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Impacto de um programa de atualização em alimentação infantil para profissionais de saúde em desfechos de saúde em crianças na idade escolar

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RESUMO

Objetivos: O objetivo geral desta tese foi avaliar o impacto de um programa de atualização em alimentação infantil para profissionais de saúde em desfechos de saúde e a influência de alimentos ultraprocessados no perfil lipídico entre crianças de baixa condição socioeconômica. Assim, desenvolveram-se dois artigos científicos que objetivaram: 1) Avaliar o impacto de um programa de atualização em alimentação infantil para profissionais de saúde nos riscos cardiometabólicos entre crianças aos seis anos de idade; 2) Avaliar a associação entre consumo de alimentos ultraprocessados na idade pré-escolar e níveis do perfil lipídicos na idade escolar. **Métodos:** O estudo original foi um ensaio de campo randomizado em Unidades de Saúde (US), na cidade de Porto Alegre, Brasil. As US foram alocadas nos grupos intervenção (n=9) ou controle (n=11). Nas unidades intervenção, os profissionais de saúde participaram de sessões de treinamento, baseado nos "Dez Passos para uma Alimentação Saudável para Crianças Menores de Dois Anos". Gestantes no último trimestre de ambos os grupos foram identificadas, convidadas a participar e inscritas no estudo como mães em potencial para receber o aconselhamento dietético, fornecido por meio dos profissionais de saúde. Os dados dietéticos foram coletados por meio de dois inquéritos recordatórios de 24 horas. Aos 6 anos, foram realizados exames de sangue para medir o perfil lipídico e níveis de resistência à insulina. **Resultados:** Os resultados mostraram que 1) Aos 6 anos de idade, foram observadas diferenças médias significativas entre os grupos intervenção e controle nos níveis de insulina (-1,05, IC 95% -1,57 a -0,53), HOMA-IR (-0,25; IC95% -0,36 a -0,13), HDL-colesterol (3,03, IC 95% 0,15 a 5,90) e triglicerídeos (-8,75 IC 95% -12,67 a -4,84). 2) Crianças com maior consumo de alimentos ultraprocessados aos 3 anos de idade apresentaram níveis mais altos de colesterol total (β 8,51 mg/dL; IC95% 1,65 a 15,37) e triglicerídeos aos 6 anos (β 9,69 mg/dL; IC95% 0,97 a 18,42) em comparação àqueles no tercil mais baixo. **Conclusões:** Intervenção na atenção primaria à saúde no início da vida foi efetiva na redução dos riscos cardiometabólicos de crianças aos 6 anos de idade. Adicionalmente, nossos resultados destacam a necessidade de estratégias eficazes para minimizar o consumo de ultraprocessados na infância.

Palavras-chaves: Estudos de intervenção. Crianças. Consumo alimentar. Alimentos ultraprocessados. Riscos cardiometabolicos.

ABSTRACT

Objective: The general aim of this thesis was to evaluate the impact of health worker training on infant feeding practices on health outcomes and the influence of ultra-processed foods on the lipid profile among children from low-income families. Thus, we developed two papers that aimed to: 1) assess the impact of health worker training on infant feeding practices on cardiometabolic risks at 6 years of age; 2) assess the association between consumption of ultra-processed foods at preschool age and lipid profile levels at school age. **Methods:** The original study was a cluster randomized controlled trial carried out in Health Care Centers in Porto Alegre, Brazil. Health centers were randomly allocated into intervention (n=9) or control (n=11) groups. In intervention sites, health workers joined training sessions on the "Ten Steps for Healthy Feeding for Children from Birth to Two Years of age". Pregnant women in the last trimester of both groups were identified, invited to participate and enrolled in the study as the potential mothers to receive the dietary counselling provided by the health workers. The dietary data were collected through two 24-hour dietary recalls. At age 6 years, blood tests were performed to measure lipid profile and insulin resistance levels. **Results:** The results showed that 1) At the age of 6 years, significant mean differences between intervention and control groups were observed in insulin (-1.05, 95% CI -1.57 to -0.53), HOMA-IR (-0.25; 95% CI -0.36 to -0.13), HDL-cholesterol (3.03, 95% CI 0.15 to 5.90) and triglycerides (-8.75 95% CI -12.67 to -4.84); 2) Children in the highest tertile of UPF consumption at age 3 years had higher levels of total cholesterol (β 8.51 mg/dL;95%CI 1.65 to 15.37) and triglycerides at age 6 years (β 9.69 mg/dL;95%CI 0.97 to 18.42) compared to those in the lowest tertile. **Conclusion:** Early life intervention in a primary care setting was effective in reducing cardiometabolic risk among children at 6 years old. In addition, our results highlight the need for effective strategies to reduce the consumption of ultra-processed foods in childhood.

Keywords: Intervention studies. Children. Food consumption. Ultra-processed foods. Cardiometabolic risk

SUMÁRIO

1 APRESENTAÇÃO

Este trabalho consiste na Tese de Doutorado intitulada: "Impacto de um programa de atualização em alimentação infantil para profissionais de saúde em desfechos de saúde em crianças na idade escolar", a ser apresentada ao Programa de Pós-graduação em Ciências da Saúde da Universidade Federal de Ciências da Saúde de Porto Alegre, em abril de 2020. As questões de pesquisa que inicialmente estimularam o desenvolvimento deste trabalho representam dúvidas importantes no cenário atual no que se refere a promoção de saúde e prevenção de doenças crônicas não transmissíveis na população infantil, e podem ser sintetizadas nas seguintes perguntas: 1) Qual o efeito a longo prazo de uma intervenção à nível de atenção primária para promover o guia brasileiro para práticas saudáveis de alimentação de crianças menores de dois anos na avaliação dos riscos cardiometabólicos na idade escolar? 2) Qual a influência das práticas alimentares na idade pré-escolar no perfil lipídico na idade escolar?

Embora seja bem estabelecido que as práticas alimentares na infância influenciam desfechos de saúde em longo prazo, ainda são poucos os estudos que avaliam o efeito no longo prazo de programas de intervenção durante a infância em países de baixa condição socioeconômica e o impacto do grau de processamento de alimentos em desfechos específicos de saúde.

Para contribuir na busca dessas respostas, o presente estudo faz parte de um projeto maior denominado "Implementação dos Dez Passos para Alimentação Saudável para Crianças Menores de Dois Anos em Unidades de Saúde", que acompanhou crianças assistidas por Unidades de Saúde da cidade de Porto Alegre até os 6 anos de idade.

Essa tese é composta pelas seguintes partes: apresentação, revisão da literatura, objetivos, e dois artigos científicos intitulados: 1) *Long-term effect of a primary care intervention to promote healthy infant feeding practices on cardiometabolic risk factors: a 6-year follow-up of a cluster randomized trial* 2) *Longitudinal associations between ultra-processed foods and blood lipids in childhood*; conclusões e considerações finais; e anexos.

2 REVISÃO DA LITERATURA

2.1 Os primeiros anos de vida e estudos de intervenção

Os primeiros 1000 dias, período entre a concepção e os primeiros dois anos de vida, são considerados uma janela crítica do crescimento e desenvolvimento humano (HOFFMAN; REYNOLDS; HARDY, 2017). A plasticidade biológica neste período constitui-se uma oportunidade única para evitar ou reduzir possíveis mecanismos epigenéticos que aumentariam a sensibilidade para o desenvolvimento de doenças (BLOCK; EL-OSTA, 2017; VICKERS, 2014), deste modo, as intervenções durante os primeiros 1000 dias para diminuir os fatores de risco ambientais são essenciais para as melhorias nas condições de saúde da população. Dentre os enfoques para o período, os programas de intervenção nutricional são cruciais considerando o impacto das práticas alimentares na saúde, bem como a formação precoce dos hábitos alimentares (BIRCH, 1999). Diversos aspectos positivos são observados em estudos de intervenção direcionados aos hábitos alimentares de crianças no início da vida, como promoção do aleitamento materno (ABBASS-DICK et al., 2015; SINHA et al., 2015) e melhorias na prática da alimentação complementar (ARIKPO et al., 2018; NGUYEN et al., 2017).

Dentre as diferentes abordagens experimentais, estudos de intervenção realizados nos serviços de saúde são promissores no que se refere a abrangência pelo maior número de pessoas, além dos benefícios potencialmente sustentados após o período de intervenção, devido ao contato repetido ao longo de vários anos entre os usuários e os serviços de saúde. Estudo de revisão sistemática avaliou o efeito da atualização em nutrição para profissionais de saúde sobre as práticas alimentares de crianças entre 6 e 24 meses (SUNGUYA et al., 2013), no qual incluiu 10 estudos conduzidos em países de baixa e média renda. Os autores concluíram programas de intervenção em nutrição para profissionais de saúde apresentam resultados positivos na frequência da alimentação, ingestão de energia e na diversidade da dieta, além de melhorar o estado nutricional das crianças.

No Brasil, VITOLO e cols. 2014, realizaram estudo de intervenção baseado nos "Dez Passos" direcionada aos profissionais da atenção primária à saúde em 20 Unidades de Saúde (US) de Porto Alegre, randomizadas em grupos intervenção e controle. As US do grupo intervenção participaram de um programa de atualização quanto às diretrizes alimentares para crianças menores de 2 anos do Ministério da Saúde. Gestantes no terceiro trimestre foram cadastradas e os desfechos foram avaliados em seus filhos. Estudo publicado demonstrou que a prevalência de aleitamento materno exclusivo no primeiro (72,3 *versus* 59,4%; RR = 1,21; IC95% 1,08 – 1,38), segundo (62,6 *versus* 48,2%; RR = 1,29; IC95% 1,10 – 1,53) e terceiro mês de vida (44,0 *versus* 34,6; RR = 1,27; IC95% 1,04 – 1,56) foi maior no grupo intervenção em relação ao controle. Além disso, aos 6 meses de idade, as crianças do grupo intervenção apresentaram melhor qualidade da dieta, avaliada por meio do *Infant and Child Feeding Index* (ICFI) (FERREIRA et al., 2019). Resultados positivos no grupo intervenção também foram observados quanto à introdução precoce de alimentos não recomendados, como açúcar de adição, gelatina, biscoito e chá. Efeitos a longo prazo da intervenção também foram observados na idade escolar. Aos 6 anos de idade, crianças do grupo intervenção, quando comparadas aquelas do grupo controle, apresentaram menor adiposidade corporal (SANGALLI et al., 2020) e menor probabilidade de constipação (SANGALLI et al., 2018)

É relevante que diferentes formas de intervenção com programas em alimentação e nutrição apresentam resultados positivos nas práticas alimentares de crianças nos primeiros anos de vida, entretanto, esses resultados estão diretamente relacionados à diferentes limitações culturais, comportamentais e sociodemográficas (HEDBERG, 2013; ICKES; HURST; FLAX, 2015). A compreensão destes fatores é necessária para que novos estudos considerem estas barreiras como estratégias de intervenção para potencializar ainda mais os resultados esperados.

2.2 Formação das práticas alimentares na infância

Os primeiros anos de vida são um período caracterizado por intenso desenvolvimento do comportamento alimentar, à medida que as crianças passam de uma alimentação exclusivamente à base de leite (materno ou substitutos do leite materno) para uma alimentação sólida, por volta dos 2 anos de idade (BIRCH; DOUB, 2014). Neste período as preferências alimentares são desenvolvidas e apresentam fundamental importância nas escolhas alimentares, principalmente de crianças, e são determinadas por uma complexa interação de fatores genéticos, ambientais e familiares (BIRCH, 1998; SCAGLIONI et al., 2018). Geneticamente, as crianças possuem preferência inata ao sabor doce e salgado e rejeição ao azedo e amargo (BIRCH, 1998) . Por isso, alimentos com alto teor de açúcar, como biscoitos, sorvete, chocolate e bolo ganham a preferência, e as verduras e legumes tendem a ser rejeitadas. Essas preferências podem ser explicadas como uma função protetora, em que os sabores mais aceitos são identificados como sinal de uma fonte de energia e nutrientes enquanto os rejeitados são percebidos como um risco pela presença de toxinas(BIRCH, 1998). No entanto, essas predisposições podem tornar-se um obstáculo para a promoção da ingestão saudável em crianças. A neofobia alimentar e aversões para os alimentos azedos ou amargos podem dificultar a introdução de, por exemplo, frutas e legumes, na alimentação da criança e deste modo favorecer o consumo de alimentos com alta densidade energética e palatáveis (VENTURA; WOROBEY, 2013)

Embora o indivíduo tenha preferências inatas por determinados sabores, o aleitamento materno e as primeiras exposições aos alimentos podem determinar preferências alimentares, que tendem a se perpetuar em todas as faixas etárias (BEAUCHAMP; MENNELLA, 2009; DE COSMI; SCAGLIONI; AGOSTONI, 2017). Nesse sentindo, os fatores ambientais serão determinantes para a formação dos hábitos alimentares dos indivíduos, sobressaindo-se das influências genéticas. Durante esse período inicial, os pais e cuidadores são os responsáveis por tomar as decisões sobre alimentação e desempenham papel crítico na formação da preferência alimentar em crianças. Grande parte da aprendizagem precoce sobre alimentação ocorre na família, ambiente que é moldado pelos pais que selecionam os alimentos da família, servem como um modelo de comportamento aos seus filhos, além de fazer uso de técnicas para incentivar o desenvolvimento de padrões e comportamentos alimentares culturalmente adequados em crianças.

As práticas alimentares nos primeiros anos de vida são determinantes e influenciam as condições de saúde em curto e longo prazo (BARKER, 2007; LANGLEY-EVANS, 2015). Deste modo, os hábitos alimentares inadequados constituem-se em relevante problema de saúde pública, estando associadas à desfechos de saúde não apenas na infância, mas também na idade adulta. Estudo longitudinal sobre a saúde infantil, ingestão de alimentos e práticas de alimentação, *Infant Feeding Practices Study II*, realizado com crianças americanas, avaliou se os padrões de exposição alimentar aos 9 meses estavam associados à dieta infantil e ao peso posteriormente aos seis anos de idade (ROSE; BIRCH; SAVAGE, 2017). Lactentes com padrões alimentares mais elevados de ingestão de frutas e vegetais no primeiro ano de vida tiveram maior consumo destes alimentos aos 6 anos. Da mesma forma, aqueles com padrão alimentar caracterizado por alimentos com alta densidade de energia (por exemplo, batatas fritas e doces) continuaram a apresentara maior consumo desses alimentos posteriormente aos 6 anos de idade, além de apresentar maior prevalência de excesso de peso.

A compreensão do impacto das formações alimentares, bem como o entendimento da vulnerabilidade das crianças ao nosso ambiente alimentar atual, é destacada como prioridade para futuras pesquisas para desenvolver estratégias baseadas em evidências para ajudar a estabelecer comportamentos alimentares saudáveis no início da vida.

2.3 Classificação dos alimentos baseada na extensão e propósito do processamento

As intensas transformações na dieta, com o aumento exponencial de alimentos e bebidas processados industrialmente, modificaram o padrão de consumo na população nas últimas décadas (POPKIN; ADAIR; NG, 2012). Entretanto, o impacto do processamento industrial e, em particular, técnicas e ingredientes desenvolvidos pela indústria alimentícia, sobre a natureza dos alimentos e em particular sobre o estado da saúde humana, ainda é pouco difundido. Até recentemente, o processamento dos alimentos era negligenciado em estudos epidemiológicos e experimentais sobre dieta, nutrição e saúde. Nessa perspectiva, um sistema de classificação de acordo com a extensão e finalidade do processamento industrial à que os alimentos são submetidos foi elaborada por Monteiro e colaboradores (MONTEIRO et al., 2010), nomeada como "NOVA" . O sistema NOVA considera todos os aspectos físicos, métodos biológicos e químicos utilizados durante o processo de fabricação do alimento, incluindo o uso de aditivos (MONTEIRO et al., 2019). A classificação divide os itens alimentares entre quatro grupos: 1) alimentos *in natura* ou minimamente processados; 2) ingredientes culinários processados; 3) alimentos processados e 4) alimentos ultraprocessados. Os exemplos dos alimentos que são incluídos em cada grupo estão apresentados na Tabela 1.

- *Alimentos in natura e minimamente processados.* Alimentos *in natura* juntamente com alimentos minimamente processados compõem o grupo 1 da NOVA. Neste grupo, os alimentos são submetidos a um processamento industrial mínimo antes de serem adquiridos e consumidos, com objetivo principal de prolongar a vida útil do alimento, permitindo seu armazenamento para uso prolongado. Esse processamento não adiciona outros produtos ou substâncias como sal, açúcar, óleos ou gorduras. Envolve limpeza, remoção de partes não comestíveis, fracionamento, pasteurização, redução de conteúdo de gordura, refrigeração, congelamento, desidratação ou procedimentos similares, conservando grande parte das propriedades nutricionais do alimento original e aumentando sua disponibilidade e segurança. Em combinações apropriadas, todos os alimentos desse grupo são a base para uma alimentação saudável.

- *Ingredientes culinários processados.* São as substâncias extraídas dos alimentos *in natura* ou minimamente processados, tais como óleos vegetais, gorduras, sal e açúcar.

  Eles são criados por processos industriais como prensagem, centrifugação, refino, extração ou mineração. Os ingredientes culinários não são consumidos isoladamente e são utilizados na preparação de outros alimentos, com refeições feitas à base de alimentos in natura ou minimamente processados.
- *Alimentos processados.* Os alimentos processados são fabricados através da adição de substâncias como o óleo, açúcar ou o sal nos alimentos in natura ou minimamente processados. Para o processamento são utilizadas técnicas como a salga, salmoura, defumação, cura, acondicionamento dos alimentos em vidros ou latas. O processamento visa aumentar a durabilidade dos alimentos, modificando e/ou aprimorando suas qualidades sensoriais.
- *Alimentos ultraprocessados.* Alimentos ultraprocessados são formulações de ingredientes, em sua maioria de uso exclusivo da indústria, que resultam de uma série de diferentes processos industriais, muitos exigindo equipamentos sofisticados e tecnologia. Esses alimentos incluem uma ampla variedade de açúcares (frutose, xarope de milho com alto teor de frutose, "suco de frutas concentrados", açúcar invertido, maltodextrina, dextrose, lactose), óleos modificados (óleos hidrogenados ou interesterificados) e fontes de proteínas (proteínas hidrolisadas, isolado de proteína de soja, glúten, caseína, proteína de soro de leite e “carne separada mecanicamente”). O processo para fabricação de alimentos ultraprocessados envolvem várias etapas como hidrólise, hidrogenação, extrusão, moldagem, pré-fritura, além da adição de corantes, conservantes, emulsificantes e outros aditivos. São alimentos com pouco ou nenhum alimento integral em sua composição, prontos ou quase prontos para o consumo, com a proposta de serem produtos duráveis, acessíveis e convenientes, palatáveis, atraentes e rentáveis.

Tabela 1. Classificação de alimentos de acordo com o grau de processamento [a]	
Classificação	**Exemplos**
Grupo 1 – Alimentos in natura ou minimamente processados. Alimentos in natura incluem todos os alimentos na sua forma animal ou vegetal de origem. Os alimentos minimamente processados são aqueles que foram alterados, mas sem que nenhum ingrediente fosse adicionado.	Frutas, verduras, legumes e cereais frescos ou congelados; leguminosas, raízes e tubérculos frescos, congelados ou secos; castanhas, nozes, amendoim sem sal; carnes, aves e peixes frescos ou congelados; leite e iogurte natural; ovos; café, chás, farinhas (trigo, milho, mandioca), temperos.
Grupo 2 - Ingredientes culinários processados Substâncias obtidas diretamente de alimentos do grupo 1 ou da natureza por processos industriais como prensagem, centrifugação, refino, extração ou mineração.	Óleos vegetais, gorduras animais, manteiga, açúcar, sal, mel.
Grupo 3 - Alimentos processados Produtos feitos com adição de sal, óleo, açúcar ou outros ingredientes do grupo 2 em alimentos do grupo 1, usando métodos de preservação, como conservas e engarrafamento, e, no caso de pães e queijos, fermentação não alcoólica.	Legumes enlatados ou engarrafados em salmoura; nozes e sementes salgadas ou açucaradas; carnes e peixes secos, curados ou defumados; peixe enlatado (com ou sem conservantes adicionados); fruta em calda (com ou sem adição de antioxidantes); pães não embalados feitos na hora; queijos.
Grupo 4 - Alimentos ultraprocessados Formados a partir de ingredientes industriais, com pouco ou nenhum alimento in natura. São alimentos prontos ou quase prontos para consumo que imitam a aparência e qualidade sensorial dos alimentos. São duráveis, convenientes, hiperpalatáveis e rentáveis.	Cereais matinais, misturas para bolo, barras de cereais; pães e produtos panificados, como bolos, doces e sobremesas; salgadinhos "de pacote", biscoitos, sorvetes, chocolates; achocolatados e bebidas lácteas, refresco em pó, refrigerantes e outras bebidas adoçadas; margarinas. Produtos pré-preparados prontos para aquecer incluindo tortas e massas e pizzas; nuggets, cachorros-quentes e outros produtos à base de carne reconstituídos; sopas e massas instantâneas e sobremesas.

[a] Adaptado de Food and Agriculture Organization of the United Nations. Ultra-processed foods, diet quality, and health using the NOVA classification system. Rome, FAO, 2019.

Estudos populacionais conduzidos em diferentes países evidenciam o aumento exponencial no consumo de alimentos ultraprocessados. Em países desenvolvidos como os Estados Unidos (BARALDI et al., 2018) e Reino Unido (RAUBER et al., 2018), estes alimentos já representam mais da metade da energia total da dieta consumida. No Brasil, LOUZADA e cols. (2015) em estudo conduzido a partir da Pesquisa de Orçamentos Familiares, mostraram que 21% da ingestão calórica da população veio a partir dos produtos prontos para consumo. Entretanto, as vendas de alimentos ultraprocessados nos países de baixa e média renda estão subindo a uma taxa desproporcional em comparação aos países de alta renda (PAHO, 2015). Por exemplo, dados provenientes do banco de dados *Euromonitor* registram um crescimento de vendas de alimentos ultraprocessados em 30% no Brasil entre 2000 e 2013, enquanto no mesmo período em países como os Estados Unidos e Canadá, as vendas caíram em países como os Estados Unidos e Canadá -9% e -7,3%, respectivamente.

2.4 Alimentos ultraprocessados: características e consequências

Desde que o sistema de classificação de alimentos NOVA foi proposto pela primeira vez em 2009, muitos estudos conduzidos em diferentes países avaliaram o impacto do consumo de alimentos ultraprocessados na qualidade da dieta, com enfoque especial aos nutrientes associados as doenças não transmissíveis. Os resultados evidenciam que o aumento do consumo destes alimentos está associado ao maior do consumo de energia, açúcar de adição, gorduras não saudáveis, sódio, e menor ingestão de proteínas e fibras (CORNWELL et al., 2018; LOUZADA et al., 2018; MARTÍNEZ STEELE et al., 2017; RAUBER et al., 2019). Além da deterioração da qualidade nutricional dos padrões alimentares, os alimentos ultraprocessados possuem características peculiares em sua composição que favorecem o seu consumo excessivo. Evidências tem demonstrado que a hiperpalatibilidade destes produtos é capaz de alterar os mecanismos de saciedade endógenos, além de induzir altas respostas glicêmicas e baixa saciedade (FARDET, 2016) e assim promover o consumo excessivo de energia (FORTUNA, 2012), que podem resultar em comportamento alimentar patológico, como a dependência alimentar (SCHULTE; AVENA; GEARHARDT, 2015). Adicionalmente, estratégias de publicidade persuasivas e agressivas pela indústria alimentícia tornam os alimentos ultraprocessados preferíveis aos alimentos in natura e minimamente processados (MALLARINO et al., 2013). Estudos evidenciam que técnicas com apelo de alegações relacionadas à saúde e nutrição, bem como design de embalagens com a inclusão de desenhos animados, cores brilhantes e letras infantis, são as estratégias mais comuns direcionadas ao público infantil, tornando-os ainda mais vulneráveis para o consumo de alimentos ultraprocessados (GIMÉNEZ et al., 2017; PULKER; SCOTT; POLLARD, 2018) .

A classificação NOVA tem sido utilizada para avaliar os possíveis impactos do consumo de alimentos ultraprocessados à saúde humana. Em adultos, estudos com amostras representativas de populações de diferentes países demonstraram associação positiva e independente entre a maior participação de ultraprocessados na dieta e obesidade (CANHADA et al., 2019; FILGUEIRAS et al., 2019; JUUL et al., 2018; JUUL; HEMMINGSSON, 2015). Nesse sentindo, recente estudo clínico randomizado investigou os efeitos da exposição de uma dieta composta por alimentos ultraprocessados comparado com uma dieta a base de alimentos não processados, que apresentavam perfis de nutrientes muito semelhantes (HALL et al., 2019). Os resultados evidenciam que com a dieta ultraprocessada, os participantes do estudo comeram, em média, 500 calorias a mais por dia e ganharam, em média, mais de 900 gramas de peso corporal em duas semanas. Foram observadas também alterações significativas em relação aos hormônios envolvidos na regulação da ingestão de alimentos durante o período das dietas. Este estudo é um marco importante na área de pesquisa em alimentação e nutrição, pois é o primeiro ensaio clínico randomizado a evidenciar a relação de causa e efeito dos alimentos ultraprocessados na saúde humana.

Na França, estudo de coorte de base populacional (NutriNet-Santé), com a participação de mais de 100000 adultos, tem avaliado longitudinalmente o efeito do consumo de alimentos ultraprocessados na saúde. Os resultados evidenciam que um aumento de 10% na proporção de consumo de alimentos ultraprocessados na dieta foi associado a um aumento significativo no risco de doenças cardiovasculares (RR= 1,12; IC 95% 1,05-1,20), câncer (RR= 1.12; IC 95% 1,06-1,18), diabetes tipo 2 (RR= 1,15; 95% IC 1,06-1,25) e mortalidade geral (RR 1,14; 95% IC, 1,04-1,27) (FIOLET et al., 2018; SCHNABEL et al., 2019; SROUR et al., 2019, 2020).

Embora muitos estudos tenham sido conduzidos para verificar o ônus de doenças atribuídas ao consumo de alimentos ultraprocessados em adultos, poucos estudos avaliaram essa relação na população infantil. Estudo longitudinal com crianças de baixa condição socioeconômica no sul do Brasil realizado por RAUBER e cols. (2015) evidenciou que o consumo de alimentos ultraprocessados na idade pré-escolar foi associado ao aumento das concentrações de colesterol total e LDL-colesterol na idade escolar. Outro estudo realizado com esta mesma população mostrou associação positiva entre o consumo de alimentos ultraprocessados e adiposidade abdominal aos 8 anos de idade (COSTA et al., 2019).

O foco nos alimentos e na qualidade geral da dieta em vez de nutrientes isolados, conforme proposto pelo sistema NOVA, podem auxiliar na compreensão da prevenção e desenvolvimento das doenças crônicas não transmissíveis, além de auxiliar na avaliação e monitoramento dos padrões alimentares da população (MONTEIRO et al., 2019). Na última década, o sistema de classificação de alimentos baseados no grau de processamento foi cada vez mais reconhecidos em relatórios e comentários da OMS, FAO e Organização Pan-Americana da Saúde (OPAS). O Brasil, desde 2014, já introduziu como princípios básicos a orientação para redução do consumo de alimentos ultraprocessados em suas diretrizes nutricionais oficiais

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3 OBJETIVOS

3.1 Objetivo principal

Avaliar o impacto de uma atualização para profissionais de saúde da atenção primária em relação às práticas alimentares no primeiro ano de vida nas condições de saúde de crianças na idade escolar

3.2 Objetivos secundários

- Avaliar o impacto da intervenção na atenção primária no primeiro ano de vida no perfil lipídico (colesterol total, HDL-colesterol, LDL-colesterol e triglicerídeos) e glicídico (glicemia, insulina, HOMA-IR) aos 6 anos de idade.
- Verificar a contribuição do consumo de alimentos ultraprocessados durante os primeiros anos de vida nas alterações do perfil lipídico (colesterol total, HDL-colesterol, LDL-colesterol e triglicerídeos) aos 6 anos de idade.
- Verificar a tendência de consumo de alimentos ultraprocessados durante a infância

4 ARTIGO 1

Long-term effect of a primary care intervention to promote healthy infant feeding practices on cardiometabolic risk factors: a 6-year follow-up of a cluster randomized trial

Submissão ao periódico *Nutrition, Metabolism & Cardiovascular Diseases*

Long-term effect of a primary care intervention to promote healthy infant feeding practices on cardiometabolic risk factors: a 6-year follow-up of a cluster randomized trial

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Abstract

Background and Aims: Early nutrition has been suggested to be an important influence for later cardiometabolic health, but information on long term effects of infant dietary intervention is limited. We assessed the long-term effectiveness of a primary care intervention to promote infant healthy feeding practices on cardiometabolic risks at 6 years of age. **Methods and Results:** A clustered field trial was conducted at health centers in Porto Alegre, Brazil, randomly assigned to the intervention (n=9) or control (n=11) group. At the intervention sites, health professionals joined a training session on the "Ten Steps for Healthy Feeding for Children from Birth to Two Years of age". Eligible pregnant women from these centers were enrolled for the follow-up of their children's health outcomes. After delivery, children were followed at 6 years of age (n=387) by interviewers blinded to treatment allocation. Blood tests were performed to measure lipid profile and insulin resistance levels. At age 6 years, children in the intervention group had lower levels of insulin (Difference -1.05, 95% CI -1.57 to -0.53), HOMA-IR (Difference -0.25; 95% CI -0.36 to -0.13), triglycerides (Difference -8.75 95% CI -12.67 to -4.84) and higher levels of HDL-cholesterol (Difference 3.03, 95% CI 0.15 to 5.90) compared to those in the control group. In addition, the intervention group had 47% lower risk of meeting high TG-to-HDL-C ratio (RR= 0.53, 95% CI 0.35 to 0.83) **Conclusion:** Early life intervention in a primary care setting was effective in reducing cardiometabolic risk after 6 years follow-up. **Trial Registration:** ClinicalTrials.gov NCT00635453.

INTRODUCTION

Nutrition during early life is known to play a role on developing infants' metabolism[1,2] and it can exert a great influence on cardiometabolic health. Over the past years, substantial attention has been given to the influence of breastfeeding duration and complementary feeding practices during infancy on later cardiometabolic risk factors, including increased blood glucose and insulin and elevated blood lipids[3–8]. In fact, preventing and controlling such metabolic risk factors is of great public health importance as they may directly affect the occurrence of cardiovascular diseases, which remains the leading cause of disease burden globally [9].

There is a need for appropriate and early preventive intervention strategies at the population level to improve the future health of children loading into adulthood considering the role of diet on future chronic diseases. Yet, fewer randomized trials have examined the long-term effects of early life dietary intervention on cardiometabolic risks[10–12], in particular, targeting developing countries. In 2008, we started a cluster randomized field trial at primary care centers to promote the "Ten Steps for Healthy Feeding from Birth to Two Years of Age". We have previously reported significant improvements in breastfeeding rates and complementary feeding practices in the first year of life[13,14], lower energy intake among children at age 3 years and lower adiposity indicators at 6 years[15]. We therefore analyzed whether our intervention could be also effective in reducing cardiometabolic risk factors among children from low-income families followed at 6 years of age.

METHODS

Study design

We conducted a cluster randomized field trial targeting selected primary health care centers that provide services predominantly to low-income families in Porto Alegre, Brazil. Of the 52 municipal health centers, 31 met eligibility criteria for the trial. Exclusion criteria were: ≤100 infant patient visits in 2006, staff-sharing between clinics, or participation in other contemporaneous, community-based dietary programs.

The randomization process took place in the research office. Of the 31 eligible health centers, 16 were initially selected via a witnessed drawing, by the principal investigator, of labeled markers from an opaque container, such that two centers would be included from each of the city's eight geo-administrative districts. Following a stratified randomization scheme, the health centers were block-randomized by district, with one center per district allocated to the intervention group and another to the control group. Four additional centers from the original 31 were randomly drawn, block-randomized at a 1:3 ratio, to maintain a balanced number of births by intervention group. This yielded 9 intervention and 11 control group centers.

Interviewers visited the intervention and control health centers from April to December 2008 to identify and enroll women who were in the last trimester of pregnancy and reported a negative HIV test. Of 736 pregnant women who were eligible, 715(97.1%) agreed to participate and answered a questionnaire about their socioeconomic status and expected due date. Contact information were obtained in order to schedule subsequent home visits. Births from May 2008 to February 2009 were included for study.

Sample size calculations were based on comparing exclusive breastfeeding rates in the two study groups. 600 mother-child pairs would be needed to detect a statistical difference between a 40% prevalence of exclusive breast-feeding up to four months of age in the intervention group[14] and a 25% prevalence in the control group, with 90% power, α of 0.5, and a design effect of 1.5. We therefore recruited 715 pregnant women to obtain the required study power, taking into account an anticipated loss to follow-up of 20%.

The study was approved by the Ethics Committee of the *Universidade Federal de Ciências da Saúde de Porto Alegre.* This study was registered on the ClinicalTrials.gov website under the identification number NCT00635453. Mothers provided informed consent on behalf of their children.

Intervention

Physicians, nurses and administrative staff of all intervention health centers participated in a training in January 2008 based on the "Ten Steps for Healthy Feeding for Brazilian Children from Birth to Two Years of Age" guideline. An experienced nutritionist conducted a structured training session for the health care team to outline the "Ten Steps" recommendations and strategies and to provide suggestions how best to incorporate these into consultations.

Printed materials were provided to the Health Care Centers for use by these professionals and for access to the Brazilian Ministry of Healthy Nutrition Department´s website. Health staff members received a pocket guide outline the "Ten Steps" for use during the appointments. Also, they received a leaflet to the mothers with a summary of the recommendations, encouraging the mothers to ask more information from the health worker if needed.

In addition, two colorful posters were provided by the research team for display in the waiting rooms sessions of health care centers with (1) information about introducing complementary food, the number of meals and food scheme; and (2) pictures of foods that should not be offered to children under two years of age (i.e. cookies, coffee, gelatin, salty foods, candy, soft drinks and snacks). The posters remained in the clinics throughout the intervention period.

In summary, the "Ten Steps" recommend: (1) providing exclusive breastfeeding until 6 months of age; (2) continued breastfeeding until two years of age with the gradual introduction of complementary foods; (3) starting complementary feeding (grains, meat, fruits) at 6 months of age 3 times daily while continuing breastfeeding; (4) providing meals at regular intervals, adjusted to the child's internal hunger cues; (5) making new foods gradually thicker until the child is able to eat a normal family meal, but foods should never be liquefied; (6) providing a variety of healthy foods every day; (7) providing a daily intake of different fruits and vegetables; (8) avoiding sugar, sweets, soft drinks, salty snacks and processed/fried foods; (9) using good hygiene practices for food preparation and handling; and (10) providing appropriate, responsive feeding when the child is ill.

Control group

In the centers randomized to the non-intervention group, clinic staff continued their routine assistance, providing the standard care without having been updated according "Ten Steps" guideline by the research team. None of the materials developed for the intervention group were provided to these clinics. All mothers were encouraged to maintain normal pediatric visits for their children.

Data collection

Mothers in both the control and intervention group were interviewed at enrollment (during pregnancy) and at follow-up home-visits at mean child ages 6 months, 12 months, 3 years and 6 years by six pairs of blinded interviewers.

Mothers were advised to seek the health care centers if any questions or doubts concerning an infant’s nutrition, diet or any health problems were raised during the interviews. Data collection by the interviewers was verified through telephone call backs to a 5% random sample of interviewed mothers. All field workers received theoretical and practical 8 hours training on data collection.

At all waves of the study, tracing and re-enrollment was attempted of children who were lost to follow-up at previous examinations.

Cardiometabolic risk factors measurements

Venous blood samples were collected at 6 years of age to assess serum lipid and glycidic profile and analyses were performed at the laboratory of the Universidade Federal de Ciências da Saúde de Porto Alegre by a blinded technician. Total cholesterol (TC), high-density lipoprotein (HDL), triglycerides (TG) and glucose levels were measured using standard enzymatic methods with an automatic analyzer (BS-120, Mindray). Low-density lipoprotein (LDL) was calculated according to Friedewald’s formula[16]. Insulin was determined by a chemiluminescence enzyme immunoassay (Immulite 1000/SIMENS).

Homoeostasis model assessment index of insulin resistance (HOMA-IR) was calculated as (insulin (μU/ml)×glucose (mmol/l))/22.5)[17] and TG/HDL-C ratio was calculated by TG over HDL-C. A high TG/HDL-C ratio was defined as $\geq$ 2.0[18].

Anthropometric measurements

At age 6 years, children were weighed barefoot wearing light clothes on a digital scale (Líder, São Paulo, Brazil) to the nearest 0·1kg, and standing height was measured on a stadiometer (AlturaExata, São Paulo, Brazil) to the nearest 0·1cm. Triceps skinfold (TSF) and subscapular skinfold (SSF) thickness were measured to the nearest 0·5mm with a caliper at the right side of the body (Lange Skinfold Caliper, BETA Tech, Inc., Cambridge, MD). WC was measured to the closest 0.1cm at the minimum circumference between the iliac crest and the rib cage using a non-stretchable tape.

Data Analysis

Statistical analyses were performed using Statistical Package for the Social Science, version 21·0 (IBM Statistics Inc, Chicago, IL, USA). All data were double entered independently by different staff members for subsequent validation in EPI-INFO, version 6·4 (CDC) and the later resolution of discrepancies. Outliers were examined by box plot analysis and 8 blood measures were excluded from further analysis.

Intent-to-treat principles were used in all analyses. We compared baseline characteristics between the participants allocated in the intervention and control groups using χ^2 and Student's t or Mann-Whitney test. Statistical significance was set at $p<0.05$ The long-term effects of the intervention on the cardiometabolic outcomes was evaluated by using the Generalized Estimation Equation (GEE) model adjusted for clustering. Data were expressed using mean differences (MD) or relative risk (RR) with 95% confidence interval (95% CI) and *P* value.

RESULTS

A total of 387 children were examined at a median age of 6.2 years (interquartile range, 6.0 - 6.5 years), representing 61.3% of the 633 originally infants at 6 months of age included in the study **(Figure 1**). Follow-up rates were similar in the intervention and control groups (64.0% and 57.8%, respectively, p = 0.112). The main reasons for losses to follow-up were refusal and moved out of area and were similar across both groups. In addition, we did not find any differences between participants at 6 years of age and those lost to study follow-up. Children with genetic diseases (n=5) and without blood data (n=79) were not included in the analyses. In total, cardiometabolic risks outcomes were available for 303 children at 6 years of age (164 intervention group *versus* 139 control group). No adverse events were reported during the intervention.

The baseline characteristics of the study participants were similar for both intervention and control groups **Table 1.** Family income was low for most families - 69.9% had a monthly income less than three times the national minimum wage (approximately US$ 565.00 ⁄month). Overall, 67.8% of the mothers did not have paid employment, 46.9% had eight years of schooling or less and 20.9% were under age 20 at the child's birth. At age 6 years, compared with the control arm, children in the intervention group had lower body fat measures, as reported previously [15].

The cardiometabolic characteristics of children by group assignment are presented in **Table 2**. At age 6 years, HOMA-IR in the intervention was on average 0.25 lower (95% CI -0.36 to -0.13) than in the control group. In addition, children in the intervention group had lower insulin levels (MD -1.05 95% CI -1.57 to -0.53). Compared with the control group, children in the intervention group had, on average, lower concentrations of triglycerides (MD -8.75 95% CI -12.67 to -4.84) and higher concentrations of HDL-cholesterol (MD 3.03, 95% CI 0.15 to 5.90). In addition, the intervention group had 47% lower risk of meeting high TG-to-HDL-C ratio (RR= 0.53, 95% CI 0.35 to 0.83) (**Figure 2**).

DISCUSSION

This follow-up of our cluster randomized trial identified a continued benefit from a dietary intervention undertaken in infancy in reducing cardiometabolic risks among children at age 6 years. Children in the intervention group had lower fasting insulin, HOMAR-IR, triglycerides and higher HDL-cholesterol levels than those in the control group.

We considered two possibilities that may explain the results on insulin resistance. First, the effect of the intervention implemented at the health centers on long-term changes in metabolism may be related to better patterns of feeding in early life. Notably, the intervention substantially increased exclusive breastfeeding duration when compared with the control arm until the third month of life (44.0% vs 34.6%)[14] and delayed the introduction of non-recommended foods among infants (e.g., added sugar, jelly, tea, and filled cookie)[13]. Lower exclusive breastfeeding rates in the control group in the first months is directly related to intake of human-milk substitutes, such as infant formula and mainly cow-milk in this population, which prevalence among infants in the first three months of life was 48.5% in the control group against 39.8% in the intervention group (p=0.057) (data not shown). Therefore, the higher content protein in cow milk and formulas, as well as higher postprandial blood glucose in non-breastfed infants, are factors responsible for the enhanced secretion of insulin[19–21], contributing to the physiologic effects of a state of compensatory hyperinsulinemia which may influence insulin levels in later life[22]. Second, we observed smaller waist circumferences and skinfolds measurements in the same children at age 6 years, a positive intervention effect on body adiposity[15]. It is well established that the adipose tissue is crucial in regulating insulin and increased adipocyte size is associated with insulin resistance[23,24]. Thus, it would be biologically plausible that our intervention has had an effect on lowering levels of fasting insulin and HOMA-IR[25,26], providing better insulin dynamics during childhood. In our study, we did not observe differences on glucose levels across study groups, what could be related to the theory that hyperinsulinemia precedes the onset of hyperglycemia[27,28].

In this study, we also observed a benefit of the intervention on lipid profile. It is possible that early exposure to dietary cholesterol in breast milk may lead to the regulation of cholesterol during childhood[29]. Similar to our results, previous reports in children have shown long-term consequences of early nutrition on lipid measurements. Mothers counseling to improve infant feeding practices promotion was effective on triglyceride and HDL levels among girls at 8 years of age[30]. Likewise, exclusive and prolonged breastfeeding had a beneficial effect at the age of 4 years on lower triglycerides, total cholesterol, and LDL-cholesterol level[6]. In addition, these changes on cholesterol metabolism may be at least partly explained by the effects of the intervention by lower energy intake of foods rich in added sugar (cookies and chocolate powder) at 3 and 6 years of age[15]. Longitudinal studies have demonstrated associations between added sugar and increased triglycerides plus lower HDL-cholesterol[31,32]. Therefore, there is consistent evidence demonstrating that early feeding practices may program long-term changes in lipid metabolism. Finally, the lower proportion of high TC/HDL ratio emphasizes our metabolic results in the intervention group. The ratio integrates information on insulin resistance and atherogenic lipid measurements related to cardiovascular risk[33]. Studies conducted in the pediatric population[34–36] have shown that the TC/HDL ration is associated mainly with insulin resistance and it may be a good predictor of cardiovascular disease in adult life.

Interventions on primary care setting hold significant promise and potentially sustained benefits beyond the intervention period because repeated contacts typically occur over a number of years. The magnitude of the difference in metabolic outcomes is small at an individual level but may have a meaningful impact at the population level. The reduced mean insulin can be translated to a reduction for later type-2 diabetes[37]. Increases in HDL is associated with a decrease in coronary heart disease risk[38], while serum triglycerides are related to the higher risk of cardiovascular disease[39,40]. Our results, in terms of public health, may potentially lead to reduced cardiovascular diseases later in life, making a prevention in primary care setting a priority.

Some potential limitations should be discussed for the full appreciation of our results. First, cautious generalization is required, since most of our sample is of low family income. However, the less privileged socioeconomic groups in Brazil are larger and more socially vulnerable. Second, the losses during the follow-up of our study are considered high, however, it is emphasized that they were similar between both groups, as well as are similar to other studies carried out in populations living in low-income urban areas. Moreover, selection bias is unlikely to be a major problem, considering the similarity in baseline characteristics between those lost and those not lost.

Conclusions

In conclusion, the effect of this early life intervention to improve the infant feeding practices in a primary care setting was sustained on lower cardiometabolic risk after 6 years follow-up. Findings produced by this study evidences that the large-scale implementation of the nutrition guideline in a National Health System could play a relevant role in the cardiovascular disease prevention.

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Table 1 – Baseline and follow-up characteristics of participants according to randomly assigned group

Variable	n*	Intervention	Control
Measured at baseline			
Boys, % (n)	633	52.5 (169)	52.7 (164)
Birth weight (g), mean SD	611	3271.60 (532.05)	3302.88 (479.19)
Maternal age at child's birth < 20 years, % (n)	633	19.3 (62)	22.5 (70)
Mother's education ≤ 8 years, % (n)	633	46.9 (151)	46.9 (146)
Mother's unemployment, % (n)	633	64.6 (208)	71.1 (221)
Marital status (married/living with partner), % (n)	633	80.1 (258)	75.9 (236)
Pre-gestational BMI (kg/m2), mean (SD)	621	24.46 (4.61)	24.64 (4.98)
Pregnancy weight gain (kg), mean (SD)	618	11.06 (6.12)	11.42 (6.74)
Monthly per capita income ($), mean (SD)	610	168.45 (138.03)	177.24 (163.71)
Measured at age 6 y – child variables [a]			
Weight (kg), mean SD	293	23.7 (5.6)	24. (5.7)
Height(cm), mean SD	293	118.7 (5.5)	119.4 (5.6)
BMIz, mean SD	293	0.6 (1.4)	0.8 (1.5)
WC (cm), mean SD	293	55.2 (5.7)	56.5 (5.9)†
TSF (mm), mean SD	293	11.5 (5.2)	12.8 (5.8)†
SSF (mm), mean SD	293	7.7 (4.9)	9.1 (6.2)†
TSF + SSF (mm), mean SD	293	19.2 (9.6)	22.0 (11.8)†

SD: standard deviation; g: grams; cm: centimeters; BMI: body mass index; WC, Waist Circumference; TSF, Triceps Skin-fold; SSF, Subscapular Skin-fold

†$p<0.05$

*n Indicates the number of responses recorded for each characteristic

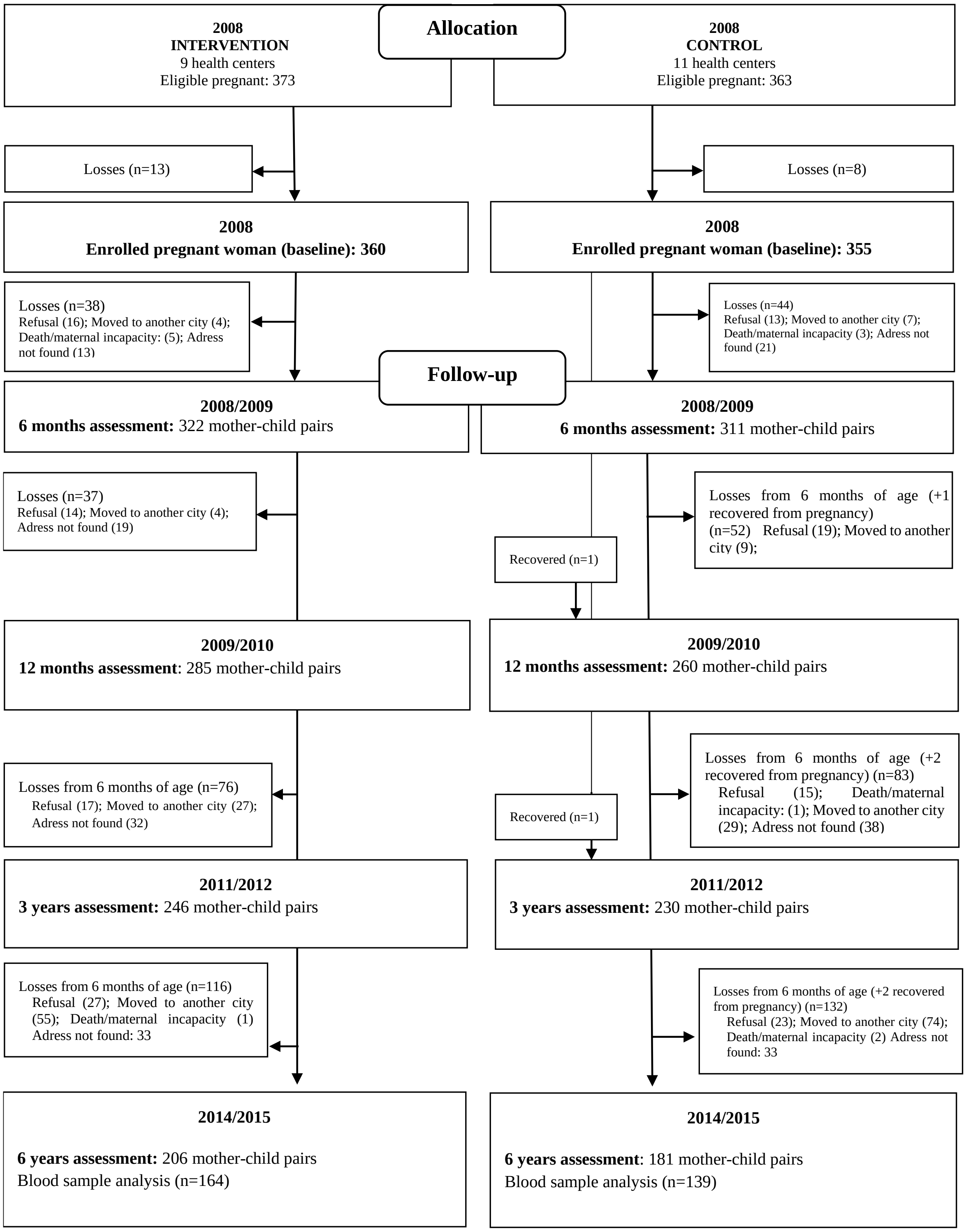
[a]Data in preparation by Sangalli et al, 2018[15] †

Table 2 – Mean (SD) of metabolic characteristics of children at age 6 years by intervention and control groups.

	Intervention (n=164)		Control (n=139)		MD (95% CI)	P
	Mean	SD	Mean	SD		
Metabolic characteristics						
Fasting glucose (mg/dL)	83.70	6.6	84.84	7.1	- 1.14 (-2.46 to 0.17)	0.089
Insulin (µU/mL)	3.29	2.0	4.34	3.3	- 1.05 (-1.57 to -0.53)	<0.001
HOMA-IR	0.68	0.4	0.93	0.7	- 0.25 (-0.36 to -0.13)	<0.001
Total cholesterol (mg/dL)	162.07	25.4	161.48	24.6	0.59 (-5.59 to 6.77)	0.852
LDL-cholesterol (mg/dL)	84.29	22.9	84.98	20.5	0.69 (-6.38 to 5.00)	0.812
HDL-cholesterol (mg/dL)	64.59	12.8	61.56	13.1	3.03 (0.15 to 5.90)	0.039
Triglycerides (mg/dL)	66.07	26.1	74.82	31.2	-8.75 (-12.67 to -4.84)	<0.001

MD, mean difference; CI, confidence interval;

Figure 1. Flow diagram of the study.



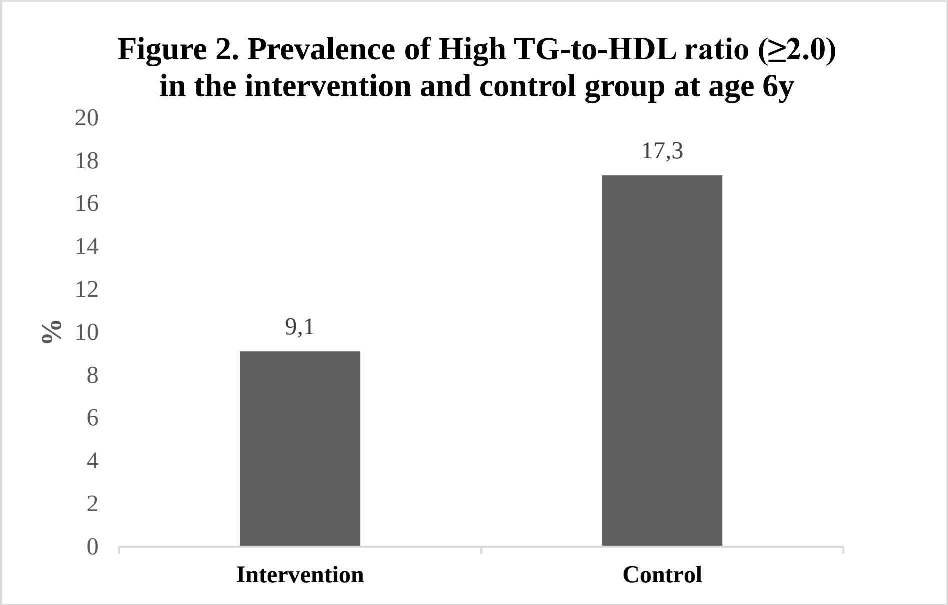


Figure 2. Prevalence of High TG-to-HDL ratio (≥2.0)
in the intervention and control group at age 6y
%
20
18
16
14
12
10
8
6
4
2
0
9,1
17,3
Intervention
Control

5 ARTIGO 2

Longitudinal associations between ultra-processed foods and blood lipids in childhood

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Longitudinal associations between ultra-processed foods and blood lipids in childhood

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Running title: ultra-processed foods and lipid profile

Keywords: ultra-processed food; children; trends; lipid profile; longitudinal studies

ABSTRACT

Emerging evidence suggests that the consumption of ultra-processed foods (UPF) plays a role in the development of chronic diseases, but evidence of their influence in children is limited. Our objective was to study longitudinal trends of UPF intake and determine their impact on blood lipids in young children. The present study was a follow-up of a randomized field trial of children (n=308) from Porto Alegre, Brazil. Dietary intake was collected using two 24-h recalls at 3 and 6 years of age and consumption of UPF was classified according to the NOVA system. At age 6 years, blood tests were performed to measure lipid profile. Contribution of UPF to total energy intake increased by 10% during the follow-up period, from 43.4% at 3 years to 47.7% at 6 years of age. Linear regression models showed that children in the highest tertile of UPF consumption at age 3 years had higher levels of total cholesterol (β 8.51 mg/dL;95%CI 1.65 to 15.37) and triglycerides at age 6 years (β 9.69 mg/dL;95%CI 0.97 to 18.42) compared to those in the lowest tertile. A positive dose-response was observed for an absolute increment of 10% of UPF on total cholesterol (β 2.76 mg/dL;95%CI 0.04 to 5.44) and triglycerides (β 3.44 mg/dL;95%CI 0.46 to 6.42). Based on our data, consumption of UPF increased significantly over time and was associated with higher blood lipids levels in children from a low-income community. Our findings highlight the need for effective strategies to minimizing the consumption of UPF in early life.

INTRODUCTION

Cardiovascular disease (CVD), a leading cause of the global burden of death and disease in adults [(1,2)], is attributed to a number of predisposing factors including low physical activity and an unhealthy dietary pattern [(3,4)]. Recent research suggests that a major contributor of unhealthy dietary patterns is a high intake of ultra-processed foods (UPF) [(5)]. Moreover, it has been reported that risk factors driving CVD, such as high serum lipid concentrations, have their origins even in early childhood [(6,7)]. High serum lipid profiles are directly affected by a poor diet, despite the fact that diet is one of the most important modifiable risk factors in the prevention of chronic non-communicable diseases [(8–10)]. However, an area that has received limited attention relative UPF intake and lipid profiles in childhood, the focus of this paper.

The global consumption of UPF, characterized as ready-to-eat and energy-dense manufactured foods, has increased dramatically [(11–14)]. Sales of UPF in low- and middle-income countries are rising at a disproportionate rate compared to high-income countries [(15)]. For example, Euromonitor reported a sales growth in UPF by 30% in Brazil from 2000 to 2013, while in the same period, sales dropped in the United States and Canada (-9% and -7.3%, respectively) [(16)]. Several studies have shown that high contribution of UPF in dietary patterns is associated with diets of lower nutritional quality [(17–19)] assessed by NOVA, a classification of foods based on their degree and purpose of industrial food processing. These findings are especially important given that that dietary patterns in this childhood often track into adulthood [(20)].

Several studies have been conducted to quantify the burden of disease attributable to specific UPF consumption. In adults, consumption of UPF has been associated with an increased risk of overweight and obesity [(21–23)], and related conditions, such as hypertension [(24)], CVD [(25)], as well as higher risk of overall cancer [(26)]. However, few studies focus on the association between consumption of UPF and risk of diseases in childhood [(27–29)]. It is critical to better understand the possible effects of these changing patterns, in particular how they may influence metabolic risk factors for non-communicable diseases in the pediatric population. Therefore, the objective of our longitudinal study was to assess trends of UPF consumption and determine the association between UPF and lipid profile in a population of children in southern Brazil.

METHODS

Study Design

This longitudinal study used data from children at 3 and 6 years of age who participated in a randomized intervention study (NCT00635453) of breastfeeding and dietary practices [30]. The intervention trial was conducted in health centers that provide primary care services predominantly to low-income families in Porto Alegre, Brazil, and the outcomes were assessed for mothers and children who received treatment at these centers. Briefly, health workers (physicians, nurses and administrative staff) of all intervention health centers participated in a training based on the “Ten Steps for Healthy Feeding for Brazilian Children from Birth to Two Years of Age” guideline and strategies to provide suggestions how best to incorporate recommendations into the consultations. From April to December 2008, all pregnant women in the last trimester at the participating health centers were invited to sign up for outcome tracking by interviewers who were blinded to the allocation status of the participants. All births occurred between May 2008 and February 2009.

The sample size initially chosen for the trial was based on the goal of detecting a difference in the prevalence of exclusive breastfeeding at 4 months [31]. A power of 90%, α of 0.5, design effect of 1.5, and a loss prediction of 20% were used to calculate the sample size, resulting in the inclusion of 360 mother-baby pairs in the intervention group and another 355 in the control group. Of 715 pregnant women who registered initially, 635 of their children were enrolled at the study at 6 months of age. A total of 476 and 387 children at 3 and 6 years of age, respectively, underwent assessment in the follow-up study. As the present study had a different aim, we proceeded to estimate if the available sample at age 6 years was sufficient to investigate the association between ultra-processed food consumption and outcomes. Assuming a correlation coefficient in the order of 0.3 and a design effect of 2, a total sample size of 226 children was required (with 90% power and α= 5%). This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethics Committee of the Universidade Federal de Ciências da Saúde de Porto Alegre. Informed consent was obtained from mothers on behalf of their children at each stage of data collection.

Data collection

Mothers were interviewed at home-visits by trained interviewers when their children were at 6 months, 3 years, and 6 years of age. Home visits for data collection by the interviewers were verified through telephone callbacks to a 5% random sample of interviewed mothers. Socioeconomic and family characteristics were obtained at recruitment. Birth weight and length, and sex were collected from the children's health records. Pre-pregnancy weight was self-reported, and mothers' height was measured during home visits when the children were six months of age and pre-pregnancy BMI was calculated. Anthropometric data of all children were obtained at 3 and 6 years using a digital scale to the nearest 0.1 kg and a stadiometer to the nearest 0.1 cm. BMI-for age z score (BMIz) was calculated based on the World Health Organization standards[32] and obesity was defined as BMI z-score >2SD for all ages.

Dietary assessment

Two multiple-pass 24-hour dietary recalls were collected for each child at ages 3 years and 6 years during the home visits on two non-consecutive days that were chosen randomly within two weeks to one month [33]. For children at age 3 years, recalls were provided by mothers or other caregivers; at age 6 years, children reported all the foods and beverages consumed the day before the interview, with help from their parents. For children who spent time with a caregiver other than the parent (e.g., during school hours), we contacted the caregiver to record all items the children consumed during the previous day. When it was not possible to obtain all available information, the participants were contacted on a different day to administer that 24h-recalls to provide accurate data for all children. Details about food types, amounts and preparation methods were recorded. Common household measures (e.g., teaspoons, tablespoons, cups, and serving sizes) were used to help mothers report the amounts of food given to their children and to standardize portion sizes. Interviews were conducted by dietitians/nutritionists and undergraduate students in nutritional sciences trained and supported in the 24-h recall method with standardized procedures, including practice interviews prior to the start of the study. The research supervisor reviewed all the dietary recalls. Dietary energy intake was estimated using the Dietwin® software program (version 2008 professional Dietwin®) and the Brazilian Food Composition Table (TACO, 2006) was preferentially used as a reference, followed by the United States Department of Agriculture chemical composition tables (USDA, Agricultural Research Service, 1998). For commercial products, we manually added all nutritional composition provided by the manufacturer to the program.

Ultra-processed food consumption

UPF was assessed using the NOVA classification system [34,35], a four-group food classification based on the extent and purpose of food processing, including unprocessed and minimally processed foods, processed culinary ingredients, processed foods, and UPF. This study focused on the NOVA group of UPF. Briefly, UPF are formulations of ingredients, most of exclusive industrial use, that result from a series of industrial processes and typically including little or no fresh food. UPF are ready to eat, drink or heat (e.g. soft drinks, sweet or savoury packaged snacks, breakfast cereal, candies, chocolate, 'instant' soups and noodles, processed meats, pre-prepared frozen dishes; and many other products). All food and drink items assessed in the dietary surveys were categorized as ultra-processed or not based on the food classification previously reported. This categorization was performed by a team of dietitians trained, supervised by researchers. Home-made recipes were identified and decomposed using standardized recipes, and the classification was applied to their ingredients. For a small number of specific food items such as pizza, there was insufficient information for classification purposes. In those cases, we used a conservative approach, such that the lower level of processing was chosen. UPF subcategories analyzed in the present study included: (1) savoury and biscuits (crackers, chips, salty snacks, cookies); (2) soft drinks (soda, sweetened juice); (3) sweets (candies, chocolate and ice cream); (4) powdered chocolate; (5) sugary milk beverages; (6) processed meats; (7) breads; (8) baby cereal; (9) margarine, mayonnaise and dressing; and (10) ready-made soup/noodle (instant noodle and dehydrated soup).

Lipid profile

Venous blood samples were collected at 6 years of age to assess serum lipid profile and analyses were performed at the laboratory of the Universidade Federal de Ciências da Saúde de Porto Alegre. Total cholesterol (TC), high-density lipoprotein (HDL-C), and triglycerides (TG) levels were measured using standard enzymatic methods with an automatic analyzer (BS-120, Mindray). Low-density lipoprotein (LDL-C) was calculated according to Friedewald's formula [36]. Cut-off values for abnormal lipid concentrations were defined according to the American College of Cardiology/American Heart Association (TC $\geq$170 mg/dL, LDL $\geq$110 mg/dL, HDL < 45mg/dL, and TG $\geq$75 mg/dL) [37].

Data Analysis

The usual dietary energy intake of UPF was estimated by the Multiple Source Method (MSM) (https://msm.dife.de)[38] that calculates dietary intake for individuals and then constructs the population distribution based on these data [39,40] . All participants were considered consumers of total energy intake and for ultra-processed food groups, a probability value of 0.5 (50 %) was used to assign the status of habitual consumer. Contribution of each subgroup of ultra-processed food to the total energy intake was calculated as a percentage of total energy.

Differences between intervention and control groups with respect to UPF consumption were analyzed and no differences at 3 (p=0.697) and 6 (p=0.606) years of age were observed. Continuous variables were expressed as mean and standard deviation (normally distributed data) or median and interquartile range (non-normally distributed data), and percent frequency. Analyses of trends in ultra-processed food consumption from age 3 years to age 6 years were conducted using Wilcoxon signed pair test and the percentage change across study period was evaluated.

Crude and multivariable linear regression models were used to determine the relationship between consumption of UPF at age 3 years on lipid profiles at age 6 years. All models were adjusted for sex, group status in early phase (intervention or control), birth weight, pre-pregnancy BMI, and family income (model 1), in addition to BMI z-score at baseline (3 years) (model 2), and for total energy intake and percentage of fat intake at age 3 years (model 3). The lowest tertile was used as the reference group and differences between strata of UPF consumption are presented as standardized regression coefficients with 95% confidence intervals (95% CI). We also estimated the change in lipid levels for a 10% increase in UPF consumption (continuous variable). Tests of linear trend were performed in all models by tertiles of UPF consumption as a continuous variable. All statistical analyses were conducted using SPSS version 21.0 (IBM Statistics Inc, Chicago, IL, USA) and statistical significance was set at $P<0.05$.

RESULTS

Of the 633 originally infants at 6 months of age included in the study, 476 and 387 children underwent assessment at the mean age of 3 and 6 years, respectively. The main reasons for loss were refusal to participate in the study and change of address (**Figure 1)**. No differences were found for sex, birth weight, maternal age at child's birth, and family income between the children who were lost to follow-up and those who remained at 6 years of age (P>0·05; data not show). The final analysis included 308 children with both complete dietary at age 3 years and blood data at age 6 years.

Characteristics of the study participants are presented in **Table 1**. Briefly, 18.9% of the mothers were under age 20 at the child's birth and 28.9% had eight years of schooling or less. Family income was low for most families - 62.5% had a monthly income less than three times the national minimum wage (approximately $804.00/month). More than half of the children were male (52.0%) and the obesity prevalence was 18% at age 3 years and 18.4% at age 6 years. Descriptive information of the lipid profile is shown in **Table 2**. Among children at age 6 years, prevalence of abnormal concentrations of TC, triglycerides, LDL-C, and HDL-C were 39.9%, 36.0%, 14.0%, and 8.8%, respectively.

Consumption of UPF represented a median of 43.4% and 47.7% of the total energy intake at 3 and 6 years of age, respectively **(Table 3).** Within food groups, the significant energy contributors were savoury and biscuits, soft drinks, and sweets in both age groups. Taken together, these UPF provided 25.8% and 28.4% of the total energy intake at age 3 and 6 years, respectively. The overall dietary contribution of UPF increased by 10% (p<0.001) during a mean follow-up period of three years. The largest relative increase among ultra-processed food groups occurred for margarine, mayonnaise, and dressing (1200%; p<0.001). There were notable changes in processed meat (58.3%; p<0.001) and bread (19.3%; p<0.001) consumption during childhood. Decreasing intake were seen for sugary milk beverages (41.0%; p<0.001) and powdered chocolate (27.5% p<0.001) over the study period.

Longitudinal associations between UPF intake and lipid profile are shown in **Table 4.** There was a positive association between UPF consumption at age 3 years and total serum cholesterol at age 6 years. In the fully adjusted model, higher UPF intake was associated with increased levels of total serum cholesterol later at age 6 years (tertile 3 *vs.* tertile 1; β 8.51 mg/dL 95%CI 1.65 to 15.37]). Similarly, a 10% increase in the consumption of ultra-processed food was associated with a 2.76 mg/dL (95%CI 0.04 to 5.44) increase in total cholesterol. Children in the highest tertile of UPF consumption had a mean triglycerides value of 9.69 mg/dL higher (95%CI 0.97 to 18.42) than those in the lowest tertile consumption in the fully adjusted model. Statistically significant associations were observed for an absolute increment of 10 in the percentage of UPF and triglycerides (β 3.44 mg/dL; 95% CI 0.46 to 6.42).

DISCUSSION

While the global consumption of UPF has increased greatly, only a few studies have reported an association between UPF intake and health outcomes in children [27–29]. Results from our longitudinal study suggest that higher UPF consumption during childhood was associated with higher levels of total cholesterol and triglycerides. In addition, we found that the consumption of UPF increased greatly during this period of early childhood. Overall, our results support the recent report of the Food and Agriculture Organization of the United Nations [5] that highlights the need for studies analyzing the impact of UPF as a risk factor for chronic non-communicable diseases in childhood.

Our data provide a comprehensive view of changes in UPF consumption from early to middle childhood. Briefly, UPF accounted for approximately 50% of total energy consumed by the children, even for those in the lowest tertile of UPF intake, the consumption of these products was particularly high in this population compared to the general Brazilian population [41]. We also found a 10% increase in total UPF consumption during the study period, suggesting a decline in diet quality the children studied. The increase in energy provided by the UPF is accompanied by a change in types of these products consumed, with the replacement of UPF targeting toddlers, such as "sugary milk beverages" and "baby cereals", by a dietary pattern based on ready-to-eat meals, such as sandwiches made with processed meat, bread and margarine, mayonnaise or dressing. Moreover, this shift in dietary patterns may be a result of complex social and environmental factors. For example, families in low-income urban neighborhoods have limited availability of healthful food and a greater availability of UPF [42–44]. Likewise, low-income groups, such as families enrolled in this study, are more likely to choose low costs foods when available [45]. Thus, providing detailed information about food consumption during childhood is necessary to develop effective strategies to prevent the chronic diseases later in life.

In regard to the development of chronic diseases, we found that higher consumption of UPF at age 3 years was significantly associated with higher blood lipid concentrations at age 6 years. There are a number of explanations for the results provided. For example, a high consumption of UPF is associated with unhealthful dietary patterns, characterized by an excess intake of energy, fat, and added sugar [18,41,46], especially among children and adolescents [47,48]. Indeed, increased total caloric intake, which is mainly driven by overconsumption of high-fat and high-sugar foods, is associated with increased lipogenesis and increased concentrations of circulating triglycerides and cholesterol [3]. Moreover, it has been reported that an excess intake of dietary sugar may be a central mediator for *de novo* lipogenesis, stimulating overproduction of hepatic triglycerides, resulting in hypertriglyceridemia [49,50]. In addition to nutrient level mechanisms, an excess intake of UPF is inversely associated with a lower intake of fruits and vegetables, foods that are known to prevent CVD [51]. Furthermore, given that obesity is a significant predictor of poor cardiometabolic health [52,53], a high intake of UPF, which has occurred following aggressive advertising and marketing of UPF [54,55], may promote obesity through a disruption of hunger and satiety [56,57]. Thus, these mechanisms support the association between UPF consumption and an unhealthy lipid profile, potentially increasing the risk of CVD.

Given the increased prevalence of cardiovascular disease throughout the world [1], our findings may be used to better elucidate the impact of UPF consumption on risk factors for CVD. For example, elevated total cholesterol and triglycerides are of critical significance since these results suggest an early vascular inflammatory response [7,58]. As the intake of UPF can continue increasing in lifelong, there is a real potential that these products may later affect the metabolism of LDL and HDL cholesterol. It is worth noting that significant changes generally occur in lipoprotein metabolism following puberty [59], which could explain the absence of association between UPF consumption and LDL and HDL cholesterol in our study. A cohort study in France reported that an increment of 10 in the percentage of UPF consumption was associated with a 12% increase in the rates of CVD in adults [25]. A longitudinal study of 8-year-old Brazilian children found an association between consumption of UPF and higher levels of total and LDL cholesterol [27], but not of higher TG. Nonetheless, our results extend this work by studying younger children who lived in a major urban center with greater access to UPF. The negative health risks of UPF consumption in the pediatric population are of particular concern as blood lipid profiles may worsen later in life as undesirable changes in eating behaviors are common during the transition from childhood to adolescence [60]. From a public health perspective, the robust evidence demonstrating the impact of UPF consumption on child health, investing in diet quality is one of the main priorities to promote cardiovascular health [61].

There are potential limitations of our study that should be discussed to fully appreciate our results. First, a number of participants were lost during follow-up, but there were no significant differences between the baseline characteristics of children who remained in the study and those lost to follow-up. Second, cautious generalization is required since the majority of our sample had low family income and may limit the applicability of our findings for more privileged populations. Third, the average of the two dietary recalls may not represent the entire distribution of usual intake due to the intra-individual variance component. Despite these limitations, our study has a number of strengths that merit attention. First, the prospective study design allowed us to assess the longitudinal association between UPF intake and lipid profile. Second, we collected detailed dietary data, including food preparation methods, ingredients used in dishes, and the brand of commercial products, which allowed us to classify foods according to the NOVA system, a valid tool for public health and nutrition research and policy [16,62,63].

In conclusion, we found that there has been a significant increase in the percentage of energy intake from UPF during childhood for children from a low-income community in Brazil. More important, we determined that a higher consumption of UPF was associated with increased blood lipids for the children in this study. The results of our study improve the understanding of how UPF intake may contribute to poor diet quality in this critical period of life. Thus, there is an urgent need for double and triple duty actions focused on minimizing the consumption of UPF in early life to reduce the risk of CVD later in life.

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Conflict of Interest

None of the authors report any conflicts of interest.

Authorship

P.S.L: formulated the research question, analyzed and interpreted the data, performed statistical analysis and wrote the manuscript;

D.J.H.: interpreted the data and statistical analysis, contributed to the drafting and critical revision of the manuscript;

F.R.: undertook data, interpreted data analysis, and critically reviewed the manuscript;

C.N.S and J.L.V: contributed to the drafting and critical revision of the manuscript;

M. R. V.: designed and conducted the study, formulated the research question, interpreted the data and the statistical analysis, and critically reviewed the article.

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Table 1. Characteristics of children and their families (n=308)[a]

Characteristics	
Maternal and family	
Maternal pre-gestational BMI ≥25 kg/m^2, n (%)	131 (38.0)
Maternal age at child's birth <20 years, n (%)	66 (18.9)
Mother's education ≤8 years, n (%)	101 (28.9)
Annual household income <US$ 3000	55 (16.0)
Child at 3y	
Age (years), mean (SD)	3.2 (0.1)
Weight (kg), mean (SD)	15.8 (2.5)
Height (cm), mean (SD)	96.7 (4.3)
BMI z-score, mean (SD)	0.9 (1.2)
Obesity, n (%)	81 (18.0)
Child at 6y	
Age (years), mean (SD)	6.3 (0.2)
Weight (kg), mean (SD)	24.1 (5.6)
Height (cm), mean (SD)	119.1 (5.7)
BMI z-score, mean (SD)	0.7 (1.5)
Obesity, n (%)	58 (18.4)

[a]Values may not equal total number of subjects in each group because of missing data; BMI: body mass index

Table 2. Mean (SD) and prevalence of alterations in lipid profile at age 6 years (n=308)

Lipid profile	Mean	SD	Abnormal values, n (%)
Total cholesterol (mg/dL)	162.4	26.8	123 (39.9) [a]
LDL-cholesterol (mg/dL)	85.1	23.1	43 (14.0) [b]
HDL-cholesterol (mg/dL)	63.0	12.7	27 (8.8) [c]
Triglycerides (mg/dL)	71.2	30.8	111 (36.0) [d]

[a] ≥170 mg/dL; [b] ≥110 mg/dL; [c] < 45mg/dL; [d] ≥75 mg/dL

Table 3 – Trends in the consumption of ultra-processed foods (% of total energy) at ages 3 years and 6 years old

	3y		**6y**		P trends	Percentage change
	Median	IQR	Median	IQR		
Ultra-processed food groups [a]						
Savoury and biscuits [b]	9.7	4.6 - 14.0	11.5	7.1 - 16.2	<0.001	18.5
Soft drinks [c]	8.1	4.7 - 10.9	8.2	5.5 - 10.3	0.752	1.2
Sweets [d]	8.0	4.7 - 11.1	8.7	4.1 - 13.4	0.021	8.8
Powdered chocolate	4.0	0.8 - 6.3	2.9	0.8 - 4.8	<0.001	-27.5
Sugary milk beverages	3.9	0.3 - 6.1	2.3	0.0 - 3.8	<0.001	-41.0
Processed meat	2.4	0.6 - 4.4	3.8	1.9 - 5.6	<0.001	58.3
Bread	3.1	0.0 - 3.7	3.7	1.5 - 5.8	<0.001	19.3
Baby cereals	1.8	0.0 - 2.7	1.3	0.0 - 1.7	0.651	-27.7
Margarine, mayonnaise and dressing	0.2	0.1 - 0.3	2.6	1.1 - 3.6	<0.001	1200.0
Ready-made soup/noodle	1.1	0.0 - 1.3	1.5	0.1 - 1.8	0.067	36.4
Total ultra-processed foods	43.4	34.3 - 51.1	47.7	41.5 - 53.8	<0.001	9.9

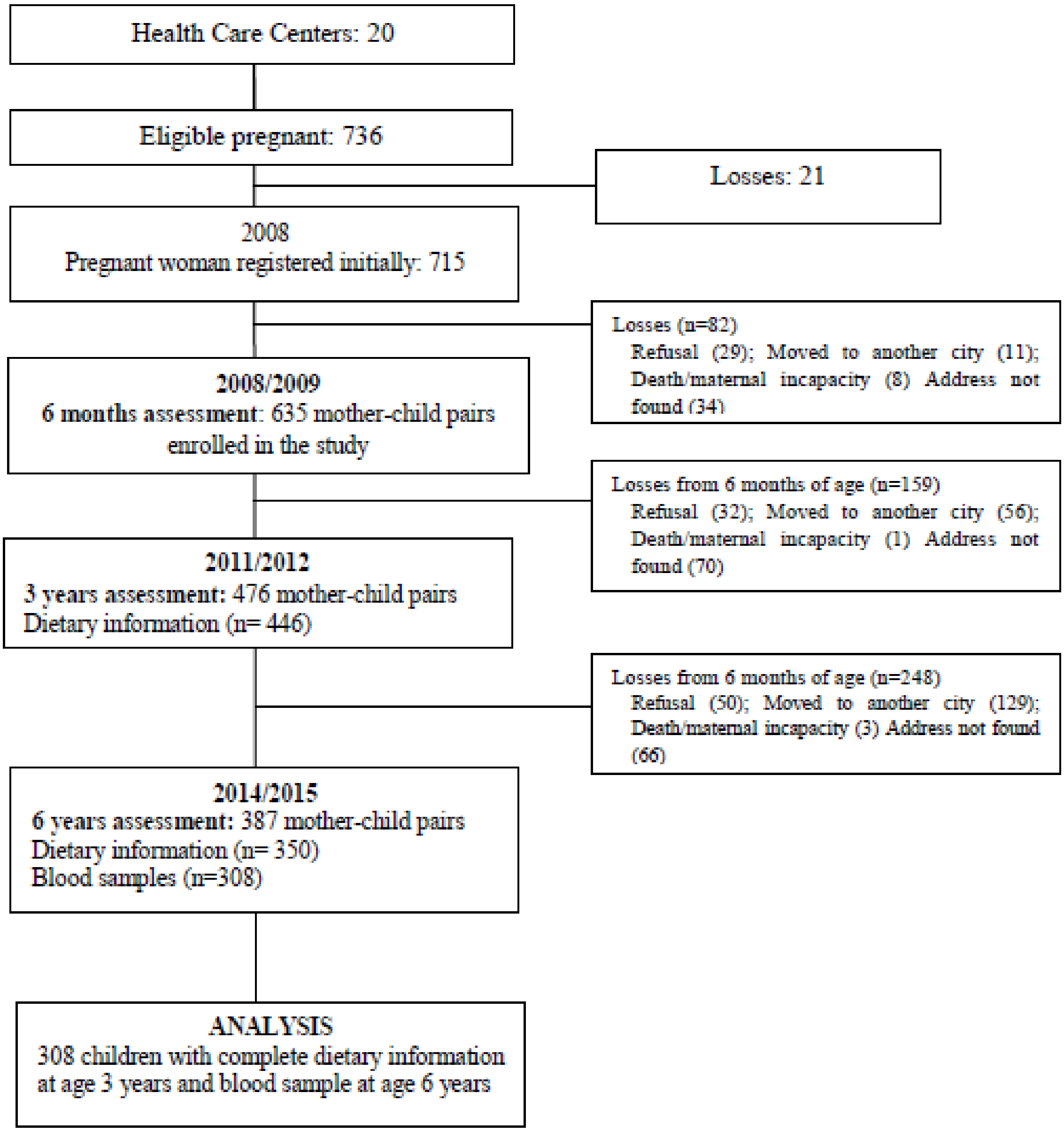
[a] Expressed as percentage of total energy intake; [b] Crackers, chips, salty snacks, cookies; [c] Soda, sweetened juice; [d] Candy, chocolate and ice cream. IQR: interquartile range

Table 4: Linear regression analyses of the association of ultra-processed food consumption at 3 years old with lipid profile at 6 years old

	Ultra-processed food consumption (% of total energy)					
	Tertile 1 29.6% (5.1- 38.2)	**Tertile 2** 44.1% (38.3 - 48.9)	**Tertile 3** 56.6% (49.0 - 85.3)		**Continuous** 10% increase	
	Reference	β (95% CI)	β (95% CI)	*P* for trend	β (95% CI)	*P* value
Total cholesterol (mg/dL)						
Crude	0	7.70 (0.51 to 14.88)	9.37 (2.84 to 15.91) *	0.016	3.08 (0.54 to 5.62)	0.017
Model 1[a]	0	7.97 (0.43 to 15.52)	9.55 (2.64 to 16.46) *	0.013	3.29 (0.59 to 6.00)	0.017
Model 2[b]	0	7.77 (-0.10 to 15.65)	8.65 (1.47 to 15.83) *	0.032	2.82 (0.07 to 5.58)	0.044
Model 3[c]	0	7.60 (-0.38 to 15.58)	8.51 (1.65 to 15.37) *	0.033	2.76 (0.04 to 5.44)	0.046
LDL-cholesterol (mg/dL)						
Crude	0	3.52 (-3.64 to 10.69)	4.64 (-0.69 to 9.97)	0.226	1.66 (-0.60 to 3.94)	0.151
Model 1[a]	0	4.16 (-3.35 to 11.69)	4.69 (-1.32 to 10.71)	0.288	1.83 (-0.68 to 4.36)	0.153
Model 2[b]	0	3.82 (-4.05 to 11.70)	3.44 (-2.83 to 9.26)	0.463	1.17 (-1.14 to 3.49)	0.322
Model 3[c]	0	4.02 (-4.13 to 12.17)	3.37 (-2.36 to 9.11)	0.467	1.18 (-1.20 to 3.57)	0.331
HDL-cholesterol (mg/dL)						
Crude	0	2.81 (-0.79 to 6.42)	2.44 (-1.77 to 6.66)	0.257	0.81 (-0.63 to 2.25)	0.271
Model 1[a]	0	2.00 (-1.40 to 5.40)	2.04 (-2.42 to 6.50)	0.444	0.66 (-0.87 to 2.20)	0.396
Model 2[b]	0	1.72 (-1.40 to 4.84)	2.03 (-2.27 to 6.33)	0.444	0.75 (-0.72 to 2.22)	0.318
Model 3[c]	0	1.76 (-1.27 to 4.80)	1.92 (-2.24 to 6.09)	0.424	0.69 (-0.71 to 2.10)	0.334
Triglycerides (mg/dL)						
Crude	0	0.58 (-7.66 to 8.83)	4.78 (-2.10 to 11.67)	0.394	1.87 (-0.72 to 4.47)	0.157
Model 1[a]	0	2.11 (-4.92 to 9.16)	7.50 (-1.02 to 16.03)	0.205	2.77 (-0.12 to 5.68)	0.061
Model 2[b]	0	3.98 (-3.93 to 11.90)	9.19 (0.01 to 18.39) *	0.117	3.31 (0.25 to 6.36)	0.034
Model 3[c]	0	2.84 (-4.49 to 10.17)	9.69 (0.97 to 18.42) *	0.085	3.44 (0.46 to 6.42)	0.024

IC: confidence interval. [a] Model 1 = adjusted for sex, group status in the early phase (intervention and control), family income, pre-pregnancy BMI, and child birth weight [b] Model 2 = Model 1 + BMI z-scores at 3 years. [c] Model 3 = Model 2 + intakes of total energy and total fat (%) at 3 years. * Difference between the first and third tertile P <0.05

Figure 1. Flow diagram of the study



6 CONCLUSÕES E CONSIDERAÇÕES FINAIS

Os resultados desta tese reforçam o impacto positivo da capacitação dos profissionais de saúde quanto às políticas públicas de alimentação e nutrição do país nos parâmetros cardiometabólicos ainda na infância. Esses resultados adicionam novas evidências quanto a importância de intervenções ainda no início da vida para as melhorias de condições de saúde da população a longo prazo. Destaca-se também a importância da preservação e defesa da atenção primária à saúde como uma forma altamente eficaz e eficiente de agir na promoção de saúde da população.

Paralelamente, o presente estudo também elucidou a compreensão do padrão alimentar ao longo das idades avaliadas por meio da classificação de alimentos de acordo com o grau de processamento, evidenciando a participação prevalente de alimentos ultraprocessados desde os primeiros anos de vida. Em uma análise longitudinal, o estudo auxiliou na compreensão do impacto do consumo de alimentos ultraprocessados no desenvolvimento de alterações sanguíneas do perfil lipídico.

Estes estudos adicionam novas evidências à literatura e reforçam o impacto das práticas alimentares ainda no início da vida nas condições de saúde à longo prazo. Por fim, sugere-se que as estratégias de intervenção, a fim de alterar estas práticas nocivas para a saúde das crianças, não estejam limitadas à assistência na atenção primária, mas que incluam ações que envolvam diferentes setores da sociedade para promover, apoiar e proteger os padrões alimentares saudáveis da população.

7 ANEXOS

7.1 Publicações científicas junto ao programa de pós-graduação

Artigos completos publicados em periódicos

Costa, C. S., Rauber, F., **Leffa, P. S**., Sangalli, C. N., Campagnolo, P. D. B., & Vitolo, M. R. (2019). Ultra-processed food consumption and its effects on anthropometric and glucose profile: A longitudinal study during childhood. *Nutrition, Metabolism and Cardiovascular Diseases*, *29*(2), 177-184.

Ferreira, V. R., Sangalli, C. N., **Leffa, P. S**., Rauber, F., & Vitolo, M. R. (2019). The impact of a primary health care intervention on infant feeding practices: a cluster randomised controlled trial in Brazil. *Journal of Human Nutrition and Dietetics*, *32*(1), 21-30.

Sangalli, C. N., **Leffa, P.S.**, de Morais, M. B., & Vitolo, M. R. (2018). Infant Feeding Practices and the Effect in Reducing Functional Constipation 6 Years Later: A Randomized Field Trial. *Journal of pediatric gastroenterology and nutrition*, *67*(5), 660-665.

7.2 Normas das revistas (endereços eletrônicos)

Revista	Normas
Nutrition, Metabolism and Cardiovascular Diseases	https://www.nmcd-journal.com/content/authorinfo
British Journal of Nutrition	https://www.cambridge.org/core/journals/british-journal-of-nutrition/information/instructions-contributors

7.3 Aprovações pelo comitê de ética

MINISTÉRIO DA EDUCAÇÃO
FUNDAÇÃO FACULDADE FEDERAL DE CIÊNCIAS MÉDICAS DE PORTO ALEGRE
COMITÊ DE ÉTICA EM PESQUISA
APROVADO PELA CARTA Nº 880/2004-CONEP/CNS/MS
RUA SARMENTO LEITE, 245 – FONE: (51) 3224.8822
CEP 90050-170 – PORTO ALEGRE – RS - cep@fffcmpa.edu.br

Of. 532/07-CEP

Porto Alegre, 06 de novembro de 2007.

Ilma. Sra.
Profa. Márcia Regina Vitolo
Nesta Faculdade

Senhora Professora

Informamos que seu projeto intitulado "Implementação dos Dez Passos da Alimentação Saudável para Crianças Menores de Dois Anos nas Unidades Básicas de Saúde.", Processo nº 226/07, foi aprovado por este Comitê, na reunião de 14 de junho 2007, conforme parecer consubstanciado nº 471-07.

Atenciosamente,

COMISSÃO CIENTÍFICA E COMISSÃO DE PESQUISA E ÉTICA EM SAÚDE

UFCSPA

COMITÊ DE ÉTICA EM PESQUISA - CEP
UFCSPA

O Comitê de Ética em Pesquisa da UFCSPA, registrado na Comissão Nacional de Ética em Pesquisa (CONEP) sob o nº 075/05 em 23/07/04, analisou o Projeto:

Projeto: 11-748 **Versão do Projeto:** **Versão do TCLE:**

Pesquisadores:
MÁRCIA REGINA VITOLO
CARLOS ALBERTO FELDENS

Título: IMPACTO DE INTERVENÇÃO NA ATENÇÃO PRIMÁRIA À SAÚDE NAS CONDIÇÕES NUTRICIONAIS DE CRIANÇAS EM IDADE PRÉ-ESCOLAR:SEGUNDA FASE DE AVALIAÇÃO DE ENSAIO DE CAMPO RANDOMIZADO POR CONGLOMERADOS

Esse projeto foi aprovado em seus aspectos éticos e metodológicos conforme as Resoluções 196/09 e demais Resoluções complementares. Toda e qualquer alteração do projeto, assim como eventos adversos graves, deverão ser comunicados a este CEP. Os TCLE, quando necessários, somente poderão ser utilizados após prévia e explícita aprovação (carimbo) de sua redação por este CEP".

Porto Alegre, 06 de maio de 2011.

José Geraldo Vernet Taborda
Coordenador do CEP/UFCSPA

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Impacto nas condições nutricionais e de saúde de crianças na idade de 6 e 7 anos que participaram de um ensaio de campo randomizado por conglomerados no primeiro ano de vida

Pesquisador: Marcia Regina Vitolo

Área Temática:

Versão: 1

CAAE: 30741714.7.0000.5345

Instituição Proponente: Universidade Federal de Ciências da Saúde de Porto Alegre

Patrocinador Principal: Conselho Nacional de Desenvolvimento Científico e Tecnológico

DADOS DO PARECER

Número do Parecer: 689.596

Data da Relatoria: 12/06/2014

Apresentação do Projeto:

O presente estudo é continuidade de um projeto (471-07 e nº 748/11 Comitê de Ética e Pesquisa da UFCSPA) desenvolvido para avaliar o impacto de atualização de profissionais da atenção primária à saúde em relação ao guia alimentar "Dez passos para uma alimentação saudável para crianças brasileiras menores de dois anos" nas condições nutricionais e de saúde de crianças assistidas por unidades de saúde da cidade de Porto Alegre.

O mesmo visa estudar se existe impacto da atualização para profissionais da atenção primária em relação às práticas alimentares no primeiro ano de vida (realizado no estudo anterior) nas condições de nutrição e saúde de crianças na idade escolar e os fatores de risco para obesidade, anemia, dislipidemias e alterações metabólicas.

Para isso, crianças na idade de 6-7 anos receberão visitas domiciliares. Os dados antropométricos e dietéticos serão coletados por estudantes de graduação e pós-graduação da Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA) por meio de questionário abordando fatores familiares, antropométricos e dietéticos. Os entrevistadores não terão conhecimento do grupo no qual as crianças pertenceram (intervenção ou controle) e serão previamente treinados para coleta de dados. Será realizada confirmação dos dados coletados em 5% da amostra por telefone. Será realizado analise de amostras de sangue na Universidade Federal de Ciências da

Saúde de Porto Alegre (UFCSPA). O deslocamento das mães e crianças, em grupos, será realizado por meio de serviço terceirizado de transporte.

Objetivo da Pesquisa:

Avaliar o impacto de uma atualização para profissionais da atenção primária em relação às práticas alimentares no primeiro ano de vida nas condições de nutrição e saúde de crianças na idade escolar e os fatores de risco para obesidade, anemia, dislipidemias e alterações metabólicas.

Avaliação dos Riscos e Benefícios:

A nível individual, as crianças terão os resultados de todos os exames e serão encaminhadas ao posto de saúde se necessário. Os resultados dessa pesquisa poderão subsidiar políticas públicas de alimentação e nutrição, sobretudo da população infantil de baixa renda.

Os riscos são pequenos e envolvem a realização de punção venosa na fossa cúbita. Os autores não descrevem os potenciais riscos de equimoses, dor local etc.

Comentários e Considerações sobre a Pesquisa:

É um estudo relevante que poderá auxiliar em políticas públicas de alimentação e nutrição na população infantil. O mesmo apresenta objetivos e metodologia claros. O mesmo foi contemplado com o Edital do Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ) Nº 14/2013-47731/2013-8.

Considerações sobre os Termos de apresentação obrigatória:

As mudanças solicitadas no termo de consentimento livre e esclarecido foram atendidas.

Os pesquisadores justificaram a falta de anuência da Secretaria Municipal de Saúde uma vez que o projeto não será realizado nas Unidades Básicas de Saúde e sim por visitas domiciliares.

Recomendações:

As sugestões foram atendidas.

Conclusões ou Pendências e Lista de Inadequações:

Parecer favorável a aprovação.

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

Considerações Finais a critério do CEP:

Término do projeto 05/2015.

De acordo com o parecer do Relator.

PORTO ALEGRE, 17 de Junho de 2014

Assinado por:
José Geraldo Vernet Taborda
(Coordenador)

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