Ann Med Res 2020;27(10):2731-6

Annals of Medical Research

DOI: 10.5455/annalsmedres.2020.04.375

Original Article

Long-term monomer elution from bulk-fill composite resins

Ayse Dundar[1], Cagatay Barutcugil[1], Sevde Gul Batmaz[1], Kardelen Yildirim[1], Oznur Gucluer[2]

[1]Department of Restorative Dentistry, Faculty of Dentistry, Akdeniz University, Antalya, Turkey
[2]Department of Endodontics, Faculty of Dentistry, Akdeniz University, Antalya, Turkey

Abstract

Aim: The aim of this study was to investigate the long-term elution of unreacted monomers from bulk-fill composite resins.
Material and Methods: Four different restorative bulk-fill composite resins (Filtek Bulk Fill, 3M ESPE; X-tra fil, VOCO; SonicFill, Kerr; and Tetric EvoCeram Bulk Fill, Ivoclar Vivadent) were used. A total of 15 samples per group (5 x 5 x 4 mm) were polymerized with light as a single layer (4 mm). Then the samples were put into 75/25% ethanol/water mixture. Evaluation of monomer release was performed by using High-Performance Liquid Chromatography device. This process was repeated after one hour, 24 hours, and 3 months. One-way analysis of variance was used to determine the differences in monomer release between groups, while the Tukey HSD test was used for multiple comparisons. The paired sample t-test was used to determine the time-dependent changes of the same material. (P < .05).
Results: Monomer release was observed in all groups. At the end of 3 months, a statistically significant increase was observed in the amount of almost all monomers released from bulk-fill composites (P <0.05).
Conclusion: It can be stated that monomer release still continues from all bulk-fill composite materials after three months.

Keywords: Bulk-fill composite; elution; HPLC; monomer

INTRODUCTION

In clinical dentistry, the highest caries rates were seen in maxillary and mandibulary molars (1). Because of limited visibility and difficulty in accessing, the restoration of posterior teeth with composite materials is tough. To alleviate these challenges, bulk-fill composites were developed. These composites provided great convenience to the clinician during the treatment by placing up to 4 mm thickness. However, as in other composites, bulk-fill composites are formed by an organic matrix and there are various monomers in their structure. Bisphenyl-glycidyl-methacrylate (Bis-GMA), urethane dimethacrylate (UDMA), triethylene glycol dimethacrylate (TEGDMA), ethoxylated bisphenol A dimethacrylate (Bis-EMA) are the common monomers used in the organic matrix (2,3). In the past, studies have shown that about 35% -77% of unreacted residual monomers were present in the polymerized composite (4,5). It has been shown that about 10% of the remaining monomers were released from the structure of the composite as a residual monomer (6). These unreacted monomers can be released from the composite into the mouth. According to the amount and type of monomers released from the composite resins, the bioavailability of the composite is gaining importance. It has been found that some of these released compounds have cytotoxic (7), mutagenic (8,9), and estrogenic (10) effects and are caused pulp, gingival and oral mucosal reactions (11-13).

The release of ingredients from resin-based dental materials has already been extensively investigated in vitro by immersion of composite samples in the various extraction solutions (14). Generally, the release is determined after 24 h or 1 week, but few studies incubated the samples for longer periods (one month, three months, and even 1 year) (15-17). Since composite restorations are expected to be used by patients for long years, it is important to investigate whether there is long term monomer release from composite materials. If long-term monomer release is present, this means that existing toxicity persists. There are many test methods for detecting the unreacted monomers released from composite resins, especially those with larger molecular structures such as BisGMA, UDMA, BisEMA (18). Gas chromatography or gas and liquid chromatography/mass spectrophotometry are currently used methods. However, High-Performance Liquid Chromatography (HPLC) is one of the most frequently used methods while evaluating the high molecular weight of unreacted monomers (19).

Received: 25.04.2020 **Accepted:** 28.09.2020 **Available online:** 22.10.2020
Corresponding Author: Oznur Gucluer, Department of Endodontics, Faculty of Dentistry, Akdeniz University, Antalya, Turkey
E-mail: gucluertuncay@hotmail.com

The aim of this study was to determine the long-term monomer elution from 4 different bulk-fill composite resins. The null hypothesis was that monomer will not be released from the bulk-fill composites during the long-term period.

MATERIAL and METHODS

Sample preparation

A total of 15 samples per composite material were prepared from 4 different bulk-fill composite materials (Filtek Bulk Fill, 3M ESPE; X-tra fil, VOCO; SonicFill, Kerr; and Tetric EvoCeram Bulk Fill, Ivoclar Vivadent) (5 x 5 x 4 mm). Materials used in this study and their properties are given in Table 1.

Teflon molds of the desired sizes were used to prepare the samples. One side of the Teflon mold was covered with a transparent strip and placed on glass. Then the bulk-fill composites were placed into this mold in the form of a 4 mm high monolayer and were sealed with transparent strip. For polymerization, a third-generation LED light curing device (ELIPAR S10, 3M ESPE, St. Paul, MN, USA) with a light output power of 1200 mW / cm^2 for the time period recommended by the manufacturer, was used. In order to verify, the irradiance at each use of the light cure unit, a calibrated radiometer (Blast LED Light Meter, First Medica, Greensboro, NC, USA) was used.

Preparation of solvent solutions

A mixture of 75% / 25% ethanol and distilled water was prepared to examine the monomer release from the bulk-fill composite samples. Next, 10 ml of prepared solution was added to amber colored small sterile glass vials. The samples were placed in vials one by one and stored at room temperature. For all material groups, measurements of monomer release were made in 3 different time periods (14). Bulk-fill composite groups (Filtek Bulk Fill (FBF), X-tra fil (XTF), SonicFill (SCF), and Tetric EvoCeram Bulk Fill (TBF)) were divided into 3 subgroups (n = 5) for measurement at 1 hour, 24 hours and 3 months. At the end of holding times, 0.5 ml of the solution from each vial containing the samples were taken up in sterile glass vials with the help of a micropipette and stored at room temperature for analysis with HPLC.

Table 1. Used materials and their properties

Material	Manufacturer	Code	Organic Matrix	Filler Loading	Inorganic filler ratio % (wt / vol)	LOT Number
Filtek Bulk-fill	3M ESPE, St.Paul, MN, USA	FBF	BisGMA, UDMA, BisEMA, procrylat resins	YbF_3, zirconium, silica	65/42.5	N719528
SonicFill	Kerr Corp., Orange, CA, USA	SCF	BisGMA, TEGDMA, BisEMA	Silicon dioxide, glass oxide	83.5/–	6383679
Tetric EvoCeram Bulk	Ivoclar Vivadent AG, Liechtenstein	TBF	BisGMA, UDMA	Ba-glass, YbF_3, PPF	79-81/-	O26276
X-tra fil	VOCO GbmH, Cuxhaven,Germany	XTF	BisGMA, UDMA, TEGDMA	(Unknown)	86/70.1	1717238

HPLC analysis

HPLC was used to determine the amounts and types of released monomers. Pure monomers were provided for the standards to be used in the calibration of the HPLC system. For this purpose, bisphenol-A glycidyldimethacrylate (BisGMA),triethyleneglycol dimethacrylate (TEGDMA), urethane dimethacrylate (UDMA), hydroxyethylmethacrylate (HEMA) and ethoxylated bisphenol-A dimethacrylate (BisEMA) monomers were used as pure and were searched as residual monomers in solvent solutions in the HPLC apparatus (14). Standard solutions were prepared in a 75% ethanol-water mixture to maintain the required concentrations and stored in a refrigerator (+4 C^0). Standard working solutions at a concentration of 5, 10, 25, 50, and 100 µg/ml were obtained separately for each monomer. When standard monomers are delivered in different concentrations, the device is both calibrated and peaks are created to determine the amount of released substance in the samples tested. Water was obtained using the Millipore refinement system in ultrasound (18.2 MΩcm at 25 C^0) and the diluted samples were passed through a 0.45 µm membrane filter before injection. Chromatographic measurements were performed using the Accela HPLC system including a thermo diode array detector and an autosampler. Thermo Xcalibur v.2.2 Software was used to control instruments and data handling. The decomposition of the monomers was carried out using Phenomenex 100-5C18 on a 250 mm x 4.6 mm column using 80% acetonitrile / 20% ultrapure water. The fluid flow rate was set at 1 ml/min. By using standard curves obtained from standard solutions, monomer amounts in the samples were calculated.

Statistics

Data were analyzed using Kolmogorov-Smirnov and Shapiro-Wilk tests for normality analysis. One-way analysis of variance was used to determine the differences in monomer release between groups, while the Tukey HSD test was used for multiple comparisons.

The paired sample t-test was used to determine the time-dependent changes of the same material. The significance level was determined as 0.05 in all statistical analysis and SPSS v.20 (IBM Software, USA) was used for the analysis.

RESULTS

The amount of monomer released from bulk-fill composite groups and the statistical differences between the groups are presented in Table 2. According to the data obtained, it was found that BisEMA, UDMA, and BisGMA were released from FBF composite. TEGDMA was not detected in any time period. An increase in the amount of monomer in all-time periods was statistically significant ($P < 0.05$) (Figure 1).

In the SCF group, while BisEMA, TEGDMA, and BisGMA were released, UDMA was not detected. The amount of BisEMA at the end of 3 months period was significantly higher than the amount at the end of the 24 h and 1 hour ($P < 0.05$) (Figure 1). It was found that TEGDMA release increased up at the end of 24 h ($P < 0.05$), but this release did not change much at the end of 3 months ($P > 0.05$).

Table 2. Amount of monomer released from bulk-fill composite groups polymerized by light curing unit

		FBF	SCF	TBF	XTF
	1 h	2.141 ± 0.555 [a]	3.688 ± 0.236 [b]	*	*
BisEMA	24 h	3.748 ± 0.252 [a]	3.406 ± 0.151 [b]	*	*
	3 m	6.962 ± 0.504 [a]	6.933 ± 0.252 [a]	*	*
HEMA			*		
	1 h	*	10.298 ± 2.779 [a]	*	28.503 ± 1.466 [b]
TEGDMA	24 h	*	41.563 ± 5.225 [a]	*	37.185 ± 9.263 [a]
	3 m	*	46.598 ± 5.419 [a]	*	89.238 ± 13.085 [b]
	1 h	7.997 ± 0.967 [a]	*	33.052 ± 9.603 [b]	27.483 ± 3.521 [b]
UDMA	24 h	13.600 ± 3.052 [a]	*	63.487 ± 8.254 [b]	30.860 ± 6.559 [a]
	3 m	35.012 ± 7.860 [a]	*	159.878 ± 9.410 [c]	128.061 ± 7.889 [b]
	1 h	9.618 ± 1.214 [a]	20.317 ± 3.253 [b]	15.702 ± 3.061 [b]	16.399 ± 3.559 [b]
BisGMA	24 h	19.021 ± 3.615 [a]	79.716 ± 5.405 [c]	39.926 ± 13.258 [b]	35.857 ± 10.648 [b]
	3 m	36.532 ± 7.111 [a]	156.473 ± 16.808 [c]	151.971 ± 7.375 [c]	84.871 ± 7.623 [b]
	1 h	19.756	34.304	48.753	72.386
Total amount of released monomer	24 h	36.368	124.685	103.414	103.903
	3 m	78.506	210.003	311.849	302.171

The average amounts (µgr / mlt) and standard deviations of monomers released from light-cured bulk-fill composite samples are shown in the table. Different lower-case letters in the same row indicate statistically different groups ($P < 0.05$). In the statistical analysis, Independent t-test was used for the comparison of two groups and one-way ANOVA and Tukey multiple comparison tests were used for the comparison of the multiple groups. (*: Monomer release could not be determined)

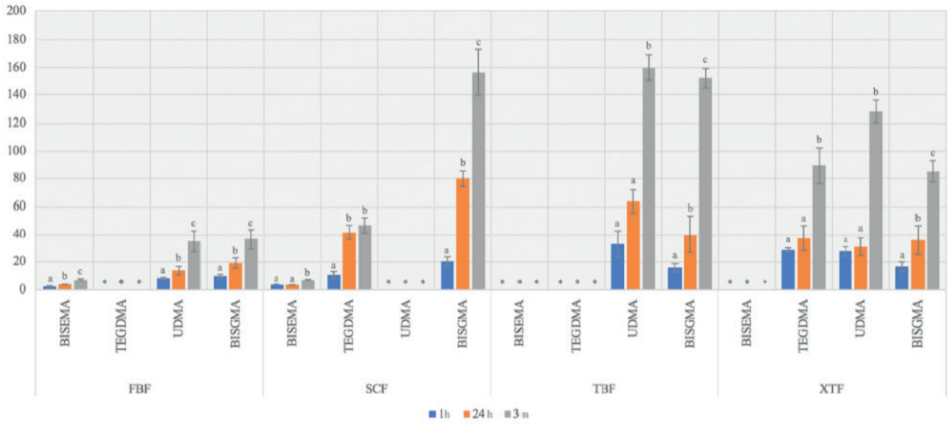

Figure 1. Changes in the amount of monomers released in bulk-fill composite samples which are polymerized by light-curing unit depending on time periods. The lower-case letters on the columns indicate statistical differences, separately for each monomer. Paired t-test was used as a statistical analysis ($P < 0.05$). (*: Monomer release not detected)

In the TBF group, UDMA and BisGMA were present in the ethanol/water solution, but BisEMA and TEGDMA were not detected in the test solution. The amount of UDMA at the end of 24 h and 1 h were not different from each other (P >0.05) (Figure 1). It was detected that the release of BisGMA increased statistically in all time periods (P <0.05) (Figure 1).

Finally, in the XTF group, it was seen that BisEMA was not present. It was detected that the amounts of TEGDMA and UDMA were similar in the first two time periods and the release was increased at the end of the 3 months (P <0.05) (Figure 1).

At the end of 3 months, the highest TEGDMA release was observed at XTF (P <0.05), (Table 2). UDMA was shown to be less released in all time periods in FBF compared with TBF and XTF; BisGMA was significantly released from SCF and TBF at the end of 3 months. However, it was shown that HEMA was not released from the bulk-fill composites in detectable amounts in HPLC. In all bulk-fill composite groups, the total amount of monomer released after 3 months was observed mostly in TBF and then in XTF (Table 2).

According to the data, after immersion in the solvent solution for 3 months, the amount of monomer released from all materials (for all monomers) was found to be higher than the amount of monomer released after immersion for 1 h (Figure 1).

DISCUSSION

According to the results of this study, it was determined that there was a monomer release from bulk-fill composites in the long-term period. Therefore, the null hypothesis that monomer will not be released from the bulk-fill composites during the long-term period was rejected. It has been reported in previous studies that unreacted monomer in composite resins may have toxicity (14, 18, 19). In this context, it is important to determine whether there is any residual monomer release from the composite materials used.

Gas Chromatography-Mass Spectrometry (GC-MS) technique has been previously used in conjunction with the Liquid Chromatography-Mass Spectrometry (LC-MS) to describe the resin composition and the substances eluted from conventional resin composites (2,20,21). However, it has been found that conventional GC-MS is a very sensitive detection method. High molecular weight monomers, such as BisGMA and UDMA, can only be identified after elution in gas chromatography (22). Therefore, the quality and quantity of residual monomers eluted from dental resin materials are generally determined using HPLC (14,23,24) which is a very powerful and widely used separation method. HPLC is more preferred than gas chromatography because the monomer is soluble in the mobile phase, and it provides more control over the elution process (25). Therefore, in this study, HPLC analysis was preferred to evaluate the release of monomers from the bulk-fill composites tested.

The deterioration of composite resins in the mouth depends on the enzymatic reactions in the saliva, the acidic conditions, and the erosive factors caused by food and beverages. To mimic these conditions, organic solvents such as ethanol, methanol, or mixtures of these solvents with water (26) should be preferred. A 75%/25% ethanol-water solution by the United States Federal Drug Administration is recommended as a liquid that mimics the food-to-mouth relationship (27) and has been used in various studies (14,28). Therefore, a 75%/25% ethanol-water solution was used in this study.

In general, polymer networks formed by the polymerization of dimethacrylates exhibit heterogeneity. In this context, some parts are tightly cross-linked while others are loosely cross-linked (19). This polymer network often contains unreacted monomers which remain trapped in gaps between polymer chains or polymer clusters. The cross-linked polymers are not normally soluble but can swell in good solvents. The solvent penetrates the matrix and expands the gap between the polymer chains (29), which causes not only the mass of the polymer chain but also the dimensions. The unreacted monomers begin to decompose. (19) In this study, it was seen that monomer elution of almost all bulk-fill composites increased in all time periods; and the amount of elution of all monomers released at the end of 3 months was found to be statistically higher than the amount released in 1 h. Alshali et al., in their study of monomer elution of various composites including bulk-fill, found that, the monomer release continued in 3 months (15). This result is compatible with the findings of our study. It was found that after 3 months, there was still monomer release, and the total amount of released monomer was greater than the amount released within 1 hour in our study. This can be explained by the fact that, as noted above, the solvent gradually expanded the gaps between the polymer chains as a result of its penetration into the composite matrix, it causes elution of monomers from the composite mass (19). The heterogeneous structure of the composite, the solvent, and the voids in the swollen mass may cause the release of unreacted monomers from the composite in the long term.

In direct composite restorations, since the area reached by the light is limited (30), the degree of conversion cannot be achieved in the composite. Therefore, they contain monomer structures that do not form a polymer network. However, while expecting residual monomer to be at very low levels in resin-containing materials polymerized in a laboratory environment, it has been reported in a very recent article that monomer is released in the long-term even from CAD/CAM blocks containing resin (31). If the monomer release has occurred in long period, even in hybrid blocks, where we expect the amount of residual monomers to be low, it seems that it is possible to evaluate monomer release in bulk-fill composites polymerized using a curing light. This shows that monomer structures cannot fully form a polymer chain.

In 2015, the European Food Safety Authority (EFSA) reduced the tolerable daily intake of BPA from 50 to 4 µg/kg bw/day (Available from http://www.efsa.europa.eu/en/topics/topic/bisphenol.htm.). BPA (Bisphenol A), the main substance of BisGMA and BisEMA, can remain as a residue in the composite and this is one of the major causes of toxicity (32). In addition to the basic monomers, BisGMA and UDMA, the co-monomer TEGDMA, is believed to have a high toxic potential (33-36). Therewithal, the low degree of conversion of the monomers is very effective in the formation of this toxic effect. In a study examining the individual conversion degrees of monomers, a conversion rate of about 70% was indicated for UDMA. However, these conversion rates were 76% for TEGDMA and 52% for BisEMA, and 39% for BisGMA due to high molecular weight and viscosity (37). In this study, all bulk-fill composites had BisGMA release. If the degree of conversion is as low as 39% and the molecular weight is high, the amount of unreacted residual monomer will be too high. However, it is seen that BisEMA, which has higher conversion rate than BisGMA as mentioned above, is released only from Filtek Bulk Fill and SonicFill. As can be seen in Table 2, other bulk-fill composite materials do not contain BisEMA. It is therefore not surprising that this monomer has not been detected in the measurements of the HPLC device. After 3 months, the amounts of all monomers released were statistically higher than those released for 1 h (Figure 1). This study showed that monomers were released from bulk-fill composites in the long term.

The first limitation of this study was that the degree of conversion and the cytotoxicity of the materials were not measured. Because of this, it is difficult to assume the relationship between the amount of monomer released, the degree of conversion and cytotoxicity. The second limitation of this study was that only one concentration of ethanol/water solution was used.

CONCLUSION

Within the limitations of this study, the following results can be highlighted:

1. All Bulk-fill composites showed monomer release.

3. Even after 3 months, the amount of all monomers' release was higher than the amount of 1 h in all bulk-fill composites. Better polymerization methods such as layering technique and high-intensity light curing unit can be preferred in the clinical use to increase the degree of conversion and decrease the cytotoxic level of composite resins.

****This work was supported by The Scientific and Technological Research Council of Turkey under Grant: 216S723. It was presented as an oral presentation at the 22nd International Scientific Congress of Restorative Dentistry Association on 30 November 2018.*

Conflict of interest: The authors declare that they have no competing interest.

Financial Disclosure: This work was supported by The Scientific and Technological Research Council of Turkey under Grant: 216S723.

Ethical approval: Since this study is not a clinical research and does not contain live-sourced experimental material, it does not require ethics committee approval.

REFERENCES

1. Demirci M, Tuncer S, Yuceokur AA. Prevalence of caries on individual tooth surfaces and its distribution by age and gender in university clinic patients. Eur J Dent 2010;4:270-9.
2. Spahl W, Budzikiewicz H, Geurtsen W. Determination of leachable components from four commercial dental composites by gas and liquid chromatography/mass spectrometry. J Dent 1998;26:137-45.
3. Ortengren U, Wellendorf H, Karlsson S, et al. Water sorption and solubility of dental composites and identification of monomers released in an aqueous environment. J Oral Rehabil 2001;28:106-15.
4. Zhu S, Platt J. Curing efficiency of three different curing modes at different distances for four composites. Oper Dent 2011;36:362-71.
5. Ferracane JL. Elution of leachable components from composites. J Oral Rehabil 1994;21:441-52.
6. Ferracane JL. Hygroscopic and hydrolytic effects in dental polymer networks. Dent Mater 2006;22:211-22.
7. Tadin A, Marovic D, Galic N, et al. Composite-induced toxicity in human gingival and pulp fibroblast cells. Acta Odontol Scand 2014;72:304-11.
8. Schweikl H, Schmalz G. Triethylene glycol dimethacrylate induces large deletions in the hprt gene of V79 cells. Mutat Res. 1999;438:71-8.
9. Visalli G, Baluce B, La Maestra S, et al. Genotoxic damage in the oral mucosa cells of subjects carrying restorative dental fillings. Arch Toxicol 2013:87:179-87.
10. Darmani H, Al-Hiyasat AS. The effects of BIS-GMA and TEG-DMA on female mouse fertility. Dent Mater 2006;22:353-8.
11. Teti G, Mazzotti G, Zago M, et al. HEMA down-regulates procollagen alpha1 type I in human gingival fibroblasts. J Biomed Mater Res A 2009;90:256-62.
12. Blomgren J, Axell T, Sandahl O, et al. Adverse reactions in the oral mucosa associated with anterior composite restorations. J Oral Pathol Med 1996;25:311-3.
13. Lai YL, Chen YT, Lee SY, et al. Cytotoxic effects of dental resin liquids on primary gingival fibroblasts and periodontal ligament cells in vitro. J Oral Rehabil 2004;31:1165-72.
14. Cebe MA, Cebe F, Cengiz MF, et al. Elution of monomer from different bulk fill dental composite resins. Dent Mater 2015;31:141-9.
15. Alshali RZ, Salim NA, Sung R, et al. Analysis of long-term monomer elution from bulk-fill and conventional resin-composites using high performance liquid chromatography. Dent Mater 2015;31:1587-98.
16. Mazzaoui SA, Burrow MF, Tyas MJ, et al. Long-term quantification of the release of monomers from dental resin composites and a resin-modified glass ionomer cement. J Biomed Mater Res 2002;63:299-305.

17. Polydorou O, Konig A, Hellwig E, et al. Long-term release of monomers from modern dental-composite materials. Eur J Oral Sci 2009;117:68-75.
18. Durner J, Schrickel K, Watts DC, et al. Determination of homologous distributions of bisEMA dimethacrylates in bulk-fill resin-composites by GC-MS. Dent Mater 2015;31:473-80.
19. Sideridou ID, Achilias DS. Elution study of unreacted Bis-GMA, TEGDMA, UDMA, and Bis-EMA from light-cured dental resins and resin composites using HPLC. J Biomed Mater Res B Appl Biomater 2005;74:617-26.
20. Michelsen VB, Lygre H, Skalevik R, et al. Identification of organic eluates from four polymer-based dental filling materials. Eur J Oral Sci 2003;111:263-71.
21. Durner J, Spahl W, Zaspel J, et al. Eluted substances from unpolymerized and polymerized dental restorative materials and their Nernst partition coefficient. Dent Mater 2010;26:91-9.
22. Geurtsen W, Spahl W, Leyhausen G. Variability of cytotoxicity and leaching of substances from four light-curing pit and fissure sealants. J Biomed Mater Res 1999;44:73-7.
23. Altintas SH, Usumez A. Evaluation of TEGDMA leaching from four resin cements by HPLC. Eur J Dent 2012;6:255-62.
24. Manojlovic D, Radisic M, Vasiljevic T, et al. Monomer elution from nanohybrid and ormocer-based composites cured with different light sources. Dent Mater 2011;27:371-8.
25. Moharamzadeh K, Van Noort R, Brook IM, et al. HPLC analysis of components released from dental composites with different resin compositions using different extraction media. J Mater Sci Mater Med 2007;18:133-7.
26. Eliades T, Eliades G, Brantley WA, et al. Residual monomer leaching from chemically cured and visible light-cured orthodontic adhesives. Am J Orthod Dentofacial Orthop 1995;108:316-21.
27. Manhart J, Kunzelmann KH, Chen HY, et al. Mechanical properties of new composite restorative materials. J Biomed Mater Res 2000;53:353-61.
28. Polydorou O, Trittler R, Hellwig E, et al. Elution of monomers from two conventional dental composite materials. Dent Mater 2007;23:1535-341.
29. Komurcuoglu E, Olmez S, Vural N. Evaluation of residual monomer elimination methods in three different fissure sealants in vitro. J Oral Rehabil 2005;32:116-21.
30. Aravamudhan K, Rakowski D, Fan PL. Variation of depth of cure and intensity with distance using LED curing lights. Dent Mater 2006;22: 988-994.
31. Barutcigil K, Dündar A, Batmaz SG, et al. Do resin-based composite CAD/CAM blocks release monomers? Clin Oral Investig. 2020 Jun 3. doi: 10.1007/s00784-020-03377-3. Online ahead of print.
32. Pongprueksa P, De Munck J, Duca RC, et al. Monomer elution in relation to degree of conversion for different types of composite. J Dent 2015;43:1448-55.
33. Goldberg M. In vitro and in vivo studies on the toxicity of dental resin components: a review. Clin Oral Investig 2008;12:1-8.
34. Geurtsen W. Biocompatibility of resin-modified filling materials. Crit Rev Oral Biol Med 2000;11:333-55.
35. Geurtsen W. Substances released from dental resin composites and glass ionomer cements. Eur J Oral Sci 1998;106:687-95.
36. Geurtsen W, Lehmann F, Spahl W, et al. Cytotoxicity of 35 dental resin composite monomers/additives in permanent 3T3 and three human primary fibroblast cultures. J Biomed Mater Res 1998;41:474-80.
37. Sideridou I, Tserki V, Papanastasiou G. Effect of chemical structure on degree of conversion in light-cured dimethacrylate-based dental resins. Biomaterials 2002;23:1819-29.