdução: O consumo mundial de açúcar triplicou nos últimos 50 anos e a sua ingesta abusiva é responsável pela resistência periférica à insulina que origina a síndrome metabólica – obesidade, *diabetes mellitus*, hipertensão arterial e doenças coronarianas.

Objetivo: Avaliar de forma objetiva o efeito da dieta fracionada e sem glicose como forma de tratamento dos distúrbios labirínticos associados às alterações da curva glicoinsulinêmica.

Método: Trata-se de um ensaio clínico controlado randomizado prospectivo. Estudo realizado com 51 pacientes divididos em dois grupos: Grupo Dieta composto por indivíduos tratados com dieta fracionada com restrição de glicose e Grupo Controle no qual os indivíduos não foram orientados em relação à dieta. Os pacientes realizaram Posturografia Dinâmica Computadorizada e Escala Análogo Visual no primeiro e trigésimo dias do estudo.

Resultados: Foi observada melhora nas condições posturográficas avaliadas e melhora clínica do grupo dieta na análise da escala análogo visual quando comparados grupo dieta e grupo controle.

Conclusão: A dieta fracionada e restritiva de glicose mostrou-se eficaz no tratamento das disfunções vestibulares associadas aos distúrbios do metabolismo da glicose.

Introduction

Global sugar consumption has tripled in the past 50 years, and its abusive intake is responsible for peripheral insulin resistance, which leads to the metabolic syndrome – obesity, diabetes mellitus, hypertension, and coronary heart disease.[1,2] An estimated 40% of individuals with weight considered normal develop some form of metabolic syndrome, as a result of glucose consumption.[3] According to the same authors, in the United States the situation has become a matter of national security, as young individuals are becoming increasingly obese and unfit for military service.

The significance of glucose metabolism disorders (GMD) can be observed in otoneurology when their high prevalence is observed in patients with labyrinth disorders.[4] It is estimated that between 30% and 90% of patients with dizziness have altered levels of blood glucose and insulin.[5–8] In recent years, several authors have investigated GMD as a cause of inner ear dysfunctions.[4,5,7,9,10] Moreover, vestibular dysfunction has been described as a new complication of diabetes and acts as a potentiating risk factor for falls in these patients.[11]

Based on the above observations, it was decided to assess the postural performance of patients with dizziness and a clinical history of GMD after a fractionated diet with glucose restriction, in order to test the hypothesis that this diet is effective in the treatment of vestibular dysfunctions associated with this condition. The aims of this study included:

1. Assess the posturography conditions on a moving platform (conditions 4, 5, 6) and the composite score in patients with body balance disorders and glucose metabolism alterations before and after a fractionated diet with glucose restriction for 30 days.

2. Assess the impact of the fractionated diet with carbohydrate restriction on the quality of life of patients with body balance disorders and glucose metabolism alterations using the visual analog scale (VAS).

Methods

This was a prospective, randomized, controlled clinical trial, previously approved by the Research Ethics Committee of the institution (No. 482/05) and registered in the Clinical Trial Protocol Registration System (NTC 02,226,536). All participants in the study signed the informed consent.

The study subjects were adults older than 18 years. They underwent all the necessary examinations to attain a final diagnosis of vestibular disorder: audiometry, videonystagmography, electrophysiological tests, and imaging tests when needed. Among these, individuals with dizziness related to food (fasting and/or after sugar intake) and who had an altered three-hour glucose tolerance test, namely: blood glucose $\leq$ 55 mg/dL; and/or blood glucose between 145 and 199 mg/dL in the second hour of the test and/or; sum of insulin levels of the second and third hours >60 U/mL were selected for study.[12–15]

Patients with complaints non-attributable to the vestibular system, orthopedic or neurological disorders that might interfere with the computerized dynamic posturography (CDP), and diabetic patients according to the American Diabetes Association (2010 and 2011) were not included in the study.[13,14]

Patients diagnosed with vestibular disorders such as Meniere's disease (anamnesis supported by the American Academy criteria) were also not included in the study.

Non-vestibular dizziness symptoms are those without labyrinthine characteristics (such as those related to

movement or vertigo), such as: syncope, visual darkening, ataxia, light headedness, head pressure.

There were no patient exclusions.

The sample consisted of 51 patients, 42 females and nine males, divided into two groups:

1. Diet Group (DG): 26 individuals who received a fractionated diet every three hours with sugar restriction.
2. Control Group (CG): 25 individuals who kept their regular diet. There were no dietary restrictions.

Patients were always randomized by the same examiner, according to the numerical order of arrival at the service. Both groups were instructed to ingest a corn starch tablet (placebo) twice a day, which was delivered by the investigator at the start of the intervention.

All study subjects were asked about the clinical characteristics of their dizziness. To quantify self-perception of body balance, the subjects answered using a VAS, in which zero meant no dizziness and ten meant the worst possible dizziness. Postural assessment was conducted by CDP through a sensory organization test (SOT), Equitest System® version 4.0 (NeuroCom Internacional – United States).

Both the VAS and the SOT were carried out at two moments of the study: the first day (D1) and after 30 days, when the dietary intervention ended (D30).

After 30 days, patients in both groups delivered the package with the placebo tablets so that the examiner could observe whether the tablets had been ingested. Adherence to the proposed dietary treatment was investigated through the question: ''Did you follow the daily diet as indicated?''

Statistical analysis

The primary variables considered were the posturographic conditions C4, C5, and C6 (conditions 4, 5, 6, which are platform-oscillating conditions) and composite score (CS), to assess the impact of vestibular responses and their effect on the final postural maintenance.[4,16–18] VAS responses were also considered, characterizing the self-perception of treatment impact on early symptoms.

For the statistical analysis the following tests were used:

- Chi-squared tests.[19]
- Student's t-test.[19]
- Fisher's exact test.[20]
- Cochran's test.[19]
- Analysis of variance (ANOVA).[19]
- Tukey's test.[19]

Results

Sample characterization

The DG consisted of 26 subjects, mean age of 45.8 ± 11.3 years. The CG consisted of 25 patients, mean age of 52 ± 13.7 years. Forty-two patients (82.4%) were females and nine males (17.6%). The values found showed normal distribution. When compared by the Student's t-test and Fisher's exact test, the groups were homogeneous regarding gender distribution ($p = 0.948$) and age ($p = 0.086$).

Table 1 C4 values in DG and CG on day one and day 30.

C4 Group	Day one Mean ± SD	Day 30 Mean ± SD	p-Value
Diet	69.24 ± 15.21	77.09 ± 9.73	0.0128
Control	62.30 ± 14.50	61.94 ± 15.22	0.9991
p-Value	0.0420	0.0002	

C4, condition 4 of posturography; DG, diet group; CG, control group.

Table 2 C5 values in the DG and CG on day one and day 30.

C5 Group	Day one Mean ± SD	Day 30 Mean ± SD	p-Value
Diet	42.75 ± 23.68	59.87 ± 16.99	0.0015
Control	44.91 ± 19.06	43.15 ± 17.29	0.9804
p-Value	0.9616	0.0028	

C5, condition 5 of posturography; DG, diet group; CG, control group.

Table 3 C6 values in the DG and CG on day one and day 30.

C6 Group	Day one Mean ± SD	Day 30 Mean ± SD	p-Value
Diet	41.17 ± 18.03	55.23 ± 15.95	0.0024
Control	45.65 ± 18.03	46.93 ± 14.66	0.9874
p-Value	0.6370	0.1390	

C6, condition 6 of posturography; DG, diet group; CG, control group.

Regarding the clinical characterization of dizziness and the results of the glucose tolerance test, the chi-squared and Cochran tests were used. The most common types of dizziness were floating (70.5%) and the feeling of imbalance (60%). The most frequent laboratory diagnosis was hyperinsulinemia, present in 76.47% of cases. Hypoglycemia occurred in 21.56% of the sample.

The ANOVA test was applied to assess variables C4, C5, C6, CS, VAS, and Tukey's multiple comparisons, which identified the significant differences.[19] When comparing posturographic conditions before and after the diet period, there was significant improvement in the DG in relation to the CG in all of them, as shown in Tables 1–4.

Table 4 CS values in the DG and CG on day one and day 30.

CS Group	Day one Mean ± SD	Day 30 Mean ± SD	p-Value
Diet	64.28 ± 11.37	73.44 ± 8.80	0.0002
Control	64.55 ± 9.62	63.95 ± 10.61	0.9838
p-Value	0.9984	0.0002	

CS, composite score; DG, diet group; CG, control group.

Table 5 VAS values in the DG and CG on day one and day 30.

VAS Group	Day one Mean ± SD	Day 30 Mean ± SD	p-Value
Diet	7.78 ± 1.75	4.04 ± 3.73	0.0002
Control	7.38 ± 2.10	6.50 ± 3.15	0.5913
p-Value	0.9347	0.0044	

VAS, visual analog scale; DG, diet group; CG, control group.

A significant improvement was observed in VAS in the DG on day 30 when compared to the first day of the study (p = 0.0002) and when compared to the CG (p = 0.0044). The results are shown in Table 5.

Discussion

The majority of the assessed cases (82.4%) belonged to the female gender, similarly to what is found in the literature. Hormonal changes in women between the fourth and fifth decades of life mark the onset of climateric period, whose manifestations may include water retention and metabolic and anxiety disorders.[4,21–23] In this age group, GMD acts as a migraine trigger and can also be responsible for triggering postural disorders.[21,24]

Anamnesis is crucial for the diagnosis of dizziness of metabolic origin, including GMD. The characteristics found in this sample do not differ from those in the literature; the most prevalent symptom was floating-type dizziness in 70.5% of patients, followed by imbalance in 60% of cases.[4]

The glucose tolerance test is considered the most important diagnostic tool in the assessment of patients with dizziness and GDM.[6,25,26] When the most frequently observed alterations are evaluated, the present results are not dissimilar from those found in the literature, and hyperinsulinemia was the most common abnormality, observed in 76.47% of cases.[10,21,27,28] Clinical trials have shown that the fractionated diet with glucose restriction plays an important role in the treatment of patients with GMD.[1,29,30] Therefore, it was decided use a diet that was fractionated every three hours, together with glucose restriction.

The literature reports the importance of the placebo effect in clinical studies that propose the validation of a certain treatment.[31,32] Approximately 35% of cases show a positive placebo response, because they generate biological phenomena that mimic pharmacological effects.[33,34] The placebo was intentionally administered to both groups so that patients would feel treated and followed by the researcher. This fact allows one to exclude the diet as a potential placebo, and instead consider that the diet was the factor responsible for the improvement of the patients assessed in the DG. Interestingly, even when explaining it to the research subjects, only one of them questioned the use of a pill containing no therapeutic effect.

At baseline, a better numeric performance in C4 of the DG when compared to the CG (p = 0.042) was observed. At the end of the study, the difference found between the groups at baseline increased to a highly significant value (p = 0.0002). The values can be attributed to improvement in vestibular-visual integration after the diet. There was a

significant improvement in the DG values on the 30th day when compared to the first measurement of C5 at baseline (p = 0.0015). Still in C5, the better vestibular performance of the DG (p = 0.0028) when compared to the CG (p = 0.9804) can be clearly observed on the 30th day of the study. As for C6, an improvement was also verified regarding the values observed on the 30th study day in the DG (p = 0.0024).

In relation to the CS, the DG results on the 30th day of the study were higher than the measures obtained on the first day (p = 0.0002), as they were also higher on the 30th day when compared to the CG (p = 0.0002).

The results demonstrate better postural performance in the DG attributed to the effect of diet on vestibular function of the subjects. Thus, this study reproduced the findings of Bittar et al. (2004),[4] who used CDP to document postural recovery improvement in patients with GMD submitted to a fractionated diet with glucose restriction.

The purpose of the VAS was to evaluate the self-perception of symptom discomfort and quantify their subjective evolution as a result of the followed diet.[31,35] A significant improvement was observed regarding the level of discomfort only in DG patients after 30 days of diet (p = 0.0002), as well as compared to the CG (p = 0.0044) in the same period. Therefore, it can be inferred that the diet had a positive influence on the self-perception of dizziness.

Conclusion

Mobile posturography, CS, and VAS showed significantly better values in patients submitted to 30 days of fractionated and glucose-restricted diet when compared to the Control Group.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Fukuda Y. Insulina, receptor de insulina e glucagon. In: Fukuda Y, editor. Açúcar: amigo ou vilão? São Paulo: Manole; 2004. p. 59–66.
2. Rask-Madsen C, King GL. Mechanisms of disease: endothelial dysfunction in insulin resistance and diabetes. Nat Clin Pract Endocrinol Metab. 2007;3:46–56.
3. Lustig RH, Schimidt LA, Brindis CD. The toxic truth about sugar. Nature. 2012;482:27–9.
4. Bittar RSM, Bottino MA, Simoceli L, Venosa AR. Labirintopatia secundária aos distúrbios do metabolismo do açúcar: realidade ou fantasia? Braz J Otorhinolaryngol. 2004;70:800–5.
5. Powers WH. Metabolic aspects of Ménière's disease. Laryngoscope. 1978;88:122–9.
6. Proctor CA, Oak R. Abnormal insulin levels and vertigo. Laryngoscope. 1981;91:1657–75.
7. Lehrer JF, Poole DC, Seaman M, Restivo D, Hartman K. Identification and treatment of metabolic abnormalities in patients with vertigo. Ann Intern Med. 1986;146:1497–500.
8. Knight LC, Saeed SR, Hradek GT, Schindler RA. Insulin receptors on the endolymphatic sac: an autoradiographic study. Laryngoscope. 1995;105:635–8.
9. Pillsbury HC. Metabolic causes of hearing loss and vertigo. Otolaryngol Clin North Am. 1981;14:347–54.

10. Rybak LP. Metabolic disorders of the vestibular system. Otolaryngol Head Neck Surg. 1995;112:128–32.
11. Agrawal Y, Carey JP, Santina CCD, Schubert MC, Minor Lloyd B. Diabetes, vestibular dysfunction, and falls: analyses from the National Health and Nutrition Examination Survey. Otol Neurotol. 2010;31:1445–50.
12. Kraft JR, Nosal A. Insulin values and diagnosis of diabetes. Lancet. 1975;305:637.
13. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33:62–9.
14. Basevi V, Di Mario S, Morciano C, Nonino F, Magrini N. Comment on: American Diabetes Association standards of medical care in diabetes: 2011. Diabetes Care. 2011;34:11–61.
15. The Endocrine Society. Workup for a hypoglycemic disorder. The Endocrine Society's: clinical/guidelines. J Clin Endocrinol Metab. 2009;94:709–28.
16. Di Fabio RP. Meta-analysis of the sensitivity and specificity of platform posturography. Arch Otolaryngol Head Neck Surg. 1996;122:150–6.
17. Ruckenstein MJ, Shepard NT. Balance function testing: a rational approach. Otolaryngol Clin North Am. 2000;33:507–18.
18. Owen BF. What can posturography tell us about vestibular function? Ann N Y Acad Sci. 2001;942:446–64.
19. Maxwell DL, Satake E. Research and statistical methods in communication disorders. Baltimore: Williams & Wilkins; 1997.
20. Magalhães MN, Lima ACP. Noções de probabilidade e estatística. São Paulo: Edusp; 2000.
21. Mangabeira-Albernaz PL, Fukuda Y. Glucose, insulin and inner ear pathology. Acta Otolaryngol. 1984;97:496–501.
22. Fonseca AS, Davidson SAV. Correlação entre tontura e disfunções do metabolismo da glicose. Braz J Otorhinolaryngol. 2006;72:367–9.
23. Oiticica J, Bittar RSM. Metabolic disorders prevalence in sudden deafness. Clinics (São Paulo). 2010;65:1149–53.
24. Sacco S, Ricci S, Degan D, Carolei A. Migraine in women: the role of hormones and their impact on vascular diseases. J Headache Pain. 2012;13:177–89.
25. Vexiau P, Legoff B, Cathelineau G. Insulin and cortisol secretion during OGTT in patients with reactive hypoglycaemia with or without clinical symptoms. Horm Metab Res. 1983;15:419–21.
26. Serra AP, Lopes KC, Dorigueto RS, Ganança FF. Avaliação da curva glicoinsulinêmica nos pacientes com vestibulopatia periférica. Braz J Otorhinolaryngol. 2009;75:701–5.
27. Lavinsky L, Oliveira MW, Bassanesi HJ, D'Avila C, Lavinsky M. Hyperinsulinemia and tinnitus: a historical cohort. Int Tinnitus J. 2004;10:24–30.
28. Kim SH, Reaven GM. Insulin resistance and hypersulinemia: you can't have one without the other. Diabetes Care. 2008;31:1433–8.
29. Spencer JTJ. Hyperlipoproteinemia, hyperinsulinism and Ménière's disease. South Med J. 1981;74:1194–200.
30. Brun JF, Fedou C, Mercier J. Postprandial reactive hypoglycemia. Diabetes Metab. 2000;26:337–51.
31. Colloca L, Petrovic P, Wager TD, Ingvar M, Benedetti F. How the number of learning trials affects placebo and nocebo responses. Pain. 2010;151:430–9.
32. Avins LA, Cherkin DC, Sherman KJ, Goldberg H, Pressman A. Should we reconsider the routine use of placebo controls in clinical research? Trials. 2012;13:44.
33. Finness DG, Katchuk TJ, Miller F, Benedetti F. Placebo effects: biological, clinical and ethical advances. Lancet. 2010;375:686–95.
34. Benedetti F. The placebo response: science *versus* ethics and the vulnerability of the patient. World Psychiatry. 2012;11:70–2.
35. Kammerlind AS, Ledin TEA, Odkvist LM, Skargren EIB. Recovery after acute unilateral vestibular loss and predictors for remaining symptoms. Am J Otolaryngol. 2011;32:366–75.