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SANDRA MARIA ABREU NOGUEIRA

INFLUÊNCIA DE UMA DIETA LIVRE DE GLÚTEN NA SENSIBILIDADE À DOR DE MULHER COM DISFUNÇÃO TEMPOROMANDIBULAR: RELATO DE CASO

FORTALEZA

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Trabalho de Conclusão de Curso (TCC) apresentado ao Curso de Odontologia da Faculdade de Farmácia, Odontologia e Enfermagem (FFOE) da Universidade Federal do Ceará, como requisito parcial à obtenção do título de Bacharel em Odontologia.

Orientadora: Lívia Maria Sales Pinto Fiamengui

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BANCA EXAMINADORA

_____

Profa. Dra. Lívia Maria Sales Pinto Fiamengui (Orientadora)

Universidade Federal do Ceará (UFC)

_____

Profa. Dra. Karina Matthes de Freitas Pontes (Coorientadora)

Universidade Federal do Ceará (UFC)

_____

Mestranda Juliana Araújo Oliveira

Universidade Federal do Ceará (UFC)

_____

Mestranda Tereza Nicolle Burgos Nunes

Universidade Federal do Ceará (UFC)

À Deus.

Aos meus pais, Célia e Ronaldo.

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APRESENTAÇÃO

Este Trabalho de Conclusão de Curso (TCC) está de acordo com o formato alternativo para TCCs e encontra-se sob o formato de artigo científico, seguindo as normas da revista “Special Care in Dentistry”.

RESUMO

A ligação entre hábitos alimentares e doenças dolorosas crônicas tem se tornado cada vez mais consistente e a eliminação do glúten da dieta de pacientes com essas desordens está se tornando uma intervenção com alto potencial para melhora clínica. O objetivo deste relato é demonstrar a redução do quadro de dor secundária a Disfunção Temporomandibular (DTM) após intervenção com uma Dieta Livre de Glúten (DLG) em mulher com dor miofascial da musculatura mastigatória e artralgia da Articulação Temporomandibular (ATM), com queixa geral descrita como 9 na Escala Visual Analógica (EVA). Foram realizados os seguintes Testes Sensoriais Quantitativos (TSQ): Teste de Sensibilidade Tátil (TST), Limiar Doloroso Mecânico (LDM), Limiar de Dor à Pressão (LDP), Somação Temporal (ST) e Modulação da Dor Condicionada (MDC), a fim de fornecer dados para a avaliação do paciente e também quantificar os efeitos do tratamento. Após um mês de intervenção com DLG, a paciente relatou uma considerável melhora da dor (1 na EVA) e foi reavaliada por TSQ. Houve aumento nos valores de LDD e LDP, indicando redução na sensibilidade à dor. A ST diminuiu e o MDC melhorou, indicando uma redução na sensibilização central e melhora na modulação da dor. A redução da hiperexcitabilidade do Sistema Nervoso Central, também, foi observada pelo aumento dos valores do LDP em todos os sítios avaliados e pela melhora nos valores da MDC. Este caso leva a crer que, quando o glúten é retirado da dieta, indivíduos com DTM podem experimentar redução da dor. A DLG parece ser um tratamento promissor para o manejo da DTM.

Palavras-chave: Transtornos da Articulação Temporomandibular, Dieta Livre de Glúten, Limiar da Dor.

ABSTRACT

The relationship between dietary habits and chronic painful disorders has become increasingly consistent, and a Gluten Free Diet (GFD) has been recognized as an intervention with high potential of clinical improvement. The present study aimed to do a case report of Temporomandibular Disorders (TMD) pain remission after treatment with a GFD of woman with myofascial pain of masticatory muscles and Temporomandibular Joint (TMJ) arthralgia. Quantitative Sensory Testings (QST), such as Mechanical Detection Threshold (MDT), Mechanical Pain Threshold (MPT), Pressure Pain Threshold (PPT), Wind-up ratio (WUR) and Conditioned Pain Modulation (CPM) were performed in order to evaluate patient´s pain mechanisms and also to quantify treatment effects. After 1 month of GFD intervention, the patient reported a considerable pain reduction. MPT and PPT values increased, indicating reduction on pain sensitivity, while WUR reduced and CPM improved, indicating a reduction on central sensitization and improvement on pain modulation. This case leads to believe that when gluten is withdrawal from the diet, individuals with TMD may experience pain reduction. GFD seems to be a promising treatment for TMD management.

Keywords: Temporomandibular Joint Disorders, Gluten-free Diet, Pain Threshold.

LISTA DE TABELAS

LISTA DE ABREVIATURAS E SIGLAS

CD	Celiac Disease
cm^2	Square centimetre
CNS	Central Nervous System
CPM	Conditioned Pain Modulation
CS	Conditioning Stimulus
GFD	Gluten Free Diet
g/mm^2	Gram square millimeter
IFN	Interferon
IL	Interleukin
kgf/cm^2	Kilogram-force per square centimetre
MCP -1	Monocyte Attractant Protein-1
MDT	Mechanical Detection Threshold
MPT	Mechanical Pain Threshold
PPT	Pressure Pain Threshold
QST	Quantitative Sensory Testings
RDC/DTM	Research Diagnostic Criteria for Temporomandibular Disorders
TMD	Temporomandibular Disorders
TMJ	Temporomandibular Joint
TNF	Tumor Necrosis Factor
VAS	Visual Analogue Scale
WHO	World Health Organization
WUR	Wind-up ratio

SUMÁRIO

INFLUENCE OF A GLUTEN FREE DIET ON PAIN SENSITIVITY OF A WOMAN WITH TEMPOROMANDIBULAR DISORDERS: A CASE REPORT

Sandra Maria Abreu Nogueira[a,1], Maria Thereza Carvalho de Magalhães Avelar [c,3], Lívia Maria Sales Pinto Fiamengui [b,2].

1 Faculty of Pharmacy, Dentistry and Nursing, Federal University of Ceará, Fortaleza-Ce, Brazil.

2 Department of Restorative Dentistry, Federal University of Ceará, Fortaleza-Ce, Brazil

3 Ceará State University, Fortaleza-Ce, Brazil

a Undergraduate student

b Professor

c Nutritionist

*Corresponding Author's Information:

Sandra Maria Abreu Nogueira

Rua Carlos Vasconcelos, 146 ap 600 – Meireles, Fortaleza-Ce, Brasil. CEP: 60115170

Phone: +55 85 999180012

Email:**sanddraman@hotmail.com**

INTRODUCTION

The relationship between dietary habits and chronic painful disorders has become increasingly consistent in the past few years, and a Gluten Free Diet (GFD) has been recognized as an intervention with high potential of clinical improvement[1-5].

Gluten is a protein complex found in grains such as wheat, rye and barley[5] and has been identified as a substance with pro-inflammatory activity[1-5]. Due to its high content of proline and glutamine, gluten is not completely digested in the gastrointestinal tract, increasing the concentration of peptides resistant to enzymatic cleavage in the intestinal lumen[3]. Those peptides may exacerbate intestinal permeability, triggering immune response[6] and causing inflamattion[7] that could reach other tissues[8].The effects of a GFD has been studied not only in celiac subjects, but also in individuals with chronic painful disorders, such as rheumatoid arthritis[9], fibromyalgia[10,11], cephalalgias[12] and irritable bowel syndrome[13].

Temporomandibular Disorders (TMD) are considered the most common cause of chronic orofacial pain[14]. Individuals with TMD show high levels of inflammatory mediators in masticatory muscles[15] and/or Temporomandibular Joint (TMJ)[16] and are predisposed to develop central sensitization[17].

Conservative treatment modalities for TMD management are several and include self-management strategies, manual therapies, exercises, occlusal splint, pharmacotherapy, counseling and others[18,19]. Their objective are mainly pain remission and function improvement due to peripheral and central sensitization reduction. Diet habits modifications may also play an important role as an additional conservative treatment modality, not only regarding food hardness, but also its composition[20]. In this scenario, GFD for individuals with TMD seems to be a promising treatment.

So, the aim of the present study was to report a case of TMD pain reduction after a GFD intervention of woman with myofascial pain of masticatory muscles and TMJ arthralgia.

CASE REPORT

A 34 years-old normossemic female attended to Orofacial Pain service of the Faculty of Pharmacy, Dentistry and Nursery, Federal University of Ceara (Fortaleza, Ceara - Brazil) with the chief complain of bilateral pain on both masticatory muscles and TMJ, described as 9 on a Visual Analogue Scale (VAS) graded from 0 to 10, for at least 7 years.

According to Research Diagnostic Criteria for Temporomandibular Disorders (RDC/DTM) - axis I, she was diagnosed with myofascial pain, TMJ arthralgia and disc displacement with reduction. The patient also had self-report of awake and sleep bruxism. Quantitative Sensory Testings (QST), such as Mechanical Detection Threshold (MDT), Mechanical Pain Threshold (MPT), Pressure Pain Threshold (PPT), Wind-up ratio (WUR) and Conditioned Pain Modulation (CPM) were performed in order to provide patient´s pain mechanisms[21] and also to quantify treatment effects[22].

MDT and MPT were performed in order to evaluate A-beta and A-delta fibers[23]. Both testes were made over masseter (body) muscle and thenar eminence using von Frey nylon filaments (North Coast, Gilroy, CA, USA), following the guidelines and recommendations for assessment of somatosensory function in orofacial pain conditions[24]. WUR evaluations were performed on the same areas using a 26g/mm^2 von Frey nylon filament, according to Costa et al (2017) proposed protocol[25].

PPT is defined as the minimal amount of pressure that can cause discomfort or pain[26]. PPT determination was carried out using a digital algometer (KRATOS, Cotia, Brazil) containing a 1cm^2 circular flat tip, which was used to apply the pressure, bilaterally, over masseter (body) muscles, anterior temporalis, TMJ and thenar eminence. Each area was tested twice and a mean value was obtained[27].

CPM was performed on the same areas, except for thenar eminence. During 1 minute, the dominant hand was immersed to the wrist on a cold water bath between 8° and 10°, controlled by a thermostat, which was the Conditioning Stimulus (CS). After 1 minute of hand immersion, and still so, another PPT measurement was performed. CPM value was considered the difference between PPT before and during CS[25].

The proposed treatment was self-management programs, GFD, occlusal splint, pharmacotherapy, physiotherapy and acupuncture. Initially, in order to evaluate the influence of GFD alone, it was suggested a 1month of GFD prescribed by a nutritionist. Previous to dietetic intervention, a complete nutritional evaluation was done in order to exclude any type of food intolerance, including signs and symptoms of gluten intolerance, sensitivity or allergy.

This case was conducted according to Helsinque II declaration. Before any procedure or intervention, the patient read and signed an informed consent.

After 1 month of GFD intervention, the patient reported a considerable pain reduction (9 to 1 on VAS) and was reevaluated through QST. Next, due to remaining complains, a conservative treatment protocol based on GFD, self-management programs and occlusal splint was prescribed.

MDT and MPT values before and after treatment are shown on the table below. After GFD intervention, MPT values increased. However, there was only a slight increase on MDT for masseter muscle and a decrease for thenar eminence for the same test.

Table1 – MDT and MPT mean values(g/mm²) and standard deviation on masseter muscle and thenar eminence before and after GFD intervention.

	MDT		**MPT**	
	Before GFD	After GFD	Before GFD	After GFD
Masseter (body)	0.017 (±0.005)	0.025 (±0.003)	2.404 (±1.582)	27.620 (±12.242)
Thenar eminence	0.229 (±0.160)	0.113 (±0.010)	6.070 (±0.594)	68.162 (±26.813)

Abbreviations: GFD, Gluten Free Diet; MDT, Mechanical Detection Threshold; MPT, Mechanical Pain Threshold.

WUR tests are important in order to evaluate the endogenous modulatory system and central sensitization process[28]. Results presented in table 2 suggest WUR improvement after GFD, showing evident result for masseter muscle.

Table 2 – WUR mean values and standard deviation for masseter muscle and thenar eminence before and after GFD.

	WUR	
	Before GFD	After GFD
Masseter (body)	4.53 (±0.54)	2.94 (±0.79)
Thenar eminence	4.13 (±2.07)	3.95 (±0.21)

Abbreviations: GFD, Gluten Free Diet; WUR, Wind-up ratio.

PPT mean values, standard deviation and the difference before and after GFD treatment expressed in kgf/cm^2 are presented on table 3. It is able to notice increased PPT values for all sites tested.

Table 3 – PPT mean values (kgf/cm²), standard deviation and PPT difference before and after GFD.

PPT	Before GFD	After GFD	Difference
Anterior Temporalis	0.503 (±0.095)	1.630 (±0.141)	1.128(±0.797)
Masseter (body)	0.388(±0.077)	0.963(±0.028)	0.575(±0.407)
TMJ	0.500(±0.028)	1.185(±0.025)	0.685(±0.484)
Thenar eminence	1.116 ±0.178)	2.371(±0.451)	1.255(±0.887)

Abbreviations: GFD, Gluten Free Diet; PPT, Pressure Pain Threshold; TMJ, Temporomandibular Joint.

PPT values before and during the conditioning stimulus and CPM values are shown on table 4. After treatment, CPM improved.

Table 4 – PPT mean values (kgf/cm²) and standard deviations, before and during CS, and CPM values before and after GFD.

	Before GFD				After GFD			
	PPT	PPT+CS	CPM (%)	CPM	PPT	PPT+CS	CPM (%)	CPM
Anterior Temporalis	0.503 (±0.09)	0.607 (±0.123)	20.67%	-0.105 (±0.219)	1.630 (±0.14)	2.070 (±0.021)	26.9%	-0.440 (±0.162)
Masseter (body)	0.388 (±0.07)	0.662 (±0.180)	70.6%	-0.275 (±0.102)	0.963 (±0.02)	1.210 (±0.091)	25.6%	-0.247 (±0.120)
TMJ	0.500 (±0.02)	0.682 (±0.017)	36.4%	-0.182 (±0.045)	1.185 (±0.02)	1.837 (±0.116)	55%	-0.652 (±0.091)

Abbreviations: CPM, Conditioned Pain Modulation; GFD, Gluten Free Diet; PPT, Pressure Pain Threshold; TMJ, Temporomandibular Joint.

DISCUSSION

Modern dietary patterns are considered risk factors for chronic painful diseases, and the World Health Organization (WHO) identifies nutrition as an important modifiable determinant[29]. In this context, the present case report aimed to evaluate the influence of a GFD prescribed by a nutritionist on chronic TMD pain complains and associated pain mechanisms.

In the present clinical case, a GFD was able to reduce pain from 9 to 1 on VAS. The assessment of somatosensory function provided important information about mechanisms underlying the patient's pain, such as hyperalgesia, pain modulation, and central sensitization[21].

MDT and MPT were performed to evaluate peripheral afferent fibers[24]. MDT results suggest a hypofunction of A-beta fibers[28]even after GFD intervention. The increase on MPT values, however, is suggestive of reduction on hyperalgesia and generalized hyperactivity for tactile stimulus related to A-delta and C fibers[28].

WUR evaluates Central Nervous System (CNS) hyper excitability. Temporal summation is obtained when repetitive noxious stimulus causes stimulation of afferent C fibers, spinal sensitization and increased pain perception[30]. When compared to values obtained from healthy individuals (2.07 for masseter muscle and 1, 53 for thenar eminence)[28], the patient exhibited heightened CNS excitability, which reduced after GFD intervention.

PPT measurement is a favorable method to determine central and peripheral sensitization and is used to evaluate deep pressure, conducted by A-delta and C afferent fibers from periphery to upper central system[24]. GFD produced an increase on PPT values for all sites tested, indicating a reduction on pain sensitivity on both trigeminal and extra trigeminal areas.

Previous studies determinated cutoff values to distinguish asymptomatic individuals from those presenting TMD. These values were 2.47 kgf / cm² for anterior temporalis[31], 1.5 kgf / cm² for masseter[31], 1.36 kgf / cm² for TMJ[32] and 3.56 kgf / cm² for thenar eminence[28]. GFD alone was able to reduce the patient´s pain complain and increase PPT values. However, according to those values, although the reduction on pain sensitivity after GFD, the patient is still considered symptomatic for TMD.

CPM evaluation verifies pain modulation produced by CNS inhibitory descending pathways[33]. The results found here suggest an efficient pain modulation system even before GFD, since the CPM values were negative. Previous studies suggest that there is not a consent

regarding how much PPT should improve during a CS to prove CPM to be considered significant. Locke et al. (2014), after evaluating healthy individuals, considered CPM to be significant when there was an increase of 5,3% on PPT[33]. On the other hand, Oono et al. (2013) suggested that the difference should be of 10% [35], while Dworkin et al. (2008) suggested that a 28% increase on PPT should be observed[34]. In the present study, CPM percentages were greater than 10% and improved after GFD.

To the best of our knowledge, there are no studies evaluating GFD as a potential treatment to TMD pain symptoms. There is evidence that patients with TMD have high levels of IL-1β, IL-6, IL-10, Tumor Necrosis Factor-alpha (TNF-α), IL-1ra and monocyte attractant protein-1 (MCP-1) than healthy individuals[36], and treatment protocols that helps reducing those cytokines levels should be emphasized.

The influence of GFD on others painful conditions have already been evaluated, and promising results were found. Isasi et al., 2014, when evaluating the influence of GFD in individuals with fibromyalgia, found a drastic reduction on generalized pain levels in 36,58% of patients[10]. Other study showed that subjects with rheumatoid arthritis had their disease activity reduced after 1 year of vegetarian GFD treatment[9]. In addition, a study evaluating GFD for one year in patients with irritable bowel syndrome, fibromyalgia and lymphocytic enteritis showed a small, however significant, improvement in pain symptoms[13].

The present clinical case leads to believe that, when establishing a GFD, the inflammation caused by gluten is reduced - and also the peripheral and central sensitization associated- explaining the clinical improvement obtained.

Gluten properties in promoting intestinal inflammation are associated with its ability to trigger cellular and humoral immune responses[7, 37]. As previously mentioned, due to high levels of proline and glutamine, gluten is not totally digested in the gastrointestinal tract. Those indigestive fragments cause enterocytes to release the protein zonulin, which causes increased intestinal permeability[6]. Non-self antigens, including gluten, gain access in to the lamina propria and activate inflammatory cells to release cytokines that cause innate immune inflammation[8].

In previous studies, zonulin was activated by gliadin in intestinal biopsies of individuals with and without celiac disease (CD)[38, 39], suggesting the capacity of gliadin to increase intestinal permeability evening subjects without CD. According to Lammers et al. (2011), gluten may also promote the release of TNF-α, IFN-γ, IL-6, IL-8, IL-10 and IL-13 in peripheral blood mononuclear cells of both patients with CD and healthy individuals[6]. A

positive association between α_2-macroglobulin plasma concentration sand gluten consumption was also observed in subjects without CD[4]. These observations suggest the spread of immune response due to gluten consumption to other body tissues beyond the intestinal mucosa[8].

This case report is not a long-term follow-up and a possible placebo effect should also be considered. Several TMD treatments are considered to be better than no one [40,41], especially because they influence the patient's expectation and beliefs about a promising treatment, increasing the probability of positive results[41]. There is evidence suggesting that placebo analgesia may be regulated by endogenous opioid mechanisms[42] and dopaminergic responses[41], which could explain the results obtained here.

This report demonstrated that gluten elimination from the diet of individuals with TMD seems to be a promising treatment for pain reduction. However, as discussed here - and demonstrated through somatosensory testings results- a GFD should be considered a coadjuvant treatment for TMD along with others therapeutic interventions.

Because this study is a case report, it does not represent the general population. Besides, it is an unprecedented intervention in the area of orofacial pain, and further studies must be developed in order to elucidate the role of gluten in TMD pain mechanisms.

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APÊNDICE A – TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

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Faculdade de Farmácia, Odontologia e Enfermagem (FFOE)

B

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO (TCLE)

Você está sendo convidada para participar, como voluntária, da pesquisa intitulada "INFLUÊNCIA DA INGESTÃO DE GLÚTEN NOS MECANISMOS SOMATOSSENSORIAIS MECÂNICOS DE MULHERES COM DOR MIOFASCIAL DA MUSCULATURA MASTIGATÓRIA". Leia atentamente as informações abaixo e faça qualquer pergunta que desejar, para que todos os procedimentos desta pesquisa sejam esclarecidos.

O objetivo da pesquisa é avaliar a influência do consumo de glúten na dor e sensibilidade na região da face em mulheres com dor nos músculos da mastigação, bem como comparar índices de qualidade de vida e qualidade do sono em mulheres que aderiram a uma dieta sem glúten. O glúten é uma substância encontrada em cereais como trigo, centeio e cevada, e está presente em alimentos como pão, macarrão, bolo, bolacha, cerveja, etc.

Ao participar, você se comprometerá a seguir uma dieta sem glúten durante um mês e a comparecer as consultas agendadas. Os efeitos adversos da exclusão do glúten parecem estar principalmente associados à menor ingestão de fibras (podendo resultar em alterações no perfil da flora intestinal). Entretanto, a adequada prescrição alimentar por nutricionista auxilia os pacientes a aderirem dieta sem glúten de forma equilibrada, sendo feita a escolha de alimentos ricos em nutrientes, naturalmente sem gluten.

Ademais, permitirá que a pesquisadora aplique três questionáros relacionados a sua saúde geral e a dor na face, como também um questionário relacionado a sua qualidade de vida e outro relacionado a sua qualidade de sono, sendo estes dois últimos aplicados em dois momentos: inicial e um mês após o início da dieta.

Alguns exames serão executados nas consultas inicial e final da sua participação. Os primeiros serão feitos utilizando alguns filamentos de nylon, onde você deverá responder várias vezes sobre a sensibilidade sentida no momento do exame de acordo com as instruções do pesquisador. Também será utilizado um aparelho capaz de medir a pressão exercida nos músculos, o qual possui uma ponta circular que fica em contato com determinadas áreas do seu rosto. Esta ponta funcionará como a ponta de um dedo fazendo pressão em determinados músculos e não machuca de forma alguma. Esse aparelho será utilizado no exame até que você relate um leve desconforto, sem que haja dor, e o valor registrado será anotado. Caso você apresente dor na face, essa dor pode aumentar levemente após o exame.

Os exames não produzirão qualquer tipo de dano físico, moral ou material, e, além disso, poderão trazer benefícios, pois, caso alguma relação entre dor na face e consumo de glúten seja encontrada em você, um novo tipo de tratamento poderá ser utilizado. Nenhum dos

procedimentos usados oferece riscos à sua dignidade. A consulta pode tornar-se cansativa devido a quantidade de questionários e testes que serão realizados.

Suas informações fornecidas serão mantidas confidenciais, respeitando sua privacidade. Você tem a garantia de receber respostas a qualquer pergunta ou esclarecimento a qualquer dúvida sobre os assuntos relacionados com a pesquisa, através do telefone da pesquisadora do projeto e, se necessário, através do telefone do Comitê de Ética em Pesquisa.

Você não terá nenhum tipo de despesa para participar desta pesquisa, bem como nada será pago por sua participação. Além disso, você tem a liberdade de deixar de participar do estudo a qualquer momento, sem que isso traga prejuízo a continuidade de quaisquer tratamentos que você esteja fazendo nessa instituição. Você não deve participar contra a sua vontade e, em caso de recusa, não será penalizado de forma alguma.

Após estes esclarecimentos, solicitamos o seu consentimento de forma livre para participar desta pesquisa. Portanto preencha, por favor, os itens que se seguem.

Dados da responsável pela pesquisa
Nome: Juliana Araújo Oliveira
Instituição: Universidade Federal do Ceará
Endereço: Rua Monsenhor Furtado s/n, Rodolfo Teófilo
Telefone da pesquisadora responsável: (85) 98170-7905
Telefone da nutricionista: (85)

ATENÇÃO: Se você tiver alguma consideração ou dúvida, sobre a sua participação na pesquisa, entre em contato com o Comitê de Ética em Pesquisa da UFC/PROPESQ – Rua Coronel Nunes de Melo, 1000 - Rodolfo Teófilo, fone: 3366-8344. (Horário: 08:00-12:00 horas de segunda a sexta-feira). O CEP/UFC/PROPESQ é a instância da Universidade Federal do Ceará responsável pela avaliação e acompanhamento dos aspectos éticos de todas as pesquisas envolvendo seres humanos.

O abaixo assinado Francilide Clemente Lima,
34 anos, RG 2001002306343, declara que é de livre e espontânea vontade que está como participante desta pesquisa.

Eu declaro que li cuidadosamente este Termo de Consentimento Livre e

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Esclarecido e que, após sua leitura, tive a oportunidade de fazer perguntas sobre o seu conteúdo, como também sobre a pesquisa, e recebi explicações que responderam por completo minhas dúvidas. E declaro, ainda, estar recebendo uma via assinada deste termo.

Fortaleza, 06 / 11 / 17

x Francileide Clemente Lira
Voluntária

Assinatura

Testemunha
(se a voluntária não souber assinar)

Assinatura

Sandra Maria Abreu Nogueira
Pesquisador que aplicou o TCLE

Assinatura

Juliana Araújo Oliveira
Pesquisador responsável

Assinatura