CLÓVIS CIRYLLO LIMONGE NETO

CARACTERIZAÇÃO *IN VITRO* DE UMA RESINA COMPOSTA *BULK FILL* CONTENDO PARTÍCULAS PRÉ-REAGIDAS DE IONÔMERO DE VIDRO (S-PRG)

Faculdade de Odontologia
Universidade Federal de Minas Gerais
Belo Horizonte
2019

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Dissertação apresentada ao Colegiado de Pós-Graduação em Odontologia da Faculdade de Odontologia da Universidade Federal de Minas Gerais, como requisito parcial à obtenção do grau de Mestre em Odontologia - área de concentração em Clínica Odontológica.

Orientadora: Profª. Drª. Cláudia Silami de Magalhães
Coorientadora: Profª. Drª Monica Yamauti

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PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

COLEGIADO DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

FOLHA DE APROVAÇÃO

Caracterização in vitro de uma resina composta bulk fill contendo partículas pré-reagidas de ionômero de vidro (S-PRG)

CLOVIS CIRYLLO LIMONGE NETO

Dissertação submetida à Banca Examinadora designada pelo Colegiado do Programa de Pós-Graduação em Odontologia, como requisito para obtenção do grau de Mestre, área de concentração Clínica Odontológica.

Aprovada em 10 de julho de 2019, pela banca constituída pelos membros:

Prof(a). Claudia Silami de Magalhaes - Orientadora
FO-UFMG

Prof(a). Emílio Akaki
Ciências Médicas de Minas Gerais

Prof(a). Soraia Macari
FO-UFMG

Belo Horizonte, 10 de julho de 2019.

UNIVERSIDADE FEDERAL DE MINAS GERAIS

PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

ATA DA DEFESA DE DISSERTAÇÃO DO ALUNO
CLOVIS CIRYLLO LIMONGE NETO

Aos 10 dias de julho de 2019, às 09:00 horas, na sala 3403 da Faculdade de Odontologia da Universidade Federal de Minas Gerais, reuniu-se a Comissão Examinadora composta pelos professores Claudia Silami de Magalhaes (Orientadora) – FO/UFMG, Emílio Akaki – Ciências Médicas de Minas Gerais e Soraia Macari – FO/UFMG, para julgamento da dissertação de Mestrado, área de concentração em Clínica Odontológica, intitulada: **Caracterização in vitro de uma resina composta bulk fill contendo partículas pré-reagidas de ionômero de vidro (S-PRG).** A Presidente da Banca, abriu os trabalhos e apresentou a Comissão Examinadora. Após a exposição oral do trabalho pelo aluno e arguição pelos membros da banca, a Comissão Examinadora considerou a dissertação:

(X) Aprovado

( ) Reprovado

Finalizados os trabalhos, lavrou-se a presente ata que, lida e aprovada, vai assinada por mim e pelos demais membros da Comissão. Belo Horizonte, 10 de julho de 2019.

Prof(a). Claudia Silami de Magalhaes

Prof(a). Emílio Akaki

Prof(a). Soraia Macari

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“A menos que modifiquemos à nossa maneira de pensar, não seremos capazes de resolver os problemas causados pela forma como nos acostumamos a ver o mundo”.

Albert Einstein

RESUMO

No ambiente bucal, as restaurações de resina composta estão sujeitas a ações físicas, provenientes do desgaste e carga oclusal, e químicas, pelo contato com a saliva e os alimentos. Os efeitos desses processos físico-químicos estão diretamente relacionados com a característica da composição do material restaurador resinoso. Ensaios laboratoriais são especialmente importantes para avaliar a resistência física e estabilidade química dos materiais restauradores. O objetivo do estudo foi realizar a caracterização *in vitro* de uma resina composta *bulk fill* contendo partículas pré-reagidas de ionômero de vidro (S-PRG) (Beautifil-Bulk, Shofu Inc). As variáveis dependentes foram resistência à flexão (FS), absorção de água (WS) e solubilidade (SL), grau de conversão (DC), liberação de monômeros em água destilada e morfologia superficial em microscopia eletrônica de varredura (MEV), após incubação da resina composta em água destilada. As variáveis independentes foram a cor da resina composta, em cinco níveis, e o tempo de armazenamento dos corpos-de-prova, em seis níveis. Os ensaios de FS, WS e SL foram realizados de acordo com a metodologia preconizada pela ISO 4049(2009). Os corpos-de-prova para os ensaios de liberação de monômeros e análise de superfície em MEV foram confeccionados com as dimensões de 15 mm de diâmetro por 1 mm de espessura , usando resina da cor A3. O grau de conversão foi determinado em corpos-de-prova cilíndricos (1 x 1 mm) com resina da cor A3. Para confecção de todos os corpos-de-prova foi utilizado o fotopolimerizador LED Radii-Cal (SDI Inc., Victoria, Austrália; 1200 mW/cm^2). Após os períodos de incubação das amostras em água destilada (10 min, 24 h, 7 dias, 30 dias, 3 e 6 meses), foram realizadas análises em cromatografia líquida de alta eficiência (HPLC) para identificação e quantificação de monômeros liberados, usando padrões de Bis-GMA e TEGDMA. Para análise de superfície, os corpos-de-prova incubados em água destilada (7 dias, 30 dias, 3 e 6 meses) receberam pulverização de 4 nm de carbono e foram avaliados em MEV (FEI - Quanta 200, FEG). Os resultados foram expressos em média e desvio padrão. Foram realizados testes de normalidade (Kolmogorov-Smirnov e Shapiro-Wilk) e de homocedasticidade (Levene). Análise de Variância (ANOVA) e teste de comparações múltiplas, e teste de Kruskal-Wallis verificaram as diferenças entre os níveis dos fatores em estudo. Foi adotado o nível de significância de 5%. Não houve diferença significativa entre as cores para as variáveis FS, WS e SL ($p>0,05$). A média (dp) do DC foi 59,37(14,49)%. TEGDMA foi identificado em todos os tempos avaliados com maiores concentrações aos 30 dias e 3 meses de armazenamento. Bis-GMA não foi detectado em nenhuma das soluções. As imagens em MEV mostraram alterações morfológicas sugestivas de rugosidade da superfície aos 6 meses de armazenamento. A resina composta Giomer Beautifil-Bulk atingiu os requisitos da norma ISO 4049(2009) para FS, WS e SL e apresentou um DC aceitável. Não houve liberação de Bis-GMA e o TEGDMA foi detectado durante todo o período de 6 meses de avaliação.

Palavras-chave: Polímeros. Resinas Compostas. Bisfenol A-Glicidil Metacrilato. Cimentos de Ionômero de Vidro.

ABSTRACT

In vitro characterization of a bulk-fill resin composite containing pre-reacted glass ionomer fillers (S-PRG)

In the oral environment, composite resin restorations are subject to physical actions, from occlusal wear and tear, and chemical actions, through contact with saliva and food. The effects of these physicochemical processes are directly related to the composition characteristic of resin restorative material. Laboratory assays are especially important for assessing the physical strength and chemical stability of restorative materials. The objective of the study was to perform in vitro characterization of a bulk fill composite containing glass ionomer pre-reacted particles (S-PRG) (Beautifil-Bulk, Shofu Inc). The dependent variables were flexural strength (FS), water sorption (WS) and solubility (SL), degree of conversion (DC), elution of monomers in distilled water and surface morphology in scanning electron microscopy (SEM). The independent variables were the shades of the composite resin, in five levels, and the storage time of the specimens, in six levels. The FS, WS and SL assays were performed according to the methodology recommended by ISO 4049:2009. For monomer elution assay and surface analysis in SEM specimens were made with 15 mm diameter and 1 mm thickness, using A3 shade resin. The degree of conversion was determined in cylindrical specimens measuring 1 x 1 mm with A3 shade resin. For the preparation of all the specimens, the Radii-Cal LED light curing unit (SDI Inc., Victoria, Australia, 1200 mW / cm2) was used. After the incubation periods of the samples in distilled water (10 min, 24 h, 7 days, 30 days, 3 and 6 months), analyzes were performed in high performance liquid chromatography (HPLC) for the identification and quantification of elution monomers using Bis-GMA and TEGDMA standards. For surface analysis, specimens incubated in distilled water (7 days, 30 days, 3 and 6 months) were sprayed with 4 nm of carbon and were evaluated in SEM (FEI-Quanta 200, FEG). The results were expressed as mean and standard deviation. Normality tests (Kolmogorov-Smirnov and Shapiro-Wilk) and homoscedasticity test (Levene) were performed. Analysis of Variance (ANOVA) and multiple comparison test, and Kruskal-Wallis test verified the differences between the levels of the factors under study. The significance level of 5% was set. There was no significant difference among the resin shades for FS, WS and SL ($p > 0.05$). The mean (SD) of DC was 59.37 (14.49)%. TEGDMA was identified at all time points with the highest concentrations at 30 days and 3 months of storage. Bis-GMA was not detected in any of the solutions. SEM images showed morphological changes suggestive of surface roughness at 6 months of storage. The composite resin Giomer Beautifil-Bulk reached the requirements of ISO 4049:2009 for FS, WS and SL and presented acceptable DC. There was no release of Bis-GMA and TEGDMA was detected throughout the 6-month evaluation period.

Keywords: Polymers. Composite Resins. Bisphenol A-Glycidyl Methacrylate. Glass Ionomer Cements.

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LISTA DE ABREVIATURAS E SIGLAS

ANOVA	Análise de Variância
ATR	Refletância Total Atenuada
Bis-GMA	Bisfenol A Glicidil Metacrilato
CANP	Área de Pico das Cadeias Alifáticas Não Polimerizadas
CAP	Área de Pico das Cadeias Alifáticas Polimerizadas
DCANP	Área de Pico das Duplas Ligações de Carbono das Cadeias Aromáticas Não Polimerizadas
DCAP	Área de Pico das Duplas Ligações de Carbono das Cadeias Aromáticas Polimerizadas
DP	Desvio Padrão
eV	Eletrons-Volt
FTIR	Espectrômetro Infravermelho por Transformada De Fourier
g	Grama
GC	Grau de Conversão
HPLC	Cromatografia Líquida de Alta Eficiência
IC	Intervalo de Confiança
LED	Light Emitting Diode (diodo emissor de luz)
M	Média dos Valores
m1	Massa Constante 1
m2	Massa Constante 2
m3	Massa Constante 3
min	Minutos
MEV	Microscopia Eletrônica De Varredura
mL	Mililitros
mL/min	Mililitros por minuto
mm	Milímetro
mm^3	Milímetro Cúbico

MPa	Megapascal
mW/cm2	Miliwatts por Centímetro Quadrado
m/z	Massa por Carga
N	Newton
n	Número de Amostra
nm	Nanômetro
p/p	Porcentagem por Peso
ppm	Parte por Milhão
SA	Absorção
SD	Desvio Padrão
seg	Segundos
SL	Solubilidade
S-PRG	Partículas De Ionômero de Vidro Pré-Reagida
rpm	Rotação por Minuto
TEGDMA	Trietileno-glicol Dimetacrilato
UDMA	Uretano Dimetracrilato
unidade/mL	Unidade por Mililitros
v	Volume
v/v	Volume por Volume
ºC	Grau Celsius
µL	Microlitro
µL/mm	Microlitro por Milímetro
µg/mm3	Micrograma por Milímetro Cúbico
µm	Micrometro

LISTA DE SIMBOLOS

%	Porcentagem

SUMÁRIO

1 CONSIDERAÇÕES INICIAIS

O tratamento restaurador com resinas compostas tem sido largamente procurado e utilizado devido ao aumento do interesse dos pacientes em restaurações estéticas e por características conservadoras durante o preparo dentário (DELAVIZ, FINER e SANTERRE, 2014; JAFFER, FINER e SANTERRE, 2002). Desde o surgimento da resina composta, as maiores mudanças ocorridas nesse tipo de material foram relacionadas às partículas de cargas inorgânicas inseridas visando a melhoria das características físicas e químicas do material (FERRACANE, 2011).

Além das resinas compostas convencionais, um novo material restaurador denominado GIOMER, foi introduzido pela Shofu Inc, que combinou as propriedades de liberação de flúor do cimento de ionômero de vidro e a resistência e estética de resinas compostas (FUSS et al., 2017; HAJIRA e MEENA, 2015; IKEMURA *et al*., 2008; SALMERÓN-VALDÉS *et al*., 2016). A principal diferença entre os compômeros e o GIOMER é a presença de partículas de ionômero de vidro pré-reagidas (S-PRG) incorporadas na matriz da resina (HAJIRA e MEENA, 2015; WIEGAND, BUCHALLA e ATTIN, 2007). As partículas S-PRG favorecem a resistência mecânica, a durabilidade e a estética de um material composto (CONDÒ *et al*., 2017), bem como a liberação de vários íons (íons flúor, íons sódio, íons silicato, íons alumínio, íons borato e estrôncio) (FUJIMOTO *et al*., 2010) que atuam em diversas funções biológicas, incluindo a liberação e recarga de flúor, efeito anti bacteriano, efeito antibiofilme e modulação de pH (HAJIRA e MEENA, 2015). A liberação de estrôncio e flúor do GIOMER protege a superfície do esmalte adjacente contra desmineralização por ataque ácido de bactérias cariogênicas (ALSAYED *et al*., 2016).

Para reduzir o estresse de contração de polimerização, recomenda-se a inserção de pequenas camadas incrementais de compósitos resinosos (2 mm), permitindo a transmissão da luz mais eficiente e aumentando o grau de conversão, com menor possibilidade de formação de fendas na interface dente-restauração

(ILIE e FLEMING, 2015; VELOSO *et al*., 2018). Para simplificar a técnica foram desenvolvidos compósitos do tipo bulk-fill que por oferecerem maior translucidez, permitindo maior dissipação de luz e incorporação de fotoiniciadores mais reativos, podem ser inseridos em cavidades em únicos incrementos de 4 a 5 mm (VELOSO *et al*., 2018).

No ambiente bucal, as restaurações de resina composta estão sujeitas a ações físicas, provenientes do desgaste e carga oclusal, e químicas, pelo contato com a saliva e os alimentos. Os efeitos desses processos físico-químicos estão diretamente relacionados com a característica da composição e microestrutua do material restaurador resinoso (FERRACANE, 2011). Ensaios laboratoriais são especialmente importantes para avaliar a resistência física e estabilidade química dos materiais restauradores, dentre os quais podemos citar: teste de resistência, teste de absorção e solubilidade, grau de conversão, análise da liberação de monômeros e avaliação de superfície por microscopia eletrônica de varredura.

A resistência do material restaurador está relacionada com as tensões que se desenvolvem de acordo com a natureza das forças aplicadas e a dimensões da restauração, incluindo forças de tensão/tração, cisalhamento e compressão (ANUSAVICE, SHEN e RAWLS, 2013). Entre os ensaios mecânicos aplicados na odontologia, um importante parâmetro para avaliar a propriedade básica de um polímero odontológico é o teste de flexão de três pontos, que possibilita determinar a resistência à flexão (ANUSAVICE, SHEN e RAWLS, 2013; GAROUSHI, VALLITTU e LASSILA, 2017; ISO 4049, 2009;). O teste de flexão se diferencia de outros ensaios mecânicos, por envolver uma força de dobramento, que resulta em complexas tensões decorrentes da combinação de tensão de compressão, cisalhamento e tração no mesmo corpo (ANUSAVICE, SHEN e RAWLS, 2013; EWEIS, YAP e YAHYA, 2018). A resistência à flexão representa o maior estresse sofrido pelo material antes da falha do material (EWEIS, YAP, YAHYA, 2018).

Os polímeros utilizados em Odontologia, como as resinas compostas, são susceptíveis a absorção de solventes, especialmente a água, e perda de componentes solúveis (solubilidade) (NOORT, 2010). Para estabilidade física e química do material é ideal que absorção e solubilidade sejam as menores possível,

pois podem influenciar negativamente na biocompatibilidade do material reduzindo suas propriedades mecânicas e a longevidade da restauração (GIANNINI *et al*., 2014). O ensaio mais simples e indicado para avaliar a absorção e a solubilidade de um polímero é feito por meio da monitorização da alteração de peso de uma amostra quando imersa na água (ISO 4049, 2009; LAGOCKA *et al*., 2015; NOORT, 2010; PORTO; ALMEIDA, 2013). A quantificação detalhada do ganho de moléculas de água ou da perda de substâncias para o solvente, como monômeros não reagidos ou partículas de carga, é um processo complexo, pois esses dois fenômenos ocorrem simultaneamente, mas em velocidades diferentes. Assim, é importante que a caracterização desses processos seja realizada separadamente: cálculo de absorção e cálculo da solubilidade (NOORT, 2010). Para isso também é muito importante que toda a água do ambiente que foi absorvida pela amostra seja removida, com o auxílio de um dessecador, antes de iniciar os testes (ISO 4049, 2009; NOORT, 2010).

As resinas compostas fotoativáveis são apresentadas em pasta única, na qual o sistema iniciador formado por uma molécula fotossensível, geralmente canforoquinona e aminas não interagem entre si quando não há exposição de luz. Entretanto, na presença de uma fonte de luz, com espectro azul com comprimento de onda aproximado de 468 nm, a molécula de canforoquinona passa para um estado excitatório interagindo com a amina para formar radicais livres que iniciam a polimerização por adição, em que monômeros com duplas ligações de carbono são convertidos em ligações simples formando uma cadeia polimérica (ANUSAVICE, SHEN E RAWLS, 2013). À medida que o processo continua, uma maior quantidade de monômeros é incorporada, resultando em aumento da viscosidade do composto e diminuição da taxa de difusão de monômeros ainda não reagidos (RUEGGEBERG *et al*., 2017). Desta forma, a avaliação do Grau de Conversão (DC) é medida em porcentagem da quantidade de duplas ligações de carbono convertidas em ligações simples. Quanto maior o DC melhores são as propriedades físico-mecânicas e químicas dos compósitos (ANUSAVICE, SHEN e RAWLS, 2013; FERRACANE, 2011; PREJMEREAN *et al*., 2016; YU, YAP e WANG, 2016). Entretanto, são alcançados valores máximos entre 50 a 70% devido ao fechamento das cadeias

poliméricas e o aprisionamento de monômeros não reagidos dentro da matriz resinosa (ANUSAVICE, SHEN e RAWLS, 2013; RUEGGEBERG *et al*., 2017; VAN LANDUYT *et al*., 2011). O DC é influenciado pela composição e espessura do material restaurador e pela transmissão de luz (ANUSAVICE, SHEN e RAWLS, 2013; YU, YAP e WANG, 2016). A espectroscopia de infravermelho por Transformada de Fourier (FTIR) equipada com dispositivo de refletância total atenuada (ATR) tem sido largamente utilizada para medir o DC de resina compostas, apresentando alta sensibilidade e especificidade (PREJMEREAN *et al*., 2016).

Devido à presença da saliva e enzimas na cavidade bucal os compósitos podem liberar monômeros não reagidos ou outros componentes da matriz resinosa (VAN LANDUYT *et al*., 2011). O processo de degradação pela ação hidrolítica e enzimática, assim como um baixo grau de conversão de polimerização, também podem potencializar o desgaste da restauração (BOURBIA *et al*., 2013; FINER; SANTERRE, 2004; JAFFER; FINER; SANTERRE, 2002; LIN *et al*., 2005; PINTO *et al.*, 2013; PUTZEYS *et al*., 2017). O principal monômero utilizado nos compósitos resinosos é o bisfenol A glicidil metacrilato (Bis-GMA), que devido sua alta viscosidade é misturado com outros dimetacrilatos, como o trietilenoglicol dimetacrilato (TEGDMA) e uretano dimetacrilato (UDMA) ou outros monômeros (FERRACANE, 2011). Há relatos na literatura de que a liberação de monômeros de resina composta são potencialmente perigosos (GUPTA *et al.,* 2012; VAN LANDUYT *et al*., 2011;), com efeitos em nível local na mucosa bucal, gengiva e polpa dentária (PUTZEYS *et al*., 2017) e em níveis sistêmicos, com efeitos teratogênicos e citotóxicos (SCHWENGBERG *et al*., 2005), morte celular (REICHL *et al*., 2006) e redução de fertilidade (AL-HIYASAT e DARMANI, 2006). O processo de liberação de monômeros é influenciado por vários fatores como a composição do compósito, o grau de conversão obtido e a constituição da solução (PINTO *et al.*, 2013). Portanto, o primeiro passo para avaliar a biocompatibilidade dos compostos resinosos é a avaliação qualitativa e quantitativa de monômeros que podem ser liberados em um ambiente controlado, onde amostras de resina compostas são imersas em solução aquosa por período específico, e o extrato é, posteriormente, analisado (PUTZEYS

et al., 2017). O método mais utilizado para avaliação de liberação de monômeros de resina compostas é por meio da Cromatografia Líquida de Alta Eficiência (HPLC) (MACAULAY *et al*., 2017; PUTZEYS *et al*., 2017; SIDERIDOU e ACHILIAS, 2005; VAN LANDUYT *et al*., 2011).

A superfície das resinas compostas pode sofrer alterações morfológicas após o processo de degradação hidrolítica, com aumento da rugosidade de superfície favorecendo manchamento e desgaste da restauração (JAFFER; FINER; SANTERRE, 2002). A avaliação ao nível microscópico para análise qualitativa dessa possível alteração morfológica é usualmente realizada por microscopia eletrônica de varredura (MEV) (FINER e SANTERRE, 2003; FINER e SANTERRE 2007; JAFFER, FINER e SANTERRE, 2002).

Embora existam diversos trabalhos na literatura sobre as propriedades físico-químicas e os processos da degradação das resinas compostas, há poucos estudos realizados com a categoria de materiais denominados GIOMER (acrônimo de *glass ionomer + polymer*). Desta forma, o presente trabalho realizou um estudo laboratorial, *in vitro*, para analisar as propriedades físico-químicas de uma resina composta do grupo GIOMER, Beautifil-Bulk (Shofu Inc., Kyoto, Japão), considerando: resistência à flexão, absorção e solubilidade, grau de conversão, liberação de monômeros em água destilada e a análise microscópica da superfície para verificar os efeitos deste processo hidrolítico.

1.1 OBJETIVO

1.1.1 Objetivo geral

Avaliar as propriedades físicas e químicas de uma resina composta comercial do tipo *bulk-fill* contendo partículas de S-PRG.

1.1.2 Objetivos específicos

- Mensurar a resistência à flexão de uma resina composta *bulk-fill* contendo partículas de S-PRG em 5 níveis de cores;
- Avaliar as propriedades de absorção e solubilidade em água de uma resina composta *bulk-fill* contendo partículas de S-PRG em 5 níveis de cores;
- Medir o grau de conversão de uma resina composta *bulk-fill* contendo partículas de S-PRG em único nível de cor;
- Quantificar a liberação de monômeros Bis-GMA e TEGDMA de uma resina composta *bulk-fill* contendo partículas de S-PRG armazenada em água destilada em 6 níveis de tempo;
- Avaliar, morfologicamente, os efeitos da liberação de monômeros sobre a superfície de uma resina composta *bulk-fill* contendo partículas de S-PRG armazenada em água destilada em 5 níveis de tempo.

2 METODOLOGIA EXPANDIDA

2.1 Delineamento experimental

Trata-se de um estudo quali- e quantitativo, experimental *in vitro*. As variáveis dependentes foram: resistência à flexão, absorção/solubilidade, grau de conversão, liberação de monômeros e características morfológicas da superfície das amostras. As variáveis independentes foram: cor da resina composta Beautifil-Bulk (Shofu Inc., Kyoto, Japão) e o tempo de armazenamento dos espécimes.

2.2 Materiais utilizados

Os materiais odontológicos utilizados no estudo estão descritos na Tabela 1. As cores das resinas compostas *bulk-fill* com partículas de S-PRG (GIOMER Beautifil-Bulk) utilizadas foram A1, A2, A3, B1, B3 e C3 (FIGURA 1). Para todos os ensaios, os compósitos utilizados foram armazenados em ambientes sem luz direta e mantidos refrigerados à temperatura de 4 ^{o}C. Antes do uso, as resinas foram retiradas do refrigerador e mantidas no laboratório sob temperatura ambiente durante 30 minutos. Os instrumentos utilizados para manipular as amostras de resina foram limpos e esterilizados para evitar contaminação. O manuseio foi realizado com luvas descartáveis. Para identificação dos padrões para o ensaio de liberação de monômeros foram utilizados o Bis-GMA e TEGDMA.

Tabela 1- Materiais, composição e fabricante empregados no estudo.

MATERIAL	COMPOSIÇÃO
Beautifil-Bulk (Shofu Inc., Kyoto, Japão)	Base: monômeros compostos por Bis-GMA, UDMA, Bis-MPEPP, TEGDMA. Parte inorgânica: partículas de vidro de alumínio flúor-boroalumíniosilicato, partículas de ionômero de vidro pré-reagidas (S-PRG). Sistema iniciador: canforoquinona. Cores \ Lote: A1 (071401); A2 (071402); A3 071403; B1 (011513); B3 (071407); C3 (081403).
Bis-GMA (SIGMA-ALDRICH, St. Louis, EUA)	Bisfenol A glicidil dimetacrilato Lot Nº: MKCF9832
TEGDMA (SIGMA-ALDRICH, St. Louis, EUA)	Trietileno-glycol dimetacrilato Lot Nº: STBG5210V

Fonte: Shofu Inc e SIGMA-ALDRICH.

Figura 1 –GIOMER Beautifil-Bulk

Fonte: http://www.shofu.com/en/products/restoratives/composites/beautifil-bulk-restorative/

2.3 Ensaio de resistência à flexão

O ensaio foi realizado no laboratório do Departamento de Odontologia Restauradora da Faculdade de Odontologia da UFMG. Um total de 25 corpos-de-

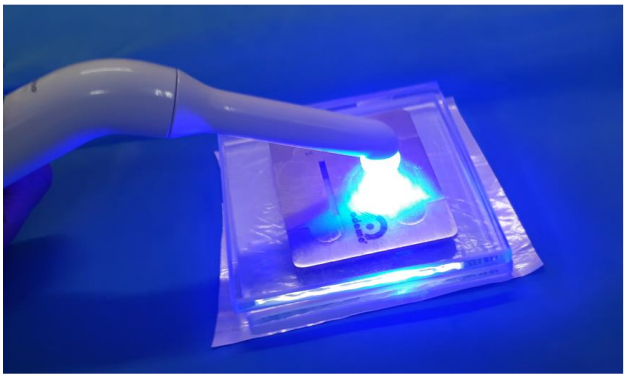
prova (n=5) foram confeccionados com resina composta Beautifil-Bulk, nas cores A1, A2, B1, B3, C3. O ensaio de flexão de 3 pontos foi realizado segundo as normas ISO 4049 (2009) e a sequência de confecção das amostras foi randomizada no programa Excel. Os corpos-de-prova foram confeccionados com auxílio de uma matriz de aço inoxidável (dimensões 25 x 2 x 2 mm, Odeme, Luzerna, Brasil) posicionada sobre uma placa de vidro e matriz de poliéster. A resina composta Beautifil-Bulk foi inserida no interior da matriz (FIGURA 2) e outra placa de vidro foi posicionada sobre o conjunto. Sobre a placa de vidro foi posicionada a ponta do fotopolimerizador com lâmpada de LED Radii-Cal (SDI Inc., Victoria, Austrália; 1200 mW/cm^2) ao centro do corpo-de-prova e o primeiro ciclo de fotoativação foi realizado (40 segundos). Subsequentemente, ambos extremos do corpo-de-prova foram fotoativados. O conjunto matriz e placa de vidro foi rotacionado em 180º para repetir o processo de fotoativação ao lado oposto do corpo-de-prova (FIGURA 3). Após os 6 ciclos de fotoativação (240 segundos), o conjunto matriz e corpo-de-prova foi imerso em água destilada a 37 ºC por 15 minutos. Os corpos-de-prova foram, então, cuidadosamente retirados das matrizes, e foi realizado acabamento com auxílio de lâmina de bisturi nº 15 para remover eventuais rebarbas de material resinoso. Os corpos-de-prova foram armazenados em água destilada a 37 ºC por um período de 24 horas.

Figura 2 – Matriz metálica (25 x 2 x 2 mm) para confecção de corpos-de-prova para ensaio de resistência à flexão

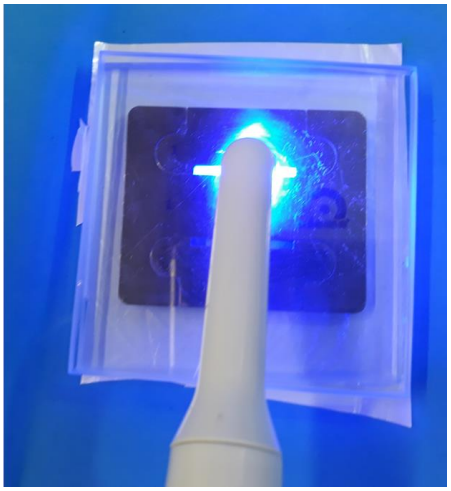
Fonte: Do autor, 2019.

Figura 3 - Confecção dos corpos-de-prova para ensaio de resistência à flexão

a



b

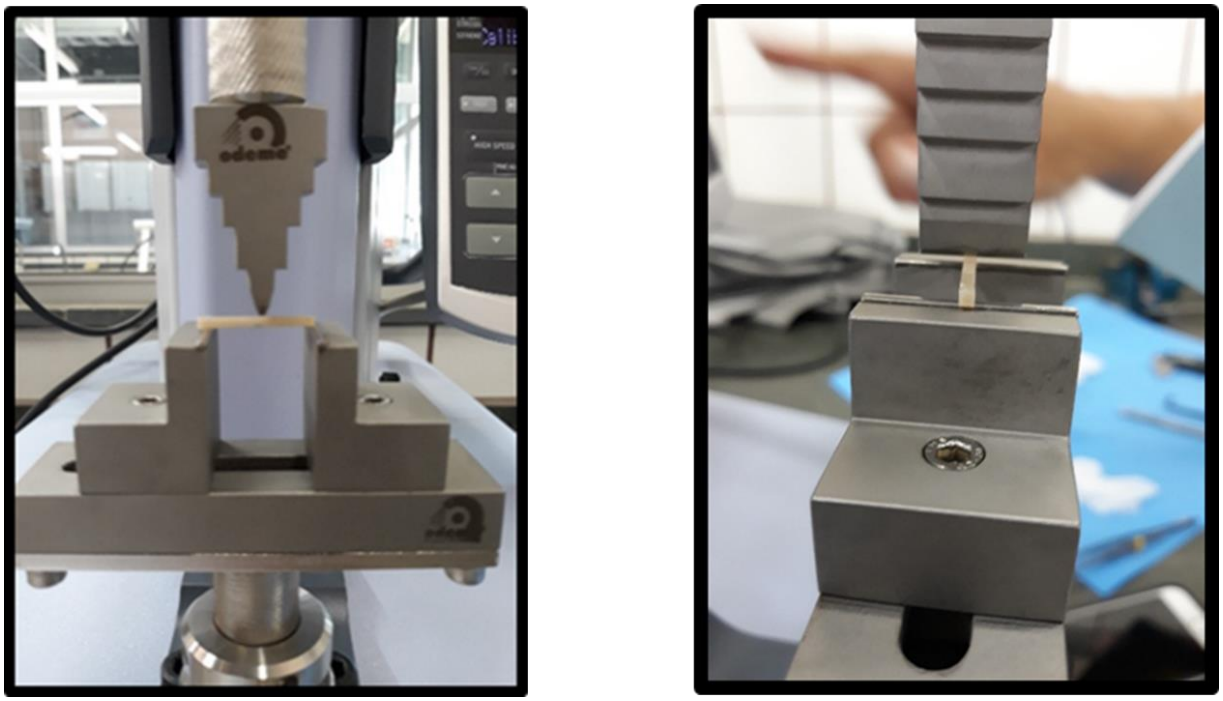


Legenda: a) Visão Frontal
b) Visão Latera
Fonte: Do autor, 2019.

Após o período de armazenagem em água destilada, foi realizada a medição da altura e espessura em três pontos de cada corpo-de-prova para obtenção de valores médios com o auxílio de um paquímetro digital (Mitutoyo, Kawaski, Japão). Os corpos-de-prova foram submetidos ao teste de flexão de três pontos utilizando a máquina universal de testes (EZ-Test, Shimadzu, Tokyo, Japão), acoplado com célula de carga (Odeme, Luzerna, Brasil) com velocidade de 1,0 mm/min até a fratura da amostra (FIGURA 4).

Figura 4 – Corpo-de-prova posicionado na máquina universal EZ-Teste para o ensaio de resistência à flexão

a b



Legenda: a) Visão Frontal
b) Visão Lateral
Fonte: Do autor, 2019.

Os valores de resistência à flexão foram calculados em Megapascal (MPa) de acordo com a fórmula:

$$\text{RESISTÊNCIA À FLEXÃO} = \frac{3xFxL}{2xbxh^2}$$

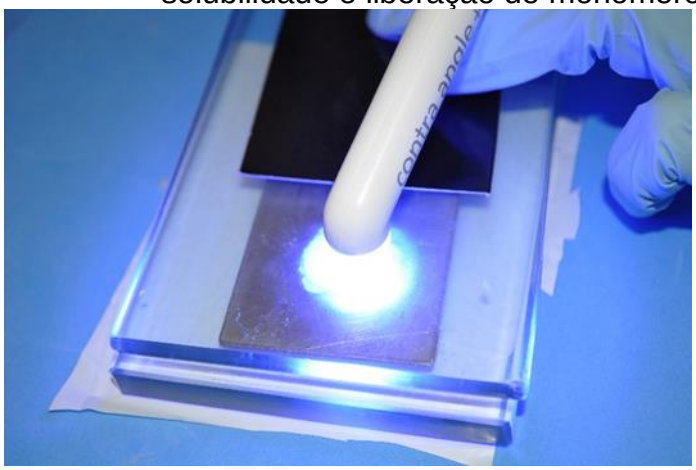
Onde: resistência à flexão (MPa); F = carga máxima (N) exercida no espécime; L = distância (mm) entre os apoios; b = largura (mm) do espécime; h = altura (mm) do espécime.

2.4 Ensaio de absorção e solubilidade

O ensaio foi realizado no laboratório do Departamento de Odontologia Restauradora da Faculdade de Odontologia da UFMG. Um total de 25 corpos-de-prova (n=5) foram confeccionados com a resina composta Beautifil-Bulk nas cores

A1, A2, B1, B3, C3. O ensaio de absorção e solubilidade foi realizado segundo as normas ISO 4049 (2009) e a sequência de confecção foi randomizada no programa Excel. A resina composta Beautifil-Bulk foi inserida no interior da matriz de aço inoxidável, apoiada sobre uma placa de vidro, com dimensões de 15 mm de diâmetro por 1 mm de espessura, posicionada entre duas placas de vidro com tiras de matriz de poliéster (Odeme, Luzerna, Brasil) (FIGURA 5). Após acomodação da resina em incremento único foi posicionada a ponta do fotopolimerizador com lâmpada de LED Radii-Cal (SDI Inc., Victoria, Australia; 1200 mW/cm^2) ao centro da amostra e o primeiro ciclo de fotoativação foi realizado (40 seg). Subsequentemente, outros 8 ciclos de fotoativação foram realizados cobrindo as dimensões do corpo-de-prova. O conjunto matriz e placa de vidro foi rotacionado em 180º para repetir o processo de fotoativação ao lado oposto do corpo-de-prova. Após os 18 ciclos de fotoativação (360 segundos) os corpos-de-prova foram cuidadosamente retirados das matrizes, e foi realizado acabamento com auxílio de lâmina de bisturi nº 15 para remover eventuais rebarbas de material resinoso. Após a confecção de todos os corpos-de-prova (FIGURA 6) os espécimes foram colocados no interior de um dessecador, contendo sílica gel dessecante a temperatura ambiente por 24 horas.

Figura 5 – Confecção dos corpos de prova para absorção e solubilidade e liberação de monômeros



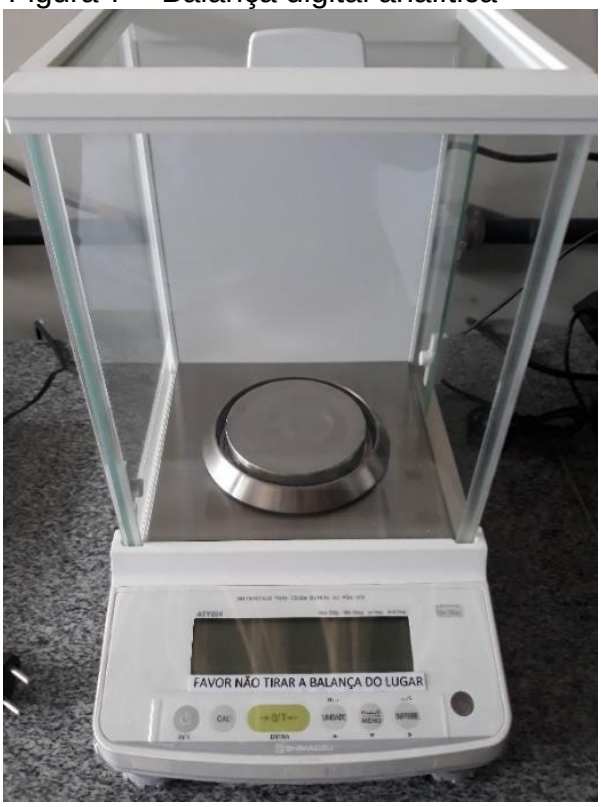
Fonte: Do autor, 2019.

Figura 6 – Corpos-de-prova confeccionados para o ensaio de absorção e solubilidade

Fonte: Do autor, 2019.

Após 24h, os corpos-de-prova foram pesados, diariamente, em uma balança digital analítica com 0,1 mg de precisão (ATY224, Shimadzu, Tokyo, Japão) (FIGURA 7), devidamente calibrada, até que foi obtida uma massa constante, denominada massa seca inicial (m1). Para determinar a massa constante de cada espécime a variação entre as massas não poderia ser maior que 0,1 mg a cada 24 horas de avaliação. A espessura e o diâmetro de cada espécime foram mensurados com o auxílio de um paquímetro digital (Mitutoyo, Kawaski, Japão) para calcular o volume de cada disco (mm^3), quando obtida a m1.

Figura 7 – Balança digital analítica



Fonte: Do autor, 2019.

Após a obtenção da m1, os mesmos corpos-de-prova foram imersos em água destilada em recipientes hermeticamente fechados contendo 10 mL de água destilada e armazenados em estufa a 37 °C por 7 dias. Os corpos-de-prova foram removidos da estufa, deixados em temperatura ambiente por 30 minutos e, em seguida, foram lavados com água destilada, suavemente secos com papel absorvente para obter a massa 2 (m2), e novamente foram armazenados e levados ao dessecador. Os espécimes foram, então, pesados diariamente até que uma massa constante (m3) foi obtida. Os valores de absorção de água (SA) (µg/mm^3) e a solubilidade (SL) (µg/mm^3) foram calculados de acordo com as seguintes fórmulas:

$$SA = \frac{m2-m3}{V}$$

$$SL = \frac{m1-m3}{V}$$

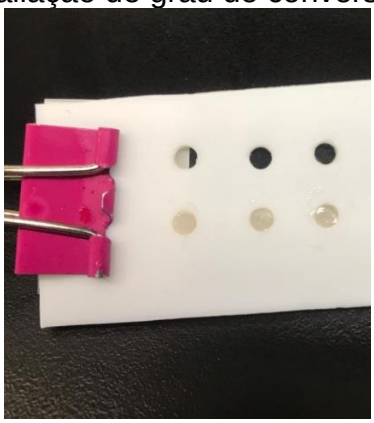
2.5 Análise do grau de conversão (FTIR-ATR)

O ensaio foi realizado no *Analytical Laboratory for Environment Science Research and Training* (ANALEST – *School of Chemistry – University of Toronto*, CA). Um total de 3 amostras (n=3) foram confeccionadas com resina composta Beautifil-Bulk na cor A3. O grau de conversão dos monômeros foi avaliado por meio de um espectrômetro Infravermelho por Transformada de Fourier (FTIR) (Nicolet iS50, Thermo Fisher, Madison, USA) equipado com dispositivo de refletância total atenuada (ATR) (FIGURA 8). A resina composta Beautifil-Bulk foi inserida no interior da matriz de teflon, apoiada sobre uma placa de vidro, com dimensões de 1 mm de diâmetro por 1 mm de espessura e fotoativada em ciclo único de 40 segundos com fotopolimerizador com lâmpada de LED Radii-Cal (SDI Inc., Victoria, Australia; 1200 mW/cm^2) (FIGURA 9).

Figura 8 – Equipamento FTIR/ATR

Fonte: Do autor, 2019.

Figura 9 – Matriz Teflon 1,0 mm x 1,0 mm para confecção de corpos-de-prova para ensaio de avaliação de grau de conversão



Fonte: Do autor, 2019.

As leituras foram realizadas para os corpos-de-prova antes e imediatamente após o ciclo de fotoativação e o DC foi calculado a partir das alterações na relação entre o pico de absorbância das cadeias alifáticas a 1636 cm^{-1} e o pico de absorbância das duplas ligações de carbono nas cadeias aromáticas a 1608 cm^{-1} nos estados polimerizados (P) e não polimerizados (N), de acordo com a seguinte equação:

$$\% \text{ Grau de Conversão} = 100 - \left[\frac{\left(\frac{CAP}{DCAP}\right)}{\left(\frac{CANP}{DCANP}\right)} x\ 100 \right]$$

Onde: CAP = área de pico das cadeias alifáticas polimerizadas; DCAP= área de pico das duplas ligações de carbono nas cadeias aromáticas polimerizadas; CANP= área de pico das cadeias alifáticas não polimerizadas; DCANP= área de pico das duplas ligações de carbono nas cadeias aromáticas não polimerizadas.

2.6 Ensaio para quantificação de monômeros liberados

O meio de escolha para incubação das amostras dos compósitos resinosos para o ensaio de liberação de monômeros foi a água destilada, totalizando

6 grupos experimentais e controles. As amostras foram preparadas em triplicata (n=3), com avaliações em curto e em longo prazo (JAFFER, FINER E SANTERRE, 2002), conforme a Tabela 2.

Tabela 2- Grupos experimentais para o ensaio de liberação de monômeros

MATERIAL	TIPO DE SOLUÇÃO	TEMPO
Beautifil-Bulk (Shofu Inc., Kyoto, Japão)	Água Destilada	10 min
		24 horas
		7 dias
		30 dias
		3 meses
		6 meses

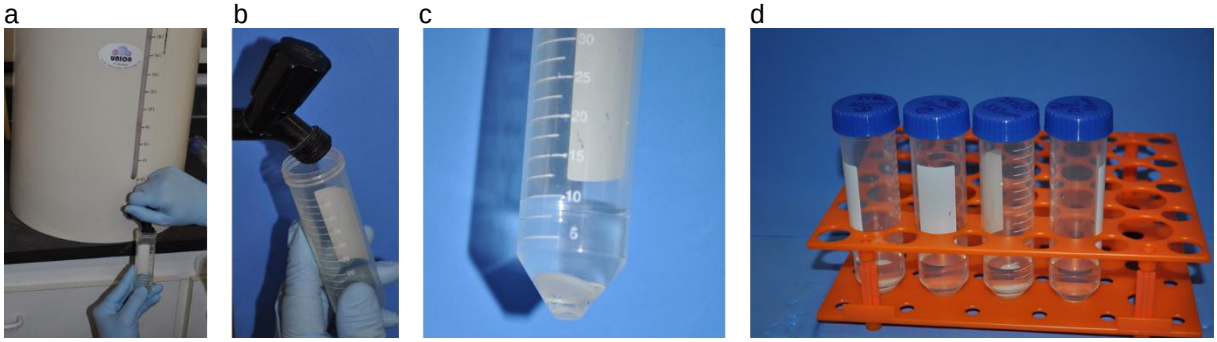
Fonte: Elaborado pelo autor, 2019.

2.6.1 Preparo das amostras para o ensaio de liberação de monômeros

Cada amostra foi confeccionada seguindo a especificação ISO 4049 (2009) para ensaio de absorção e solubilidade, utilizando matriz metálica com 15 mm de diâmetro por 1mm de espessura, cor A3, posicionada entre duas placas de vidro com tiras de matriz de poliéster. Essas amostras foram fotoativadas utilizando aparelho com lâmpada de LED Radii-Cal (Radii, SDI; 1200 mW/cm^2), cuja ponteira foi posicionada diretamente sobre a placa de vidro (FIGURA 5). Após acomodação da resina em incremento único, a ponta do fotopolimerizador foi posicionada sobre a placa de vidro, ao centro da amostra, e o primeiro ciclo de fotoativação foi realizado (40 segundos). Subsequentemente, outros 8 ciclos foram realizados cobrindo as dimensões do corpo-de-prova. O conjunto matriz e placa de vidro foi rotacionado em 180º para repetir o processo de fotoativação ao lado oposto do corpo-de-prova (Figura 4) Após os 18 ciclos de fotoativação (360 segundos), os corpos-de-prova foram cuidadosamente retirados das matrizes, e foi realizado acabamento com auxílio de lâmina de bisturi nº 15 para remover excessos de material resinoso. Em seguida, foram inseridos em tubos tipo Falcon, contendo 10 mL de água destilada e

acondicionados em estufa a 37 ºC. Para cada intervalo de tempo utilizou-se um tubo Falcon preenchido apenas com água destilada como grupo controle (FIGURA 10). A espessura e o diâmetro de cada espécime foram mensurados com o auxílio de um paquímetro digital (Mitutoyo, Kawaski, Japão) para calcular a área de superfície de cada disco (mm^2).

Figura 10 – Armazenamento dos corpos-de-prova para ensaio de liberação de monômeros



Legenda: a e b) Coleta de 10 mL água destilada do destilador
c) Amostra posicionada com água destilada no tubo Falcon estéril
d) Amostras 1, 2 e 3 e tubo controle sem amostra para armazenamento no primeiro tempo

Fonte: Do autor, 2019.

O experimento ocorreu por um tempo total de 6 meses e as análises das soluções foram realizadas em curto e longo prazo considerando 10 minutos, 24 horas, 7 dias, 30 dias, 3 meses e 6 meses.

Após completar o primeiro tempo de 10 minutos, os corpos-de-prova foram removidos dos frascos com a solução de água destilada, e, em seguida, lavados com água destilada, suavemente secos e inseridos em novos frascos com uma nova solução e recolocadas na estufa a 37 ºC. O tubo tipo Falcon com a água destilada onde permaneceu a amostra foi mantido congelado a -20 ºC. O procedimento foi repetido, respeitando o intervalo de tempo com as mesmas amostras inseridas em novos tubos com água destilada, mantidos no congelador até finalizar o período total de 6 meses.

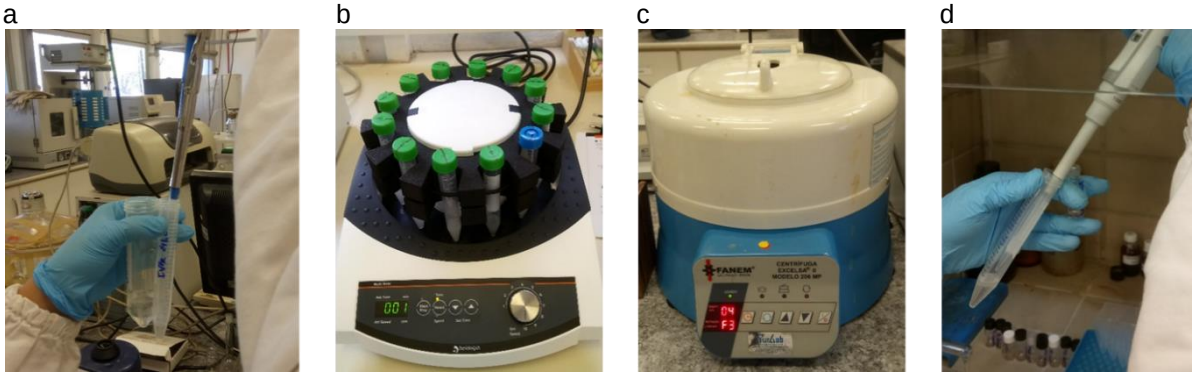
2.6.2 Preparo das amostras para avaliação no HPLC

Após o período completo de incubação das amostras, os tubos com as soluções mantidas congeladas, foram enviados ao laboratório do Instituto de Química (NovaCrom) da Universidade de Campinas (UNICAMP).

O procedimento de preparo de amostra foi adaptado de Michelsen *et al*. (2012) e realizado da seguinte forma: 1 mL da amostra e 1 mL de acetato de etila grau HPLC foram transferidos para um tubo Falcon de 15 mL (FIGURA 11a), agitou-se o tubo por 1 minuto em vortex (FIGURA 11b) e centrifugou-se por 4 minutos a 3000 rpm (FIGURA 11c). Retirou-se 0,5 mL do sobrenadante e transferiu-se para um frasco de vidro (FIGURA 11d). Repetiu-se esse procedimento por 3 vezes. Ao final, obteve-se 1,5 mL do extrato em acetato de etila, evaporou-se sob fluxo de nitrogênio esse volume e ressuspendeu-se o extrato seco em 0,5 mL de fase móvel. A amostra foi filtrada em filtro de seringa de 0,45 µm para um vial e acondicionada no amostrador do cromatógrafo.

Figura 11 – Preparo da amostra para análise no HPLC

a b c d



Legenda: a) Transferência das amostras para tubo Falcon
b) Vórtex utilizado para preparo das amostras
c) Processo de centrifugação das amostras
d) Tranferência para o frasco de vidro

Fonte: Do autor, 2019.

2.6.3 – Preparo dos padrões para análise no HPLC

Foram preparadas soluções estoque dos padrões de Bis-GMA e TEGDMA, em acetonitrila grau HPLC, na concentração de 10,0 µg/mL e a partir dessas, realizaram-se as seguintes diluições para se obter as soluções de trabalho (Tabela 3).

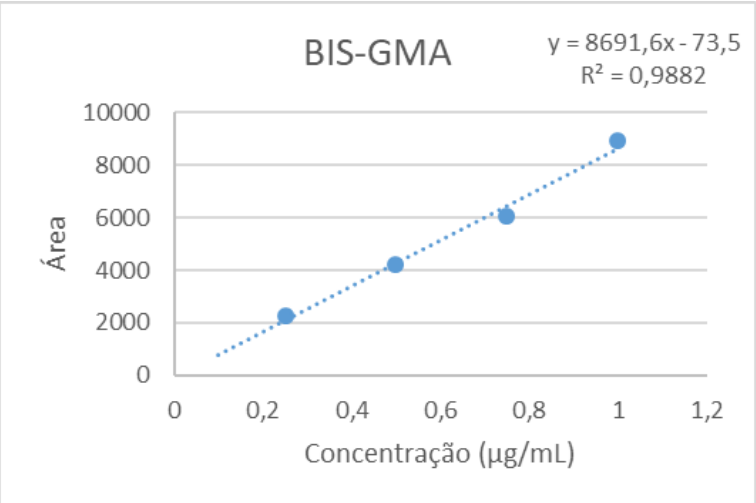
Tabela 3 – Diluições para soluções de trabalho no HPLC

Bis-GMA (µg/mL)	**TEGDMA (µg/mL)**
-	0,10
0,25	0,25
0,50	0,50
0,75	0,75
1,00	1,00

Fonte: Elaborado pelo autor, 2019.

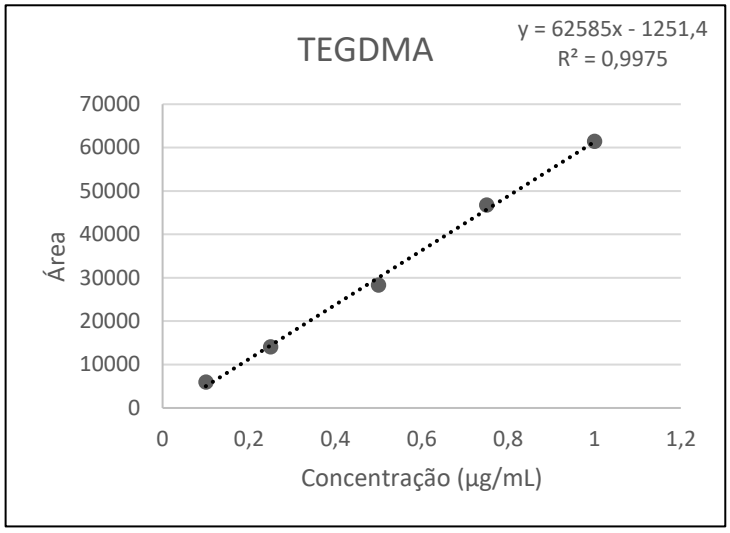
Estas soluções foram filtradas em filtro de seringa de 0,45 µm para um vial, acondicionada no amostrador do cromatógrafo e injetadas. Construiu-se a curva analítica utilizada para a quantificação das amostras (Gráficos 1 e 2).

Gráfico 01 – Curva analítica do Bis-GMA



Fonte: Elaborado pelo autor, 2019.

Gráfico 02 – Curva analítica do TEGDMA



Fonte: Elaborado pelo autor, 2019.

O método cromatográfico utilizado empregou Coluna NovaPack (C18 3,9 mm x 150 mm x 4 µm) (Waters Corporation, Milford, USA) com modo de eluição isocrático, volume de injeção 10 µL, vazão 0,5 mL/min e com fase móvel acetonitrila: acetato de amônio 10 mm 65:35 (v/v).

As condições do espectrômetro de massas para o Bis-GMA (modo MRM) foram: íon precursor (m/z) 513,19 Da, íon filho (m/z) 142,9 Da, voltagem do cone 25 V, energia de colisão 20 eV. Para o TEGDMA (modo MRM), as condições foram: íon precursor (m/z) 286,97 Da**,** íon filho (m/z) 112,9 Da**,** voltagem do cone 25 V**,** energia de colisão 12 eV.

Desta forma, foi possível identificar e quantificar a presença ou ausência dos monômeros Bis-GMA e TEGDMA.

2.7 Análise morfológica da superfície por microscopia eletrônica de varredura (MEV)

Como o objetivo de avaliar o efeito da liberação de monômeros da resina Beautifil-Bulk foram confeccionados 5 corpos-de-prova em matrizes de aço com

dimensões de 15 mm de diâmetro por 1 mm de espessura na cor A3. Um corpo-de-prova foi mantido a seco e os demais foram armazenados em água destilada, à temperatura de 37 ºC, nos mesmos intervalos empregados no ensaio de liberação de monômeros: 7 dias, 30 dias, 3 meses e 6 meses (JAFFER; FINER; SANTERRE, 2002). Não foram avaliados os corpos-de-prova armazenadas no período de 10 min e 24 horas devido ao curto tempo para uma possível alteração na superfície.

Após o período de incubação os corpos-de-prova foram lavados com água destilada, suavemente secados e levados ao Centro de Microscopia da UFMG. Os corpos-de-prova foram submetidos à pulverização de 4 nm de carbono em sua superfície, utilizando o equipamento para metalização (MD20, Bal-Tec, Vaduz, Alemanha) (FIGURA 12). Após a metalização, os corpos-de-prova foram levados ao microscópio eletrônico de varredura (FEI - Quanta 200, FEG, Eindhoven, Holanda).

Figura 12 – Metalização dos corpos-de-prova para avaliação em MEV

a b c

Legenda: a) Posicionamento dos corpos-de-prova na matriz
b) Metalizadora (MD20, Bal-Tec)
c) Corpos-de-prova metalizados
Fonte: Do autor, 2019.

2.8 Análise estatística

A partir dos dados obtidos foram realizadas análises estatísticas e descritivas, onde os resultados foram expressos como média dos valores (M) e desvio padrão (DP). Foram realizados testes de normalidade (Kolmogorov-Smirnov e

Shapiro-Wilk) e de homocedasticidade (Levene). Os dados obtidos dos ensaios de resistência à flexão e absorção apresentaram distribuição normal e homocedasticidade. Assim, foi empregada Análise de Variância (ANOVA) e teste de comparação múltipla para identificação de diferenças entre os níveis dos fatores em estudo. O ensaio de liberação de monômeros não apresentou distribuição normal, mas cumpriram os preceitos de homocedasticidade sendo realizado o teste não-paramétrico Kruskal-Wallis. Para os dados de solubilidade, em que os pressupostos de normalidade ou homogeneidade falharam, foi aplicado teste não paramétrico de comparação Kruskal-Wallis Test. Em todas as situações, foi adotado o nível de significância de 5%.

3 ARTIGOS

3.1 Artigo

- Os dados obtidos foram compilados na forma de artigo a ser submetido ao periódico *Journal of Applied Oral Science* (Qualis A2). O texto foi adequado nas normas desse periódico após as correções sugeridas pela banca examinadora durante a defesa.

Title: *In vitro* characterization of a bulk-fill resin composite containing S-PRG fillers

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ABSTRACT

Objective: The aim of the study was to analyze the physico-chemical properties of a bulk-fill resin composite containing S-PRG fillers. Materials and methods: The dependent variables were flexural strength (FS), water sorption (WS) and solubility (SL), degree of conversion (DC), long-term elution of monomers in distilled water and surface morphological analysis after incubation in distilled water. The independent variables were shade of the composite resin and storage time of the specimens. Descriptive statistical analyzes of data was made.Results were expressed as mean values and standard deviation. Normality tests (Kolmogorov-Smirnov and Shapiro-Wilk) and homoscedasticity tests (Levene) were performed. The data obtained from the tests of FS and WS showed normal distribution and homoscedasticity. Thus, Variance Analysis (ANOVA) and multiple comparison test were used to identify differences among the levels of the factors under study. The monomer release assay did not present normal distribution but fulfilled the precepts of homoscedasticity and the non-parametric Kruskal-Wallis test was performed. For the SL data, in which the normality or homogeneity assumptions failed, a Kruskal-Wallis Test non-parametric test was applied. In all situations, the significance level of 5% was adopted. Results: There was no significant difference among the resin shades for FS, WS and SL variables ($p > 0.05$). The mean of DC 59.37(14.49) %. For elution monomers the highest amounts of TEGDMA were eluted after 30 days and 3 months of storage. BisGMA could not be detected in any of the solutions. SEM images showed morphological changes suggestive of surface roughness at 6 months of storage. Conclusion: The composite resin Giomer Beautifil-Bulk reached the requirements of ISO 40409: 2009 for FS, WS and SL standards and presented an acceptable DC. There was no elution of BisGMA, and TEGDMA could be detected throughout the 6-month period of evaluation.

Key words: Dental resins. Physical and Chemical Properties. Fourier-transform infrared spectroscopy. Bisphenol A-Glycidyl Methacrylate. Methacrylates.

INTRODUCTION

Resin composites are subjected to physical actions, due to wear and occlusal loading, and chemical, by the humidity of saliva and food. The effects of these physico-chemical processes are directly related to the composition of resin restorative materials.[1] Laboratory tests are especially important to evaluate the physical resistance and chemical stability of restorative materials.

The strength of the restorative material is related to the stresses that develop according to the nature of the applied forces and the dimensions of the restoration, including tensile, shear and compression tension.[2] Three-point flexural is a valuable test to evaluate flexural strength.[3,4] The differential of the flexural test with other mechanical tests is that because it is a folding force, it results in complex tensions arising from the compression, shear and tensile stress relationship in the same body[2]. Flexural strength means the greatest stresses to the material before failure.[2]

Resin composites are susceptible to solvent absorption, especially water, and loss of soluble components.[1] For physical and chemical stability of the material it is ideal that the sorption and solubility is the lowest possible as it can negatively influence the biocompatibility of the material reducing its mechanical properties and longevity of the restoration.[5] Also, a direct relation with the stability of the composite is its percentage of degree of conversion (DC). The higher the DC the better the physical-mechanical and chemical properties of the composites,[1,6,7]but values are reached between 50 and 70% due to the closure of the chains polymerization and trapping of unreacted monomers within the resin matrix.[8,9]

Due to the presence of saliva and enzymes in the oral cavity the elution of unreacted monomers or other components of the composite resin matrix may occur..[9] The process of degradation by the hydrolytic and enzymatic action can increase the wear of the restoration[10-14], as well as a low degree of polymerization conversion.[15] The elution of composite resin monomers are potentially hazardous[9,16] at the local level as mucosa, gingiva and dental pulp[15] and systemic levels such as teratogenic and cytotoxic effects[17], cell death[18] and fertility reduction[19]. The degradation of the surface of the composite resins can undergo morphological alterations with increased surface roughness favoring staining and wear of the restoration.[13] The most commonly used method for evaluating the elution of composite resin monomers is by means of High-Performance Liquid Chromatography (HPLC)[20,15,21,9] and Scanning Electron Microscopy (SEM) is usually used to analyze the surface of the degraded specimes.[22,23,13]

GIOMER is a class of resin materials introduced by Shofu Inc., which combined the fluorine release properties of glass ionomer cement and the strength and aesthetics of composite resins.[24-27] The main difference between the compomers and the GIOMER is the presence of pre-reacted glass ionomer particles (S-PRG) incorporated in the resin matrix which enables the release of fluoride and other ions.[26,28] Recently, a GIOMER bulk-fill resin composite has been introduced to simplify the restorative technique. Because of its higher translucency, allow greater light dissipation and incorporation of more reactive photoinitiators, this type of resin can be inserted into cavities in single increments of 4 to 5 mm.[29]

Therefore, the present *in vitro* study analyzed the physical-chemical properties of a GIOMER resin composite, Beautifil-Bulk, considering the shade of the composite resin and storage time of the specimens.

MATERIAL AND METHODS

Experimental design

This was a qualitative and quantitative, *in vitro* experimental study. The dependent variables were flexural strength (FS), sorption (WS) and solubility (SL), degree of conversion (DC), elution of monomers and morphological analysis of the samples surface. The independent variables were shade of the composite resin and the storage time of the specimens. The shades of the GIOMER bulk-fill restorative material (Beautifil-Bulk, SHOFU Inc.) used were A1, A2, A3, B1, B3 and C3. For all assays, the materials used were kept at 4 °C prior to use, the resins were removed from the refrigerator and kept in the laboratory at room temperature for 30 minutes. Glove and instrument handling were cleaned and sterilized to prevent contamination. BisGMA and TEGDMA were used to identify the standards for the monomer elution assay. The Radii-Cal LED light curing unit (SDI Inc., Victoria, Australia, 1200 mW/cm^2) was used to photactivate all the samples for 40 sec. The materials and chemicals used are described in Table 1.

Flexural strength assay

A total of 25 specimens (n=5) were prepared with Beautifil-Bulk resin in shades A1, A2, B1, B3, C3, according to ISO 4049:2009,[3] with the aid of a stainless-steel matrix (dimensions 25 x 2 x 2 mm, Odeme, Luzerna, Brazil). After 24 h water storage at 37 ºC, the samples´ dimensions were measured with a digital caliper with a precision of 0.01 mm (Mitutoyo, Tokyo, Japan) and the three-point bending test was performed using the universal

test machine (EZ-Test, Shimadzu, Tokyo, Japan) at a rate of 1.0 mm/min until fracture of the sample. The values of FS were calculated according to the equation:

FS= $\frac{3xPxD}{2xWxh^2}$

Where,

FS = flexural strength (MPa)
P = the maximum load, in newtons, exerted on the specimens;

L = the distance, in millimeters, between the supports (20 mm);

W = the width, in millimeters, of the specimens measured prior to testing;

h = the height, in millimeters, of the specimens measured prior to testing.

Sorption and Solubility Assay

A total of 25 specimens (n = 5) were prepared with the same Beautifil-Bulk shades as previously described, following ISO 4049:2009[3] and using a stainless-steel matrix (dimensions 15 x 1 mm, Odeme, Luzerna, Brazil). The specimens were kept in a desiccator containing desiccant silica gel at 23 °C (±1 ºC) for 24 h. They were weighed daily on an analytical digital scale (ATY224, Shimadzu, Tokyo, Japan) until there was no variation of 0.1 mg and a constant mass, called the initial dry mass (m1) was obtained. Dimensional measurements from each sample were taken with digital caliper with a precision 0.01mm (Mitutoyo, Tokyo, Japan) to calculate volume (V) of each disc (mm^3). Subsequently, the same specimens were immersed in distilled water in individual vials containing 10 mL of distilled water and stored in an incubator at 37 °C for 7 days. The specimens were removed from the incubator, left at room temperature for 30 minutes, and then rinsed with distilled water, gently dried with absorbent paper to obtain mass 2 (m2), and again stored inside a desiccator. The specimens were weighed daily until a constant mass (m3) was obtained. WS ($\mu g/mm^3$) and SL ($\mu g/mm^3$) values were calculated according to the following equation:

WS = $\frac{m2-m3}{V}$

SO = $\frac{m1-m3}{V}$

Degree of conversion (DC)

A total of 3 samples (n=3) were prepared with Beautifil-Bulk, shade A3. The DC of the monomers was evaluated using Fourier Transform Infrared (FTIR) spectrometer (Nicolet iS50, Thermo Fisher, Madison, USA) equipped with attenuated total reflectance (ATR) device. The resin composite was inserted into the Teflon matrix, placed on top of a glass slab and photoactivated in a single cycle according to the manufacturer's recommendations. The DC was calculated from the changes in the ratio of the absorbance peak of the aliphatic

chains (CA) to 1636 cm^{-1} and the absorbance peak of the carbon double bonds in the aromatic chains (DCA) at 1608 cm^{-1} in (DCAP) and unpolymerized (CANP; DCANP), according to the following equation:

$$\% \text{ DC} = 100 - [\ \frac{\left(\frac{CAP}{DCAP}\right)}{\left(\frac{CANP}{DCANP}\right)} x\ 100\ ]$$

Elution of monomers assay

Beautifil-Bulk samples (shade A3) were made following the ISO 4049:2009[3] specification for WS and SL assay as described above (n=3) and were incubated in distilled water. Short- and long-term evaluations were conducted.[30,13] The incubation periods were 10 min, 24 hours, 7 days, 30 days, 3- and 6-months. Each specimen was incubated in individual vials containing 10 mL of distilled water at 37 °C. After each storage period, the specimens were removed from the vials, rinsed with distilled water, gently dried and inserted into new vials with a fresh water and stored at 37 °C. Storage solutions were kept frozen at -20 °C. The procedure was repeated respecting the time interval. A control (blank) group solution was prepared which consisted of 10 mL distilled water without resin discs to assure that the source of monomer elution would be the material and not the vial. The dimensions of the samples were taken to calculate the surface area.

The elution assay was adapted from Michelsen, et al.[31] (2012) and carried out as follows: 1 mL of the sample and 1 mL of HPLC grade ethyl acetate were transferred to a 15 mL vial, vigorously agitated for 1 minute and centrifuged for 4 minutes at 3000 rpm. 0.5 mL of the supernatant was removed and transferred to a glass vial. This procedure was repeated 3 times. At the end, 1.5 mL of the ethyl acetate extract was obtained, the volume was evaporated under nitrogen flow and the dried extract was resuspended in 0.5 mL of mobile phase. The sample was filtered through a 0.45 µm syringe filter into a vial and placed in the chromatograph sampler. Stock solutions of the BisGMA and TEGDMA standards were prepared in HPLC grade acetonitrile at the concentration of 10.0 µg/mL and from these the following dilutions were performed to obtain working solutions (Table 2). These solutions were filtered on a 0.45 µm syringe filter into a vial, wrapped in the chromatograph sampler and injected. The analytical curve used for the quantification of the samples was constructed (Figure 1 and 2). The chromatographic method used was from NovaPack Column (Waters Corporation, Milford, USA) (C18 3.9 mm x 150 mm x 4 µm) with isocratic elution mode, 10 µL injection volume, flow rate 0.5 mL/min and mobile phase acetonitrile: ammonium acetate 10 mm 65:35 (v/v). Mass spectrometer conditions for BisGMA (MRM mode): precursor ion (m/z) 513.19 Da, son ion (m/z) 142.9 Da, cone voltage 25 V, collision energy 20 eV. For the

TEGDMA (MRM mode): precursor ion (m/z) 286.97 Da, son ion (m/z) 112.9 Da, cone voltage 25 V, collision energy 12 eV. In this way, it was possible to identify and quantify the presence or absence of the Bis-GMA and TEGDMA monomers.

Surface morphological analysis by SEM

Discs (15 x 1 mm) of resin composite, shade A3, were prepared (n=3). A sample was kept dry and the others incubated in distilled water, at 37° C, at intervals of 7 days, 30 days, 3 months and 6 months.[13] It was not incubated in the period of 10 min and 24 h due to the short time for a possible change in the surface of the specimen. After the incubation period the samples were washed with distilled water and gently dried. The specimens were subjected to the metallization machine to spray 4 nm of carbon on their surface, using metallization equipment (MD20, Bal-Tec, Vaduz, Germany). After the metallization the samples were taken to the scanning electron microscope (FEI - Quanta 200, FEG, Eindhoven, Netherlands).

Statistical analysis

From the data obtained were descriptive statistical analyzes, where the results were expressed as mean values and standard deviation. Normality tests (Kolmogorov-Smirnova and Shapiro-Wilk) and homoscedasticity tests (Levene) were performed. The data obtained from the tests of FS and WS showed normal distribution and homoscedasticity. Thus, Variance Analysis (ANOVA) and multiple comparison test were used to identify differences between the levels of the factors under study. The monomer release assay did not present normal distribution, but fulfilled the precepts of homoscedasticity and the non-parametric Kruskal-Wallis test was performed. For the SL data, in which the normality or homogeneity assumptions failed, a Kruskal-Wallis Test non-parametric test was applied. In all situations, the significance level of 5% was adopted.

RESULTS

Flexural strength

The results of FS obeyed normal distribution and homecedasticity. The means and standard deviation of the FS in table 2. There was no significant statistical difference among the shades for FS ($p = 0.249$).

Sorption and Solubility

The results did not present statistically significant difference for both dependent variables. The means and standard deviation are described in Table 2. There was no significant statistical difference among the shades for WS ($p = 0.819$) and SL ($p = 0.559$).

Degree of conversion

After triplicate analysis by FTIR / ATR the mean DG with standard deviation was 59.37(14.49)%. The analysis was performed immediately after photopolymerization and no statistic was performed.

Elution of monomers assay

Neither BisGMA nor TEGDMA were detected in the control solutions. BisGMA was not detected in any of the solutions. Figure 3 shows the punctual elution of TEGDMA over 6 months. There was a significant difference for median TEGDMA elution over 6 months (p=0,027). The highest amounts of TEGDMA were eluted at 30 days and 3 months of storage. From 3 months there was a significant decrease in the elution, but the values did not achieve the initial levels (10 min). Figure 4 shows the cumulative elution values of TEGDMA for each period. There was a significant increase in the amount of eluted monomer from 10 min and 24 h to 3 and 6 months, and there was also a significant increase from 7 days release to 6 months (p=0.015).

Surface morphological analysis by SEM

The morphological surface of the composite resin sample with S-PRG particles can be seen in Figure 5 (10.000x magnification). A suggestive difference was observed on the surface of samples that were incubated for 6 months (figure 4d), which showed more porous with exposure of particles fillers when compared to samples that were not incubated (Figure 5a). This suggests that, during the final incubation process, the samples had a higher elution of unreacted monomers.

DISCUSSION

The flexure tests are generally used to indirectly evaluate and to estimate the clinical performance of restorative materials.[2,32-36] The ISO 4049:2009[3] recommends a FS value greater than 80 MPa for class 2 and type 1 materials (intra-oral photoactivated materials). For the shades evaluated in this study, the requirements for FS met ISO standard. Pigments concentration levels from different resin shades did not affect the mechanical properties of the material.

The overall mean FS value of different resin shades was 89.77±9.98 MPa. This result is also very consistent with previous reports, that used the same material, and the FS value was 92.06±10.11 MPa[36] after incubation for 7 days in distilled water and 86.60±3.57 MPa[2] after incubation for 7 days in artificial saliva. On the other hand, other FS results from the

same material were higher (118.86 ±8.26 MPa[37]; 131.2± 6.9 MPa[33]) than that found in the present study. Generally, changes in *in vitro* mechanical test results for the same material are related to the DC or the type of solution and incubation time prior to the assay.However, it was not possible to identify relationship between the DC and FS values compared to the results of our study. Tsujimoto et al.[33] (2017) did not identify significant differences between the results for FS for high and low viscosity GIOMERS bulk fill and high and low viscosity bulk fill resins.

The sorption of water molecules by hydrophilic monomers of the resins and solubility of resinous matrix components exposed to the humid environment of the oral cavity represent one of several mechanisms of deterioration that can result in hydrolytic degradation and rupture of the union of the resin particles, besides elution of unreacted monomers and other components of the resin matrix.[38] Therefore, low sorption and low solubility in aqueous media are desirable characteristics in restorative materials, such as composites.[38] The WS and SL are influenced by the resin composition, i.e., the polymer matrix and the amount of inorganic filler particles. The resin matrix is more susceptible to water effect and is prone to the release of unreacted monomers.[39,40] In this study, the mdian value for the different resin shades was 16.87±0.80 μg/mm^3 for WS and -2.74±0.60 μg/mm^3 for SL. GIOMER Beautifil-Bulk complied with the requirements of ISO 4049:2009[3] with values lower than 40 μg / mm3 for WS and 7.5 μg / mm^3 for SL. The literature reported WS values range from 13.6 to 18.3 μg/mm^3 and SL range from 0.7 to 0.9 μg/mm^3 for S-PRG filler containing materials.[39,41] Misilli e Gönülol[42] reported WS values range from 10,67 a 11,34 μg/mm^3 and SL range from -2,64 a -1,83 μg/mm^3 for three bulk fill resin composites. The negative value of solubility indicates the possibility of incomplete dehydration of the materials. This may be indicative of a low level of solubility rather than the complete absence of dissolution. It is probable due to hydrolytic chemical reactions that resulted in the formation of hydrogen bonds by connecting the absorbed water molecules to the polar groups of the polymer chains, which could not be completely removed.

In the present study, the average DC was 59.37±14.49%. Ilie and Fleming[43] (2015) and Yu, Yap and Wang[7] (2017) evaluated the DC of 2.0 mm thick samples, and Beautifil-Bulk achieved 43% and 46% of conversion, respectively. The thinner specimens (1.0 mm) from our study probably allowed better light transmittance and promoted a higher DC than that of other studies.

Eluted monomers of resin composites have potential impact on the biocompatibility and structural stability of the restoration[9,44] and there are concerns that resin-based materials

may be toxic.[18] The chemical composition of the material and its DC are related to elution of monomers.[44,11,9] For monomer release assays, various types of solvents can be used to incubate the samples, e.g., water and aqueous mixtures as cell culture media, artificial or human saliva, buffer solutions and organic solvents using mixtures based on ethanol or methanol.[9] In this current study, the choice for distilled water was made because it was the same medium used to store the samples in the other experiments (FS, WS and SL). BisGMA could not be detected in our study in any period of evaluation. This result agrees with those from Lagocka, et al[45] (2018), that did not detect BisGMA for up to 21-day incubation period of Beautifil-Bulk Flow in water distilled. These findings can be justified by the properties of the Bis-GMA molecule which presents high molecular weight, high viscosity, low mobility and it is hydrophobic.[46] On the other hand, the TEGDMA molecule has low molecular weight, high mobility, it is hydrophilic and is used in the composite resins as diluent to allow better handling.[1] Consequently, TEGDMA is generally eluted more easily than high molecular weight molecules like BisGMA.[45,46] Therefore, the presence of TEGDMA at each evaluation period in distilled water over 6-months has confirmed previous reports that it is possible that composite materials continue to elute certain monomers after a long incubation period in vitro.[9,46] Additionally, a systematic review [46] stated that there is a weak but significant correlation between the exposed surface of the tested sample and the release, while none correlation can be found for volume.

CONCLUSION

The resin composite containing S-PRG fillers, Beautifil-Bulk, reached the requirements of ISO 4049:2009[3] concerning flexural strength, water sorption and solubility, and presented an acceptable degree of conversion. There was no elution of BisGMA, but TEGDMA was detected throughout the 6-month evaluation period.

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Conflicts of interest

The authors do not have conflicts of interest.

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Table 1- Materials and chemicals used in the study.

MATERIAL	COMPOSITION
Beautifil-Bulk (Shofu Inc., Kyoto, Japão)	Resin matrix: monomers composed of BisGMA, UDMA, Bis-MPEPP, TEGDMA. Inorganic flller: S-PRG filler based on fluoroboroaluminosilicate glass, polymerization initiator, pigments and others. Shades (Lot Nº): A1 (071401); A2 (071402); A3 071403; B1 (011513); B3 (071407); C3 (081403).
BisGMA (SIGMA-ALDRICH, St. Louis, USA)	Bisphenol-A-glycerolate-dimethacrylate Lot Nº: MKCF9832
TEGDMA (SIGMA-ALDRICH, St. Louis, USA)	Triethylenglycol-dimethacrylate Lot Nº: STBG5210V

Table 2 - Mean (SD) of sorption (WS, n = 5, μg/mm^3), solubility (SL, n = 5, μg/mm^3), flexural strength (FS, n = 5, MPa)

	WS	SL	FS
A1	16.77±0.59	-2.98±0.93	89,73 (5,22)
A2	16.79±1.09	-2.81±0.64	81,43 (12,98)
B1	16.63±1.05	-2.56±0.40	89,49 (14,20)
B3	17.24±0.66	-2.40±0.56	97,44 (8,68)
C3	16.94±0.62	-2.93±0.50	90,76 (8,80)

Legends for figures

Figure 1 - BisGMA analytical curve

Figure 2 - TEGDMA analytical curve

Figure 03 - Graph of median punctual elution (µg/mL) of TEGDMA over 6 months storage in distilled water. The “x” inside each box refers to the mean value of TEGDMA elution

Figure 04 – TEGDMA elution rate over 6 months storage in distilled water

Figure 5. SEM analysis of samples: a) prior to incubation; b) after 7 days; 4) after 30 days; d) after 6 months

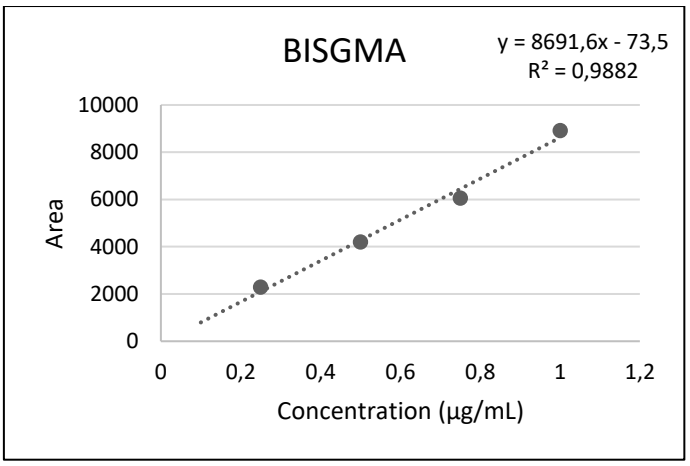

Figure 1 - BisGMA analytical curve

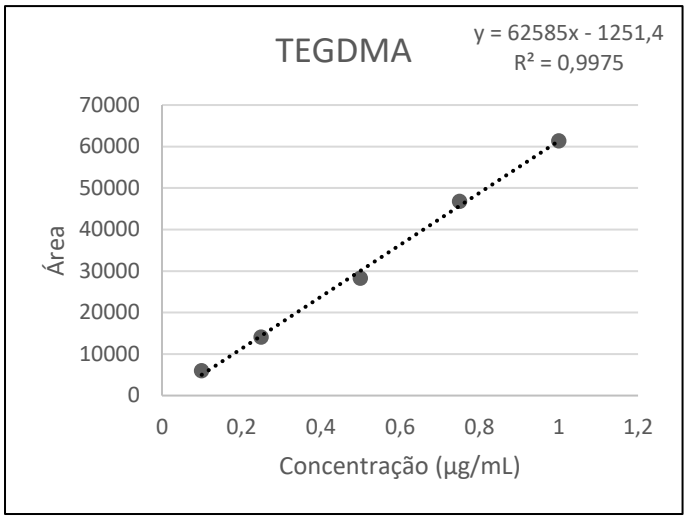

Figure 2 - TEGDMA analytical curve

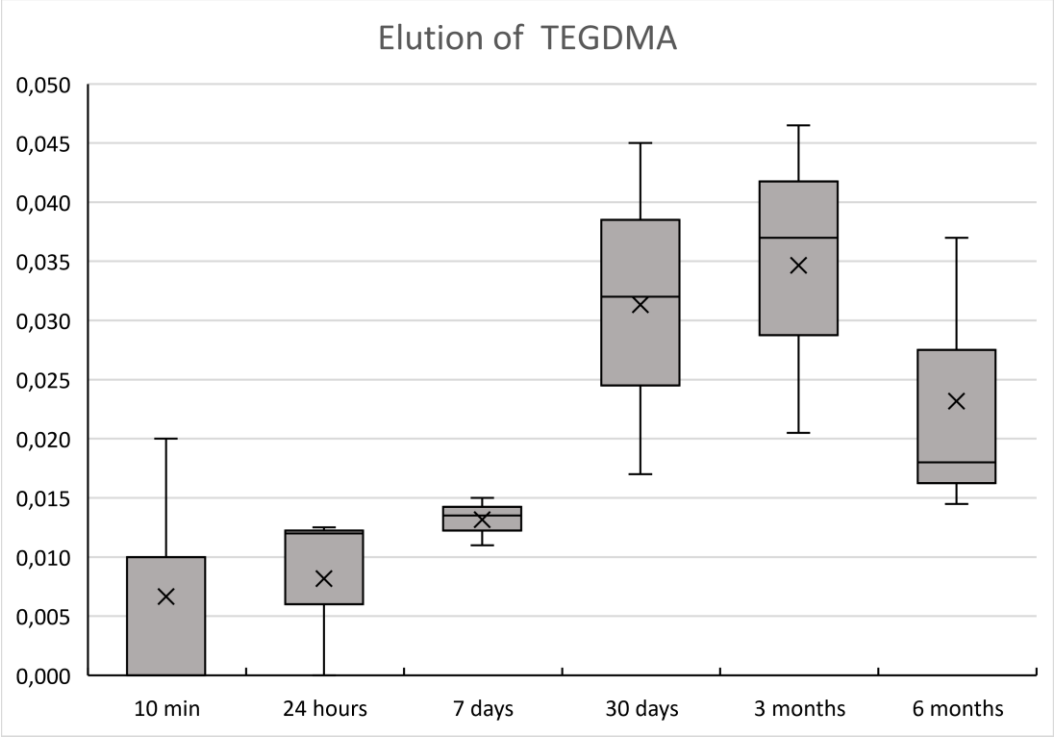

Figure 03 - Graph of median punctual elution (µg/mL) of TEGDMA over 6 months storage in distilled water. The “x” inside each box refers to the mean value of TEGDMA elution

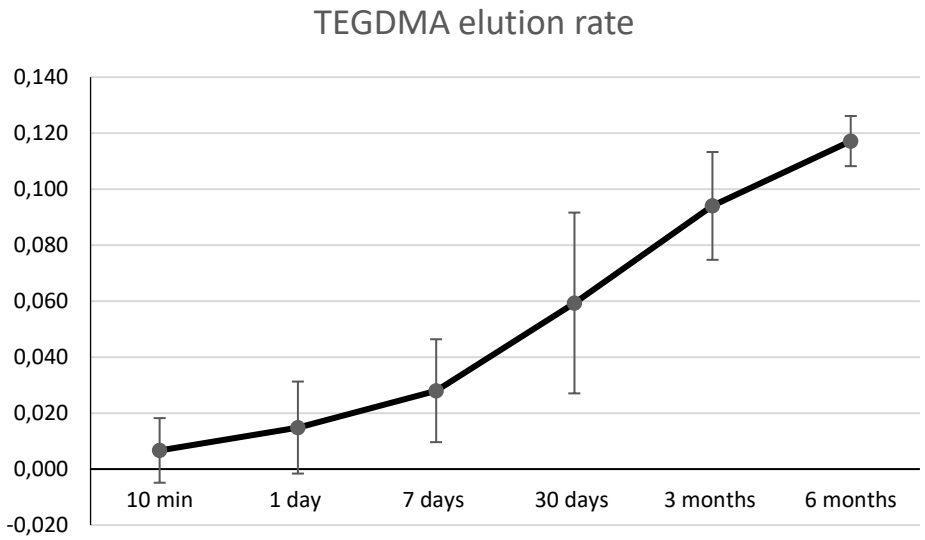

Figure 04 – TEGDMA elution rate over 6 months storage in distilled water

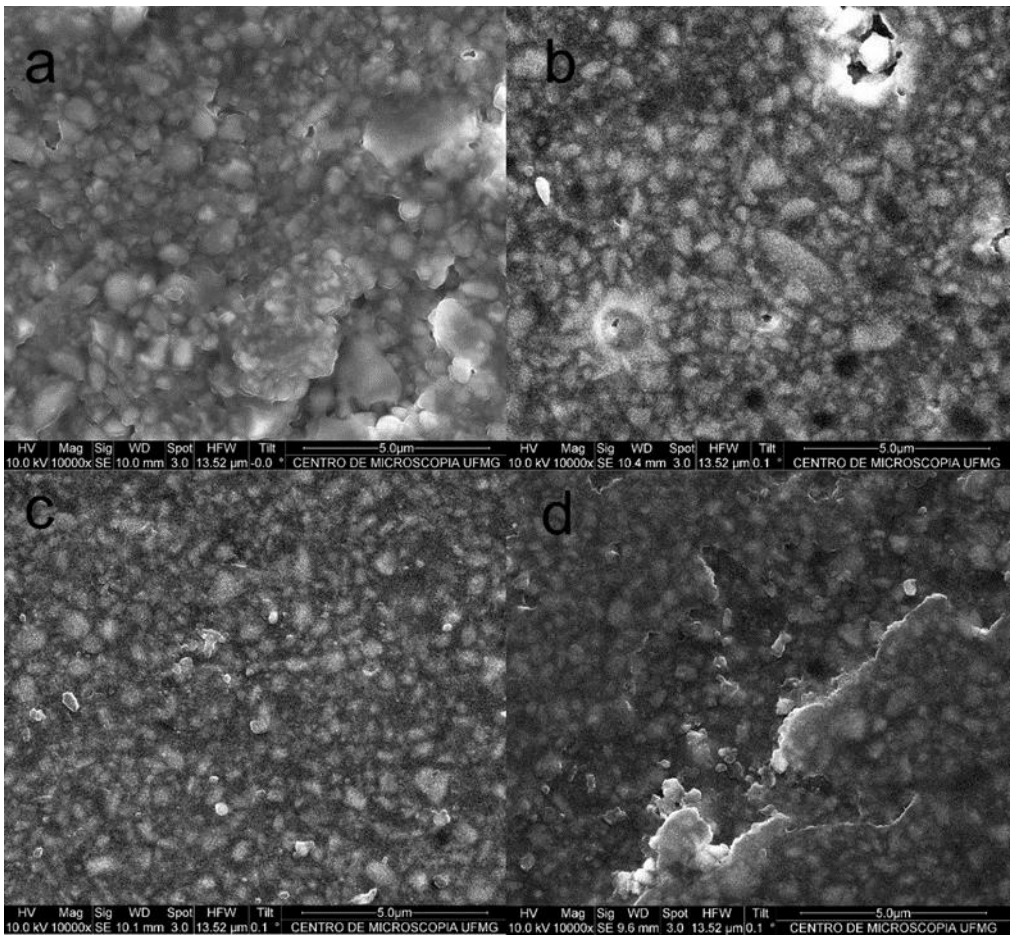

Figure 5. SEM analysis of samples: a) prior to incubation; b) after 7 days; 4) after 30 days; d) after 6 months

4 CONSIDERAÇÕES FINAIS

O compósito restaurador GIOMER Beautifil-Bulk apresentou resultados adequados de acordo com norma ISO 4049 (2009) para os ensaios de resistência à flexão, absorção e solubilidade. Os valores médios foram 89.77 (±9.98) MPa para resistência a flexão, 16,87 (±0,80) μg/mm^3 para absorção e -2,74 (±0,60) μg/mm^3 para solubilidade. O grau de conversão do compósito restaurador GIOMER Beautifil-Bulk foi 59.37 (±14.49) %, sendo considerado adequado comparado aos valores relatados na literatura de outros compósitos do tipo *Bulk-Fill*. Ao ensaio de liberação de monômeros não foi identificado o monômero Bis-GMA em nenhuma amostra, mas o monômero TEGDMA foi encontrado em todos os tempos, apresentando maiores quantidades em 30 dias e 3 meses de armazenamento. Após 3 meses, houve uma diminuição significativa na eluição, mas os valores não atingiram os níveis iniciais (10 min). A avaliação morfológica da superfície dos corpos-de-prova do compósito restaurador GIOMER Beautifil-Bulk, armazenados em água destilada, apresentou imagem sugestiva de maior rugosidade no período de 6 meses de incubação. Embora, no presente estudo, tenha sido utilizado um único compósito restaurador, a possibilidade de realização de cinco ensaios laboratoriais para avaliação das características físicas e químicas do material foi relevante em relação a outros estudos. Também tivemos a oportunidade de realizar uma revisão sistemática abordando o desempenho clínico dos materiais restauradores GIOMERS, o que contribuiu para o atual conhecimento sobre o material. As limitações do presente estudo foram a possiblidade de avaliar apenas dois monômeros presentes na constituição da Beautifil-Bulk, devido ao alto custo do ensaio, e poucos estudos publicados na literatura com o mesmo material para comparação dos resultados obtidos nos ensaios *in vitro.* Estudos de liberação de monômeros que puderem avaliar a liberação de todos os monômeros presentes na constituição do compósito restaurador Beautifil-Bulk e em soluções com preparos enzimáticos, que simulam a constituição da saliva humana, se fazem necessários para maximizar a compreensão sobre a estabilidade química do compósito.

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PRODUÇÃO CIENTÍFICA (2017-2019)

- Apresentação de trabalho científico

"**RESISTÊNCIA FLEXURAL DE UMA RESINA COMPOSTA CONTENDO PARTÍCULAS PRÉ-REAGIDAS DE IONÔMERO DE VIDRO (S-PRG)**" de autoria de Clóvis Ciryllo LIMONGE NETO*,Tassiana Cançado Melo SÁ, Francisco Ivison LIMEIRA, Cláudia Silami de MAGALHÃES, Monica YAMAUTI, apresentado no XIV Encontro Científico da Faculdade de Odontologia da Universidade Federal de Minas Gerais, no período de 07 a 09 de novembro de 2018.

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Clinical performance of GIOMER restorative composites in comparison to different types of dental restorative materials: a systematic review and meta-analysis

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Abstract

Purpose: To analyze the clinical effectiveness of GIOMER restorative composites in permanent teeth. *Methods:* A systematic review with a meta-analysis was conducted based on the PRISMA Statement. Clinical trials that evaluated the clinical performance of GIOMER restorative composites in permanent teeth compared to any other dental material were included. A meta-analysis was performed for the marginal adaptation and surface roughness

criteria between GIOMER restorative composite and resin-modified glass ionomer cement (RMGIC) at the 6- and 12-month follow-ups. The quality of available evidence was evaluated by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE). *Results:* Six studies fulfilled the inclusion criteria. In these studies, GIOMER restorative composites were compared with different types of dental restorative materials, such as composite resin, glass ionomer cement (GIC), and RMGIC. Dental restorations were evaluated by the modified USPHS (the United States Public Health Service) criteria in all included studies. Two studies were suitable for the meta-analysis, which showed a significant difference between GIOMER and RMGIC surface roughness at the 6-month (OR = 6.56, IC = 2.38–18.13) and 12-month (OR = 8.76, IC = 3.19–24.07) follow-up. No significant difference between GIOMER restorative composites and RMGIC for marginal adaptation was found at the 6-month (OR = 1.54, IC = 0.59–4.02) and 12-month (OR = 1.36, IC = 0.51–3.60) follow-up. The certainty of the evidence was low for marginal adaptation outcome and moderate for surface roughness outcome. In conclusion, the GIOMER restorative composites presented similar performance to RMGIC concerning the marginal adaption and better surface roughness when compared to RMGIC.

Clinical relevance: GIOMER restorative composites could be an alternative for direct restorations in permanent teeth with better surface roughness when compared to RMGIC.

Introduction

Due to the demand for esthetic procedures and the advocacy for the minimum removal of dental tissues during dental preparation, composite resins have been widely used in

Restorative Dentistry.[1,2] Several studies have demonstrated the clinical evidence of the survival of this restorative material.[3-5] On the other hand, composite resins are susceptible to failures due to their physical and chemical properties,[6] as well as the risk of secondary carious lesions adjacent to the restorations.[7]

Materials through which fluoride is released, such as glass ionomer cements (GICs), have the capacity to neutralize the pH of the saliva with proven efficacy for control and the reduction of bacterial growth.[8] The release of fluoride and strontium ions forms an acid-resistant layer and reinforces the dental structure, converting hydroxyapatite into fluorine-apatite and strontium-apatite with proven anti-cariogenic efficacy.[8] GICs are widely used for restorations in deciduous teeth or as temporary restorations in permanent teeth due to their properties of low resistance and weight loss over time, which, ultimately, lead to the increase of roughness on their surface and the consequent accumulation of plaque.[4]

GIOMER is a new class of restorative material introduced by Shofu Inc, which combines the fluoride-releasing properties of glass ionomer cement and the strength and aesthetics of composite resins.[9-11] The main difference between GIOMER materials and compomers is the presence of pre-reacted glass ionomer particles (S-PRG) incorporated into the resin matrix.[10,12] S-PRG particles enable the mechanical strength, durability, and aesthetics of a composite material ,[13] as well as the release of various ions (fluorine ions, sodium ions, silicate ions, aluminum ions, borate ions, and strontium ions)[14] that provide multiple biological functions including the release and recharge of fluoride, an anti-plaque effect, an anti-biofilm effect, and pH modulation.[10]

There are several studies in the literature on the clinical efficacy of composite resins, however there are few studies comparing this clinical efficacy with fluoride-releasing

materials as GIOMER. Thus, the objective of the present systematic review and meta-analysis was to compare the clinical performance of GIOMER restorative composites with the clinical performance of restorations performed with other types of direct restorative materials. The null hypothesis of this study is that the clinical performance of GIOMER restorative composites is similar to the clinical performance of restorations with other types of direct restorative materials.

Material and Methods

Protocol and registration

This systematic review and meta-analysis were registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42018110634. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was followed.[15]

Eligibility criteria

This systematic review and meta-analysis aimed to answer the following question: Is there any difference in the clinical performance of dental restorations with GIOMER restorative composite in permanent teeth compared to other direct restorative materials? The PICO question described below was applied.

(P) Population - adults or adolescents with restorations in anterior or posterior permanent teeth.

(I) Intervention - restorations with GIOMER restorative composite.

(C) Comparison - restorations with other restorative material.

(O) Outcome - primary outcome: clinical performance of dental restorations evaluated by postoperative sensitivity, color match, marginal adaptation, anatomic form, surface roughness, staining, marginal staining, secondary caries, retention criteria, and the influence of isolation (rubber dam or cotton roll) on the primary outcome.

Randomized clinical trials comparing the clinical performance of dental restorations with GIOMER restorative composite and restorations with other restorative materials performed in permanent teeth of adults or adolescents were included. Letters, literature reviews, case reports, case series, non-randomized clinical trials, *in vitro*, and *in situ* studies were excluded. Restrictions on language or date of publication was not imposed in any way.

Information sources and search strategy

In September 2018, electronic searches were performed in the following databases: PubMeb, Web of Science, Scopus, Medline Ovid, and the Cochrane Library. A grey literature search in Google Scholar, limiting the search to the first 300 hits was performed. Manual searches of the reference list of the included articles were also carried out. In May 2019, an update of the search was carried out to verify if there were any new potential publications.

The search strategy for PubMed, Web of Science, Medline Ovid, and Cochrane Library was as follows: [giomer OR s-prg OR pre-reacted glass ionomer OR s-prg filler OR beautifil]. For Scopus, the search strategy was tailored according to the characteristics of the database.

Study Selection

Endnote Web (Clarivate Analytics, Philadelphia, US) was used to manage the bibliographic references. Any duplicated references were removed upon identification. Titles and abstracts were evaluated independently by two review authors (CCLN and AMN), who

applied the eligibility criteria. The full text of the references with insufficient information in the titles and abstracts was also evaluated by the two review authors. The references that fulfilled the eligibility criteria were included. If any divergence between the review authors took place, a third review author (MY) decided if the reference should be included or otherwise.

Data collection process and data items

Data collection of the included articles was carried out by two review authors (CCLN and AMN). Divergences were also resolved by a third review author (MY). The following data were collected from the included articles: identification of the study (last name of the first author and year of publication), study design, period of follow-up, age of participants, total number of restorations, and total number of the participants at study's onset, type of dental materials assessed and number of restorations per group at the end of the study, isolation method, evaluation criteria, outcomes evaluated, and results.

Risk of bias in individual studies

The risk of bias assessment of the included articles was performed by two review authors (CCLN and AMN) according to the Cochrane Risk of Bias Tool for Randomized Clinical Trials (http://handbook.cochrane.org). The aspects of bias were evaluated individually in order to assess the selection, performance, attrition, reporting, and detection bias.

Six domains were assessed: random sequence generation, allocation concealment, blinding of outcome assessors, blinding of participants and personnel, incomplete outcome data, and selective outcome reporting. A low risk, an unclear risk, or a high risk of bias were

used to classify each domain. Divergences between the two review authors were resolved by a third review author (DCA).

Synthesis of results

Included studies with methodological homogeneity were incorporated into the meta-analysis. The results of the meta-analysis were reported as odds ratio (OR) and 95% confidence intervals (CI). In the meta-analysis, statistical heterogeneity was assessed by means of the I^2 statistics.[16] Analyses with a value of I^2 greater than or equal to 40% were classified as having a high statistical heterogeneity and the random effect model would be used. Analyses with a value of I^2 lower than 40% were classified as having a low statistical heterogeneity and the fixed effect model would be used. The meta-analysis was performed using the software Review Manager (Rev.Man), version 5.3 software (Review Manager. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Additional analysis

Depending on the outcomes evaluated in the included studies, subgroup analyses were carried out considering the results of two clinical performance criteria (surface roughness and marginal adaptation) at two follow-up periods (six and twelve months). For studies that analyzed other clinical performance criteria, only these two criteria were incorporated into the meta-analysis.

Quality of evidence rating and strength of recommendations grading

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)[17] system was used to analyze the quality of the evidence and the strength of recommendations using the GRADEpro GDT online software. The selected outcomes were marginal adaptation and surface roughness six and twelve months after restoration with

GIOMER and RMGIG. For each one, the GRADE evaluated the number of studies included in the meta-analysis, the studies' design, risk of bias, inconsistency, indirectness, imprecision, and other considerations, such as publication bias. The evidence could be downgraded in one or two levels according to the seriousness of the limitation. The certainty of the assessment of the outcome could be classified as high, moderate, low, or very low.

Results

Study selection

The searches across the five electronic databases retrieved 910 references. After the removal of duplicates, 552 references remained. Titles and abstracts were assessed, and ten articles were selected for the evaluation of the full text. Among the ten articles, four studies were excluded because the focus of the analysis was on periodontal outcomes and not outcomes related to the clinical performance of the restorative material.[18-21] Therefore, six studies fulfilled the eligibility criteria and were included in this systematic review and meta-analysis.[22-27] No study meeting the eligibility criteria was identified in Google Scholar or in the reference list of the included studies. Figure 1 displays the process of the study selection of this systematic review and meta-analysis.

Characteristics of included studies

The characteristics of the included studies are described in Table 1. Two studies compared composite resin and GIOMER.[22,25] One study used two types of GIOMER.[23] One study compared RMGIC and GIOMER.[24] In one study,[26] composite resin and GIOMER were compared with bases pre-filled with RMGIC or compomer. One study compared restorations with RMGIC, GIC, and GIOMER.[27]

In two included studies, rubber dam isolation was used.[22,23] In three studies, cotton rolls were used.[24,25,27] In one study, no information on the isolation method was provided.[26] In four included studies, Class IV restorations were evaluated.[22-24,27] In one study[23], both carious and non-carious cervical lesions were evaluated, and Class I restorations with only one type of GIOMER were assessed. In two studies, Class II restorations were evaluated [25,26]. The minimum period of the follow-up period was six months, and the maximum was 72 months. The participants' age ranged from 16 to 75 years. The total number of restorations evaluated in the included studies was 547.

Risk of bias within studies

In all included studies, information on the blinding of participants and personnel was unclear.[22-27] In one study, the random sequence generation and the allocation concealment were of a low risk of bias and the authors reported that the cards were sequentially numbered and placed in opaque and sealed envelopes.[27] Three included articles presented a low risk of bias[24,25,27] (Jyothi *et al*., 2011; Dijken *et al.*, 2013; Priyadarshini *et al.*, 2017) and three presented an unclear risk of bias[22,23,26] for the blinding of the outcome assessor. In regards to incomplete outcome bias, only one included study showed an unclear risk of bias[26] and five showed low risk of bias. [22-25,27] For selective reporting, two included studies presented a low risk of bias[24,27], three presented a high risk of bias[22,23,25], and one presented an unclear risk of bias.[26] No other bias was observed in any of the included studies. Figure 2 displays the assessment of the risk of bias for each included study, and Figure 3 shows a summary of the risk of bias assessment.

Synthesis of results and subgroup analysis

Two included studies were incorporated into the subgroup analyses.[24,27] One subgroup analysis compared marginal adaptation between GIOMER and RMGIC, six months and twelve months after the restoration placement. The subgroup analysis showed no difference with respect to marginal adaptation between GIOMER and RMGIC at 6 months (OR = 1.54, CI = 0.59–4.02, I^2 = 38%) and 12 months (OR = 1.36, CI = 0.51–3.60, I^2 = 31%) after restoration placement (Figure 4). One subgroup analysis compared surface roughness between GIOMER and RMGIC, six and twelve months after restoration placement. RMGIC was 6.56 times more likely to present Bravo scores six months after restoration placement than GIOMER (OR = 6.56, CI = 2.38–18.13, I^2 = 0%). RMGIC was 8.76 times more likely to present Bravo scores twelve months after restoration placement than GIOMER (OR = 8.76, CI = 3.19–24.07, I^2 = 0%) (Figure 5). In all subgroup analyses, the fixed effect model was used.

Quality of evidence rating and the strength of recommendation grading

The certainty of the evaluation of the outcomes marginal adaptation and surface roughness, after dental restoration with GIOMER materials and RMGIG, was low for marginal adaptation (6- and 12-month follow up) and moderate for surface roughness (6- and 12-month follow up) (Table 2).

Discussion

The present systematic review and meta-analysis was conducted due to the lack of evidence of the clinical efficacy of GIOMER restorative composites. One of the most important properties of GIOMERS is the ability to release and recharge fluoride to prevent secondary caries.[9,28,29] RMGIC materials were also associated with a higher reduction of

demineralization in adjacent hard tooth tissue under caries challenge than composite resins without fluoride.[30] There are no other systematic reviews comparing the clinical efficacy of GIOMER restorative composites with different types of restorative materials.

In the studies included in this systematic review and meta-analysis, dental restorations were evaluated by the United States Public Health Service (USPHS) criteria.[22-27] However, those studies did not explicitly mention if CONSORT recommendations were followed. It would have been very helpful if the studies had used those recommendations to write, review, or assess reports. The CONSORT statement collaborates to improve the quality of randomized clinical trials. In addition, no study cited the protocol registration number for *in vivo* trials in any specific database.

The present systematic review and meta-analysis included six studies that evaluated the clinical performance of materials in the short- and long-term periods. [22-27] In general, the present results demonstrated that the clinical performance of GIOMER restorative composite was like that of RMGIC, concerning marginal adaption and surface roughness. The included studies employed different designs regarding the type of cavity (Class I, II, V) and restorative material (GIOMER, composite resin, GIC, and RMGIC). Thus, it was only possible to perform the meta-analysis of two outcomes using two studies.[24,27] The subgroup analyses of both outcomes compared GIOMER with RMGIC in non-carious Class V restorations at the same time periods (6- and 12-months).

In the included studies, the GIOMER restorative composites used were Beautifil, Beautifil II, and Reactmer. This class of material has properties of GIC related to fluoride release and fluoride recharge along with better esthetics, resistance, and easy polishing.[23] PRG-technology is classified into two categories: F-PRG (full reaction type), with which the

entire filler particle is attacked by polyacrylic acid, and the S-PRG (surface reaction type), with which only the surface of the glass filler is attacked by polyacrylic acid, and a glass core remains. In fact, S-PRG has replaced F-PRG. A previous Reactmer (Shofu, Kyoto, Japan) used F-PRG technology, but this material was indicated only for cervical cavities.[23] Current versions of the Beautifil resins and FL-Bond adhesive system (Shofu, Kyoto, Japan) developed using S-PRG technology are indicated for Class I through Class VI cavities.[23] Beautifil II is considered a second-generation GIOMER introduced into the market.[27]

Two studies were suitable for meta-analysis. One subgroup analysis showed a significant difference between GIOMER and RMGIC with respect to the surface roughness at the 6- and 12-month follow-up. In both studies, the restorations were submitted to polishing procedures to get the surfaces as smooth as possible.[22-27] Several factors related to the restorative procedures, the characteristics of composites, and the operator may affect the surface roughness. According to some authors, increased surface roughness enlarges the area available for bacterial adhesion[31] and biofilm formation. This could happen in the case of the absence of good polishing or a smooth state, which could lead to secondary caries[31] and inflammation of gingival tissue.[10,18,31-34] The presence of biofilm is one of the factors that may stimulate surface degradation,[31] compromising the longevity of resin composite restorations.

Moreover, no significant difference between the marginal adaptation of GIOMER and RMGIC restorations was found at the 6- and 12-month follow-up. Jyothi *et al*.[24] and Priyadarshini *et al*.[27] also reported that GIOMER presented a better color match and worse retention than GIC.

The GIOMER restorative composites were considered suitable as definitive restorative materials.[22-24,26,27] Dijen *et al*.[25] found a higher failure rate in GIOMER than in composite

resin due to fracture or secondary caries. However, Matis *et al.*[22] have not found a significant difference between GIOMER and composite resins in all the evaluated periods and outcomes. Saveanu & Dănilă[26] reported that GIOMER restorative composite presented an inferior quality for marginal staining and color match when compared with composite resin. This was the only study included in this systematic review and meta-analysis that used the compomer and RMGIC as a restorative base, using the composite resin or GIOMER as a restoration for enamel in class II cavities.[26]

There is still poor information on this type of material. The major limitation of this study was the scarce number of non-randomized clinical trials using GIOMER materials. Therefore, it was unfeasible to perform subgroup analyses with other outcomes. For future research, it would be convenient to follow the CONSORT's recommendations for designing and reporting studies, in particular regarding the blindness of operators and evaluators. A detailed report of the results is highly relevant to describe the gross values of the analysis of each outcome in each period for the eventual meta-analyses.

Conclusion

The GIOMER restorative composite presented a similar performance to that of RMGIC restorations concerning marginal adaption. However, GIOMER presented better surface roughness when compared to RMGIC. It is still premature to assert that the clinical behavior of GIOMER restorative composites is similar to the clinical performance of restorations with other types of direct restorative materials. Randomized clinical trials with long-term follow-ups are still necessary to compare the clinical performance of GIOMER restorative composites and other materials.

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Conflicts of interest

The authors do not have conflicts of interest.

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Table 1. Characteristics of the included studies.

Author **Year** **(Country)**	**Study Design**	**Follow-up** **(months)**	**Age of participants**	**Initial number of restorations and participants**	**Type of dental materials and final number of restorations per group**	**Isolation method**	**Evaluation criteria**	**Outcomes**	**Results**
Matis *et al.* 2004 **(USA)**	Split mouth Randomized Clinical Trial	6, 18, and 36	Mean age = 45 years Range = 30–75 years	80 restorations (Class V) 30 individuals	**Microfield Composite** (Scotchbond Multi-Purpose Plus Dental Adhesive + Silux Plus[a]) = 39 **GIOMER** (FL-Bond + Beautifil[b]) = 39	Rubber dam and retraction cord when necessary	Modified USPHS	**POS, MA, AF, SR, S, MS, SC,** and **R**	**POS, MA, AF, SR, S, SC, R:** There were no significant differences in the evaluated periods among all the evaluated outcomes. **MS:** 7 teeth exhibited margin with discoloration restored with Beautifil and 4 with Silux Plus, but without significant differences. Neither material was significantly different from each other in the outcomes evaluated. Both materials meet the clinical portion of the Acceptance Program Guidelines for Dentin and Enamel Adhesives Materials established by

									the American Dental Association.
Sunico *et al.* 2005 **(Phillippines)**	Split mouth Randomized Clinical Trial	6 and 24	Mean age = 35 years Range = 20–50 years	62 restorations (42 Class V and 20 Class I) 15 individuals	**GIOMER** (Imperva FluorBond[b] + Beautifil[b]) = 20 Class V and 20 Class I) (Reactmer[b] + Reactmer Bond[b]) = 21 Class V	Rubber dam	Modified USPHS	**POS, CM, MA, AF, SR, MS, SC,** and **R**	**POS, CM:** There was no significant differences in the evaluated periods for both materials. **MA:** There were significant differences for MA in CL V restorations with Beautifil at periods evaluated ($p < 0.05$). **MA, MS:** Both GIOMER materials presented failures in marginal adaptation, marginal discoloration, and wear in the evaluated periods. **MA, AF, MS** were the criteria that had the most Charlie and Delta ratings at both six months and two years for the Reactmer CL V restorations. **SC:** 20% of restorations with Reactmer showed secondary caries at the 24-month evaluation. **SR:** Not

									reported. **R:** At 6 months, 19% (n = 4) of the restorations with Reactmer dislodged and after 24 months another restoration was lost. While for Beautifil, any restoration lost retention. Beautifil CL V restorations were better retained then Reactmer CL V restorations in the evaluated periods. At 24 months, there was an 80% success rate for Beautifil and only a 71% success rate for Reactmer.
Saveanu & Dănilă **2010** **(Romania)**	Split mouth Randomized Clinical Trial	6, 12, 24, and 36	Mean age = not reported Range = 16–55 years	90 restoration (Class II)	**Composite Resin with RMGIC** (Filtek Supreme[a] + Vitrmer[a]) = 24 **GIOMER with RMGIC** (Beautifil[b] + Vitremer[a]) = 23 **GIOMER with Compomer Flow**	Not reported	Modified USPHS	**POS, CM, MS,** and **R**	**POS:** There was higher sensitivity for composite resin restorations compared to restorations made with GIOMER, but without significant difference. **CM:** There were no significant differences at 6 and 12 months. But with 24 months, restorations with composite resin showed 33,33 (8) score Alpha, while restorations with GIOMER showed only 4.34 (1) score Alpha with significant differences (p<

					(Beatutifil[b] + Dyract Flow[e]) = 21 **Composite Resin with Compomer Flow** (Filtek Supreme[a] + Dyract Flow[d]) = 22				0.05). **MS:** There were significant differences at 12 months for restorations with p = 0037 with favor to composite Resin with rating Alpha (95.65%) and GIOMER with rating Alpha (73.91%), the rest is bravo. **R:** None of restorations lost in the evaluated periods.
Jyothi *et al.* 2011 **(India)**	Split mouth Randomized Clinical Trial	15 days, 6 and 12 months	Mean age = not reported Range = 20–60 years	80 restorations (Class V) 32 individuals	**RMGIC** (Fuji II LC[c]) = 40 **GIOMER** (FL-Bond II[b] + Beatufil II[b]) = 40	Cotton Rolls, saliva ejector and gingival retraction cords	Modified USPHS	**POS, MA, SR, S, MS,** and **R**	**SR:** There were significant differences in the evaluated periods. GIOMER-exhibited a superior surface finish compared to RMGIC. **MA, R:** There were no significant differences in the evaluated periods. **POS, S, MS:** There was no marginal discoloration, staining, and postoperative sensitivity for all the restorations.

Dijken **2013** **(Sweden)**	Split mouth Randomized Clinical Trial	12, 24, 36, 48, 60, and 72	Mean age = 57.1 years Range = 24–77 years	115 restorations (Class II) 54 individuals	**Hybrid Resin** (G-Bond[c] + Gradia Direct Posterior[c]) = 58 **GIOMER** (FL-Bond[b] + Beautifil[b]) =53	Cotton Rolls and suction device	Modified USPHS	**POS, CM, AF, MA, SR, MS,** and **SC**	**POS:** No post-operative sensitivity was reported. **CM:** There was a significant decrease in color match at the period evaluated for both materials ($p < 0.05$). **AF:** There were no significant differences in the evaluated periods. **MS:** There were changes for both materials, but this was significantly higher for the GIOMER material **MA, SC:** During the total period evaluated, 5 (8,5%) restorations with composite resin and 9 (17,7%) restorations with GIOMER failed due to receding caries or fracture ($p < 0.05$). **SR:** Not reported.

Priyadarshini *et al.* 2017 (India)	Split mouth Randomized Clinical Trial	6 and 12	Mean age = not reported Range =35–65 years	120 restorations (Class V) 20 individuals	**RMGIC** (Self Conditioner[c] + Fuji Filling LC[c]) = 40 **GIC** (Ketac N100 Nano Ionomer Primer[a] + Ketac N100[a]) = 40 **GIOMER** (FL Bond II LC[b] + Beautifil II[b]) = 40	Cotton rolls, saliva ejector, and gingival retraction cords	Modified USPHS	**POS, CM, MA, SR, MS,** and **R**	There was a significant reduction for some outcomes such as **CM** and **SR** for RMGIC, **R** for GIOMER, **MS,** and **CM** for GIC, after 12 months with $p < 0.05$. **CM, SR, MS, R:** There was a significant difference with $p < 0.05$ from 6 to 12 months for all materials. **R:** GIV and RMGIC restorations were better retained than GIOMER restorations in the evaluated periods with significance differences. **MS:** It was higher for GIC than others material with significance differences. **CM:** GIOMER was better than GIC and RMGIC in the evaluated periods. **SR:** GIOMER was better than RMGIC with a significance

									difference. **POS, MA:** There were no significant differences in the evaluated periods.

RMGIC = Resin-Modified Glass Ionomer Cement; GIC = Glass Ionomer Cement; POS = Postoperative Sensitivity; CM = Color Match; MA = Marginal Adaptation; AF = Anatomic Form; SR = Surface Roughness; S = Staining; MS = Marginal Staining; SC = Secondary Caries; R = Retention. [a] = 3M Dental Products, St. Paul, Minn; [b] = Shofu, Kyoto, Japan; [c] = GC Corp., Tokyo, Japan; [d] = 3M ESPE, St. Paul, USA; [e] = Dentsplay Sirona, Sidney, Australia.

Table 2. GRADE quality of evidence.

Outcome	**Nº of studies**	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI)**	**Quality**
Marginal adaptation 6 months	2	randomized trials	serious [a]	not serious	not serious	serious [b]	none	OR 1.54 (0.59 to 4.02)	⊕⊕◯◯ LOW
Marginal adaptation 12 months	2	randomized trials	serious [a]	not serious	not serious	serious [b]	none	OR 1.36 (0.51 to 3.60)	⊕⊕◯◯ LOW
Surface roughness 6 months	2	randomized trials	serious [a]	not serious	not serious	not serious	none	OR 6.56 (2.38 to 18.13)	⊕⊕⊕◯ MODERATE
Surface roughness 12 months	2	randomized trials	serious [a]	not serious	not serious	not serious	none	OR 8.76 (3.19 to 24.07)	⊕⊕⊕◯ MODERATE

CI: Confidence interval; **OR:** Odds ratio.
a. The evidence has been downgraded by one level because of serious concern regarding the risk of bias. According to the Cochrane Tool, most information is from studies at moderate risk of bias.
b. The evidence has been downgraded by one level because confidence intervals cross threshold.

Illustrations

Fig 1. Flowchart of study selection

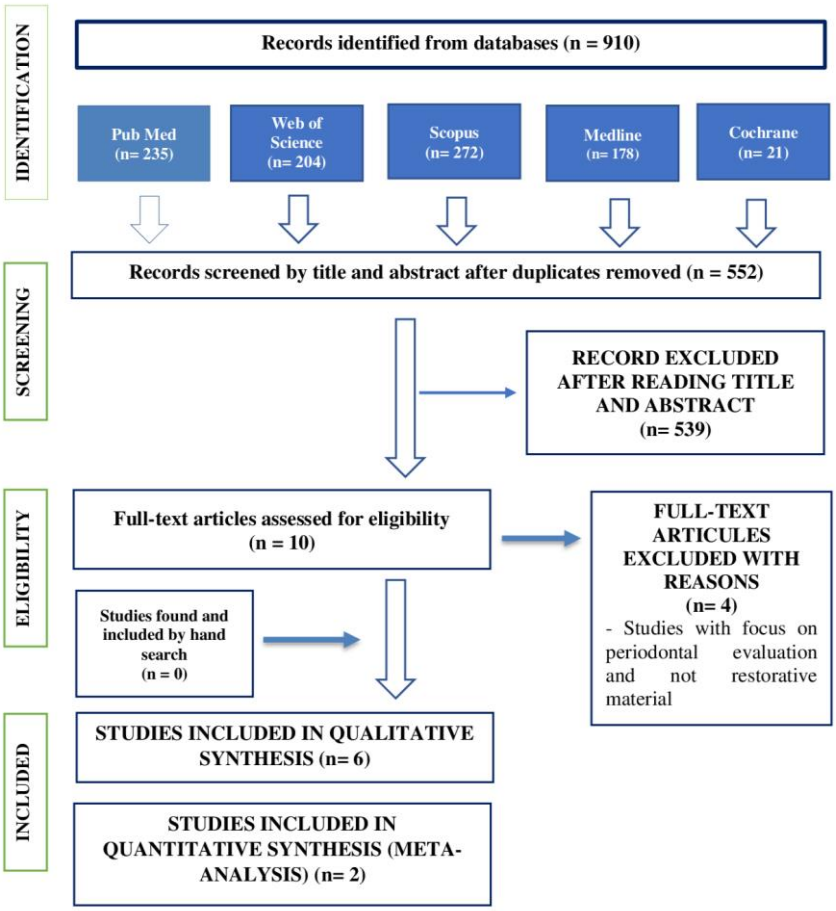

Fig 2. The assessment of risk of bias for each included study

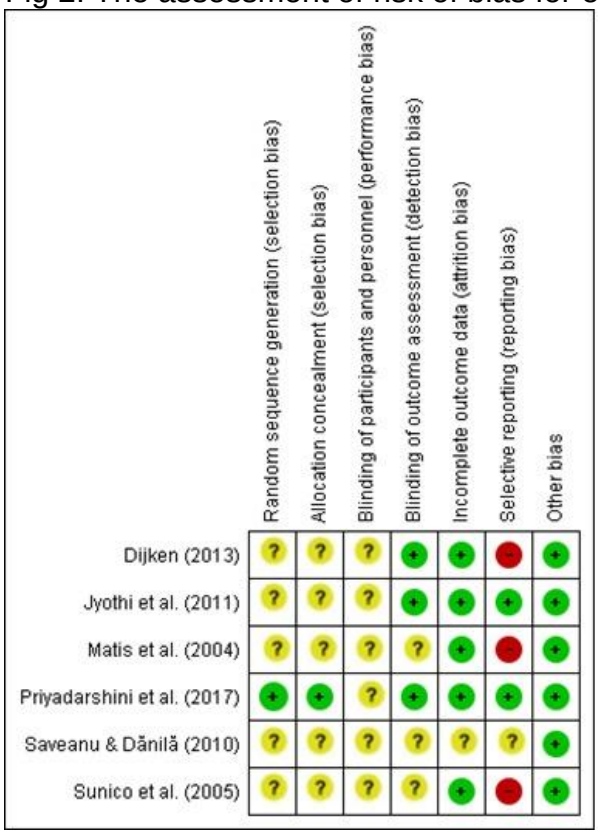

Fig 3. Summary of the risk of bias of the include studies

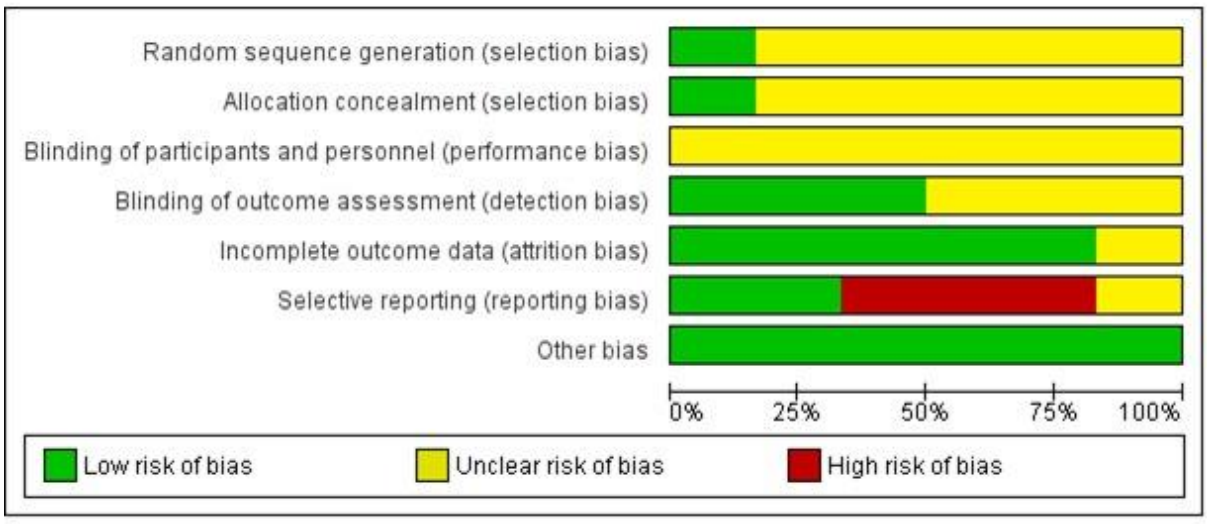

Fig 4. Forest Plot for marginal adaptation between GIOMER and RMGIC at six- and 12-months

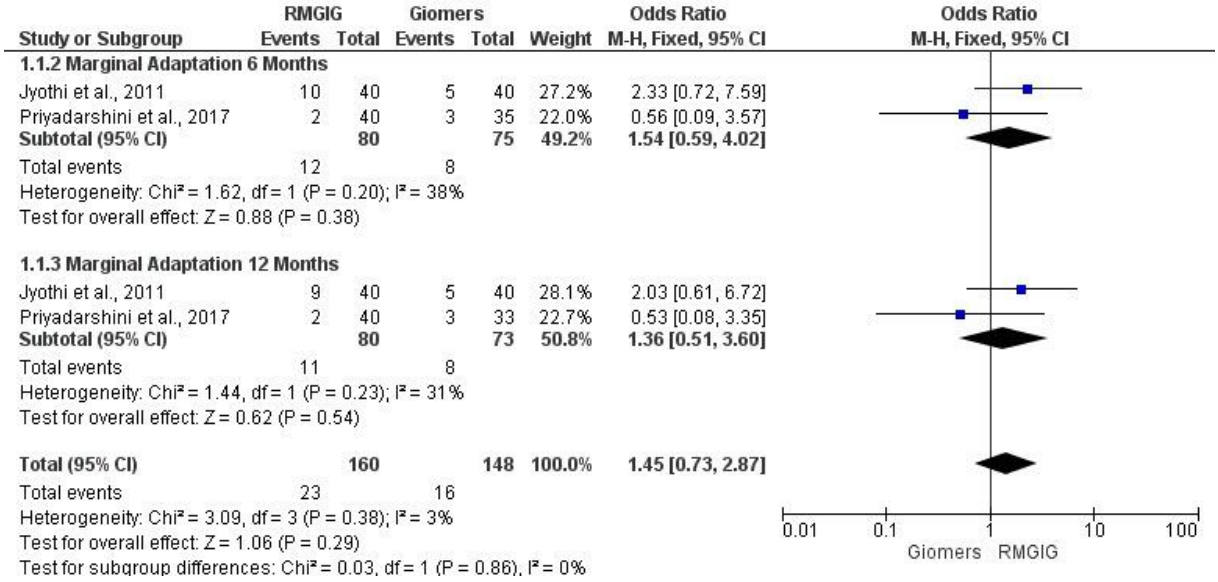

Fig 5. Forest Plot for surface roughness between GIOMER and RMGIC at six- and 12-month