Eur. J. Prosthodont. Rest. Dent., Vol.18, No. 3, pp 139-145
Printed in Great Britain

doi:10.1922/EJPRD_903Mickenautsch07

Absence of Carious Lesions at Margins of Glass-Ionomer Cement (GIC) and Resin-Modified GIC Restorations: A Systematic Review

Steffen Mickenautsch*, Martin J Tyas†, Veerasamy Yengopal‡, Luciana B Oliveira§ and Marcelo Bönecker¶

Abstract - *This systematic review sought to quantitatively answer the question as to whether, in tooth cavities of the same size, type of dentition and follow-up period, resin-modified glass-ionomer (GIC) restorations, when compared to conventional GIC restorations, offer a significant caries preventive effect, as measured by the absence of caries lesions at the margin of restorations. Six databases were searched for articles in English, Portuguese or Spanish until 07 May 2009. Four articles were accepted and 22 separate datasets extracted. The difference between both types of material were computed as Relative Risk (RR) with 95% Confidence Interval (CI). No meta-analysis was undertaken due to aspects of clinical/methodological heterogeneity. The results of the extracted datasets ranged between RR 0.90 (95%CI 0.81 – 1.01) and 1.08 (95%CI 0.71 – 1.63; p>0.05) indicating no difference in the caries preventive effect between both types of materials. Further high-quality randomized control trials are needed in order to confirm these results.*

KEY WORDS: Glass-ionomer cement, caries, systematic review

INTRODUCTION

Secondary caries is the most common reason for replacing restorations[1] and an ideal restorative material would have, as one of its properties, the ability to prevent demineralization and/or promote remineralization at the cavity margin. Since ionic fluoride has been shown to reduce the incidence of caries at the population level, both in the water supply[2] and in other vehicles such as toothpaste[3], considerable attention has been focused on fluoride-containing restorative materials.

The earliest fluoride-releasing restorative material was silicate cement (now superseded). Anecdotal evidence of its caries-preventive effect was related to the paucity of reports of secondary caries seen in association with silicate cement despite its high intra-oral solubility[4]. This observation led to the inclusion of fluoride into restorative materials such as amalgam and resin-based materials, although published evidence of an anti-caries effect was not observed[5].

The glass-ionomer cements (GIC) that were introduced clinically in the early 1970s contained fluoride as a necessary part of the manufacturing process. This originated in part from silicate cement that also contained fluoride[6]. Thus, there was considerable interest in the effect of GIC on the adjacent tooth structure in terms of its purported anti-caries effect; as to whether it could influence the demineralisation-remineralisation cycle. The original glass-ionomer cements, now generally referred to as 'conventional' glass-ionomers (C-GIC), hardened in the tooth cavity because of an acid-base reaction between the fluoroaluminosilicate glass powder and the polyalkenoic acid liquid. However, they were sensitive to water uptake and loss in the first hours or days after setting, and this led to the development of 'resin-modified' GICs (RM-GIC): approximately 10% of the set material is resin, usually hydroxyethylmethacrylate (HEMA) [7].

Published studies that have examined the association of secondary caries with C-GIC restorations have reported variable findings. A retrospective study of 1283 C-GIC restorations, reported a failure rate of 7%, none being due to secondary caries[8]. Conversely, a further study investigated the reasons for replacing 412 C-GIC restorations and reported that almost half were replaced because of secondary caries[9]. A qualitative systematic review without meta-analysis found no evidence for or against the inhibition of secondary caries by C-GICs[10] and a subsequent literature review[5] confirmed this report. However, in a recent systematic review with meta-analysis, significantly less caries lesions were observed on single-surface C-GIC restorations in permanent teeth after 6 years compared to restorations with amalgam (Odds ratio 2.64 – 95%CI 1.39 – 5.03, p = 0.003)[11]. The advantages of meta-analysis over qualitative or narrative synthesis are that it provides the chance to detect whether a treatment effect is statistically significant (p<0.05) and improves estimation of the effect by quantifying its outcome, resulting in a more precise estimation[12]. No systematic review with meta-analysis regarding the caries-preventive effect of RM-GIC has been published. A combining of the recently confirmed anticariogenic properties of C-GIC[11] with the more water-resistant

* BDS, PhD
† BDS, PhD, DDSc
‡ BDS, MPH, MDENT
§ BDS, MSc
¶ BDS, MSc, PhD

characteristics achieved by inclusion of HEMA[8] would greatly benefit restorative treatment. Thus, this systematic review sought to quantitatively answer the question as to whether, in tooth cavities of the same size, type of dentition and follow-up period, RM-GIC restorations, when compared to C-GIC restorations, offer a significant caries preventive effect, as measured by the absence of caries lesions at the margin of restorations.

MATERIALS AND METHODS

Data collection

Five Anglophone databases (Biomed Central; Cochrane Library; Directory of Open Access Journals; PubMed; Science-Direct) and one Lusophone database (Literatura Latino-Americana e Caribenha em Ciências da Saúde – LILACS) were systematically searched for articles reporting on clinical trials up to 07 May 2009. The string of MeSH and text search terms with Boolean operators: *"Glass Ionomer Cements AND Dental Caries OR Root Caries AND resin modified glass ionomer cement"* was used to search the Anglophone databases and the strings of text terms: *"agentes cariostáticos [Descritor de assunto] and cimentos de ionômeros de vidro [Descritor de assunto] and cárie dentária",* as well as *"cariostatic agents [Descritor de assunto] and glass ionomer cements [Descritor de assunto] and dental caries [Descritor de assunto]"* were used to search LILACS. Articles were selected for review from the search results on the basis of their compliance with the inclusion criteria:

1. Titles/abstracts relevant to topic;
2. Published in English, Portuguese or Spanish;
3. Two-arm longitudinal clinical trial.

Where only a relevant title without a listed abstract was available, a full copy of the article was assessed for inclusion.

Article review

Only articles that complied with the inclusion criteria were reviewed further. Two reviewers (VY and SM) independently reviewed full copies of articles in accordance with the exclusion criteria[13]:

1. No random or quasi-random allocation of study subjects;
2. Not all entered subjects accounted for at the end of the trial;
3. Subjects of both groups not followed up in the same way;
4. No computable data reported for both control (comparison) and test groups.

Where several articles had reported on the same trial over similar time periods, the article covering the trial most comprehensively in accordance with the exclusion criteria was accepted. Disagreements between reviewers were resolved by discussion and consensus.

Data extraction from accepted trials

The outcome measure was the absence of caries lesion at the margin of restorations. Individual dichotomous datasets including the number of caries-free restorations (n) and total number of evaluated restorations (N) for both the control (comparison) and the test groups were extracted from each article. Where possible, missing data were calculated from information given in the text or tables. In addition, authors of articles were contacted in order to obtain missing information. Disagreements between reviewers during data extraction were resolved through discussion and consensus. It was anticipated that some of the studies eligible for inclusion would be split-mouth in design (quasi-randomized trials). The split-mouth study design is commonly used in dentistry to test interventions and has the advantage of enabling an individual to serve as both subject and control. In this study design one or more pairs of teeth (e.g. primary molars) form the unit of randomization. These pairs are, strictly speaking, not independent and should be analysed as "paired data" on a per-child basis. However, as in other similar reviews[14], in order to prevent exclusion of data, split mouth trials were included and the pairs were analysed independently.

Quality of studies

The quality assessment of the accepted trials was undertaken independently by two reviewers (VY and SM) following Cochrane guidelines[15]. Trials not included in this review were used to pilot the process. Subsequently, a quality assessment rating scored by both reviewers was derived by consensus. The following quality criteria were examined:

(1) Generation of randomization sequence (allocation), recorded as:

(A) adequate - e.g. computer-generated random numbers, table of random numbers;

(B) unclear - unclear or not reported;

(C) inadequate - e.g. case record number, date of birth, date of administration, alternation.

(2) Allocation concealment, recorded as:

(A) adequate - e.g. central randomization, sequentially numbered sealed opaque envelopes;

(B) unclear - unclear or not reported;

(C) inadequate - e.g. open allocation scheule, unsealed or non-opaque envelopes

(3) Blind/masked outcome assessment, recorded as:

(A) yes;

(B) unclear;

(C) no;

(D) not possible

STATISTICAL ANALYSIS

A random effects model in RevMan Version 4.2 statistical software (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2003) was used. Differences in treatment groups were computed on the basis of Relative Risk (RR) with 95% confidence intervals (CI). Datasets were assessed for their clinical and methodological heterogeneity, following Cochrane guidelines[16]. Datasets were considered to be heterogeneous if they differed in type of dentition (primary or secondary), cavity type, caries status at baseline, fluoride exposure from other sources and follow-up period. Chi^2, degree of freedom (df) and the percentage of total variations across datasets (I^2) were used in assessing statistical heterogeneity[17]. Only identified homogeneous datasets (clinical and methodological homogeneity) were combined for meta-analysis. Studies were assigned a Mantel-Haenszel weight directly proportional to their sample size.

RESULTS

An initial search of PubMed resulted in 220 articles, of which four[18-21] complied with the inclusion and exclusion criteria and were selected for review. A subsequent search of the other four Anglophone databases and the one Lusophone database generated no further results. All four reviewed articles reporting on randomized[18] and quasi-randomized control trials were accepted[19-21]. Table 1 provides information about quality aspects assessed for the accepted trials. Random allocation of subjects was rated A (Adequate) in one trial[21], B (Unclear) in one[20], and two trials[18,19] were rated as C (Inadequate). The random allocation in the latter two was rated inadequate because one trial alternated allocation of the two materials[18] and the other used a preconceived allocation table in order to ensure that each material was placed in the more anterior, middle or posterior tooth position an equal number of times[19]. As the used allocation mode in both trials made allocation concealment impossible, the quality of allocation concealment in these trials was also rated as C (Inadequate). The allocation concealment of the remaining two trials[20,21] was rated as B (Unclear). All B ratings were based on the lack of information in the text.

From the four accepted articles, 22 separate computable dichotomous datasets relevant to the review question were extracted. The main characteristics of the datasets are described in Table 2. Clinical and methodological heterogeneity between all datasets was observed. The datasets differed in type of dentition; type of restored cavity; fluoride exposure and follow-up period. Furthermore, two articles presenting eight separate datasets, did not report on the caries status of subjects in the different groups at baseline[18,20] and three articles, including 12 separate datasets, did not report on fluoride exposure from other sources[18,20,21]. For that reason, no meta-analysis was conducted and statistical heterogeneity was not further assessed. The Relative Risk (RR) with 95% Confidence interval (CI) of the separate datasets, ranging from 0.90 (95%CI 0.81 – 1.01) to 1.08 (95%CI 0.71 – 1.63), showed no difference ($p>0.05$) between the two materials with regard to absence of caries on restoration margins (Figure 1).

DISCUSSION

The aim of this quantitative systematic review was to explore whether in tooth cavities of the same size, type of dentition and follow-up period, RM-GIC restorations remained as free of secondary caries as did C-GIC restorations. Despite the identification of 220 articles dealing with dental caries and glass-ionomer cements, only four fulfilled the selection criteria. Often in systematic reviews, restrictive exclusion criteria concerning methodological aspects are used to limit the inclusion of bias and so strengthen the external validity of the results. One of the methodological considerations in systematic reviews concerning topics of therapy is selection of randomized control trials (RCT) that follow only a parallel group design[13]. Besides randomized parallel-group studies, the split-mouth study design is commonly used in dentistry to test interventions and includes the advantage of having an individual serve as both experimental subject and control. However, it has been suggested that split-mouth studies should be regarded as "quasi-randomized", as the common practice of including patients with at least one pair of treatable teeth results in exclusion of other potential study subjects and thus introduces a selection bias[22]. For this reason systematic reviews should, strictly speaking, not include split-mouth trials. There is a risk, however, that some useful trial data would be excluded from the review, thus weakening the overall clinical value. Therefore, in order to increase the inclusion envelope in this review, split-mouth quasi-random study designs and their data[19-21] were included and analyzed independently. Further aspects in the methodology of this review might have contributed to limitations in its results: (i) not all relevant publications were listed in the selected databases; (ii) not all relevant publications were published in English, Portuguese or Spanish. Thus, some relevant studies may not have been identified. Despite

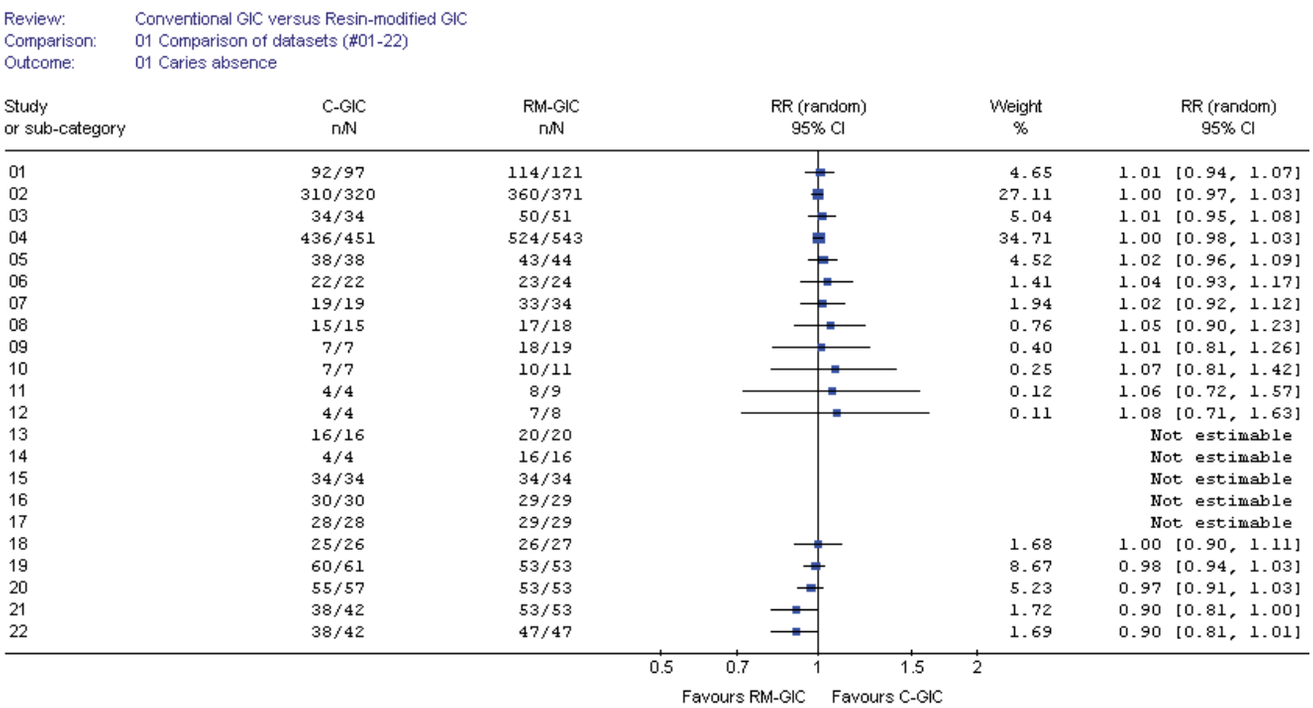
Table 1. *Quality assessment of randomized/quasi-randomized control trials*

Article	*Selection bias*		*Detection bias*
	Random allocation	*Allocation concealment*	*Evaluator blinding*
Qvist V *et al.* (2004)[18]	C	C	B
McComb D *et al.* (2002)[19]	C	C	D
Brackett WW *et al.* (1999)[20]	B	B	A
Hübel S and Mejáre I (2003)[21]	A	B	C

Table 2. *Main characteristics of datasets from randomized and quasi-randomized control trials.*

Article	*DS*	*Study type*	*Outcome measure*	*RM-GIC*	*C-GIC*	*Study subjects Age*	*Dentition*	*Type of restored cavity*	*Caries status at baseline*	*Fluoride exposure from other sources*	*Follow-up Period*
Qvist V *et al.* (2004)[18]	01	RCT	Caries absence	Photac Fil	Ketac Fil	>3 years	Primary	Class I	No info	No info	8 years
	02							Class II			
	03							Class III+V			
	04							All types			
McComb D *et al.* (2002)[19]	05	Split-mouth	Caries absence	Vitremer	Ketac Fil	>18 years	Permanent	Class V	Patients with at least 3 cervical carious lesions / All patients had received prior radiation therapy involving head and neck	Independent from Fluoride exposure	6 months
	06									No Fluoride exposure	
	07									Independent from Fluoride exposure	12 months
	08									No Fluoride exposure	
	09									Independent from Fluoride exposure	18 months
	10									No Fluoride exposure	
	11									Independent from Fluoride exposure	24 months
	12									No Fluoride exposure	
	13									Fluoride exposure	6 months
	14										12 months
Brackett WW *et al.* (1999)[20]	15	Split-mouth	Caries absence	Photac Fil	Ketac Fil	Median 45 years	Permanent	Cervical abrasion/ abfraction lesions	No info	No info	6 months
	16										12 months
	17										18 months
	18										24 months
Hübel S and Mejáre I (2003)[21]	19	Split-mouth	Caries absence	Vitremer	Fuji II	4-7 years	Primary	Class II	Mean defs 4.7 (SD = 2.9)	No info	<12 months
	20										12-23 months
	21										24-35 months
	22										>35 months

DS = Number of dataset; RCT = Randomized control trial; RM-GIC = Resin-modified glass-ionomer cement; C-GIC = Conventional glass-ionomer cement; SD = Standard deviation.



N = Total number of evaluated restorations; n = Number of restorations without caries; RR = Relative risk; CI = Confidence interval; C-GIC = Conventional glass-ionomer cement; RM-GIC = Resin-modified glass-ionomer cement "Not estimable" = Results of both groups the same (= RR 1.00); "Study or sub-category" = Number of dataset

Figure 1. *Comparison results in caries absence on restoration margins between both materials*

these considerations, in PubMed only 1.8% of the initially identified 220 articles were randomized/quasi-randomized control trials reporting the comparison of RM-GIC with C-GIC. Moreover, no further eligible articles were identified in the other databases. It can therefore be assumed that there is a general lack of published studies on this topic and the inclusion of further data sources might not have resulted in the selection of more articles.

Although trials with statistically significant results have been shown to be more likely to be published in English[23], non-English language trials may contribute in average 17.5% to the weight in individual meta-analyses and a decrease in average precision (Inverse of standard error) of meta-analysis results from 8.34 down to 7.68 after exclusion of non-English language trials was observed[24]. For this reason it was decided to search, besides English databases, also the well-known Lusophone database LILACS and to include, besides English language articles, also publications in Portuguese and Spanish.

The quality of the four accepted trials related to internal validity was assessed, using a structured checklist[15]. The assessment outcome indicated that the results of the trials might be limited by selection and detection bias (Table 1). Such bias or systematic error may affect studies, by causing either an over- or under-estimation of the treatment effect of an investigated clinical procedure. The overestimation of such effect has been observed to be the most common[25]. A 41% treatment effect overestimation due to selection bias, caused by lack of allocation concealment during the randomization process alone has been reported[26]. Since none of the trials accepted in this review included or reported on allocation concealment, their results need to be interpreted with caution.

Quantitative assessment, through calculation of the relative risk (RR) with 95% Confidence interval of the 22 dichotomous datasets showed no statistical differences in caries absence between RM-GIC and C-GIC (Figure 1). Qvist *et al.* (Datasets # 01-04) used a C-GIC (Ketac Fil) and an RM-GIC (Photac Fil) for 451 and 543 restorations respectively, in various cavities in deciduous teeth[18]. No information was provided on randomization. Restorations were followed for a maximum of 8 years. However, by then 60% of restorations could not be evaluated because of tooth loss. Three percent of both types of GIC restoration had secondary caries diagnosed during the study period. McComb *et al.* (Datasets # 05-14) restored cervical caries lesions in 45 high-caries-risk patients[19]. Each patient received three restorative materials in the same quadrant: Ketac Fil C-GIC; Vitremer RM-GIC (3M ESPE); and a non-fluoride containing resin composite (Z100, 3M ESPE). In total, 50 sets of restorations were placed and, after 24 months, only one of the GIC restorations, which was an RM-GIC, had developed secondary caries. Brackett *et al.* (Datasets # 15-18) restored non-carious cervical lesions (NCCL) with either a C-GIC (Ketac Fil; 3M ESPE, Seefeld, Germany) or an RM-GIC (Photac-Fil; 3M ESPE)[20]. Thirty-four pairs of restorations were placed and the allocation of the two materials to the patients was random. After 2 years, 15% of restorations were not available for examination and there was one caries lesion associated with each of the GICs, both being in the same patient, among the 85% of restorations examined. Hübel and Mejàre (Datasets # 19-22) also compared C-GIC (Fuji II; GC Corp, Japan) and RM-GIC

(Vitremer)[21]. However, the restorations were in approximal cavities in deciduous teeth. A mainly split mouth design with random allocation was used, with 62 C-GIC and 53 RM-GIC restorations. After 3 years, four Fuji II restorations and zero Vitremer restorations had developed secondary caries. However, no statistical tests for this evaluation criterion were reported. There is therefore no evidence from the two trials in permanent teeth[19,20] that any difference exists in the incidence of secondary caries adjacent to C-GIC and RM-GIC restorations. In deciduous teeth, the findings are equivocal: one study[18] found no difference between C-GIC and RM-GIC with respect to secondary caries, while the other study[21] found significantly more failures of the C-GIC, but mostly due only to loss of retention.

The lack of difference between RM-GIC and C-GIC with respect to secondary caries may be due to their similar fluoride release characteristics[5]. Wiegand *et al*. have extensively reviewed the dynamics of fluoride release and recharge characteristics of several fluoride-containing materials, including the glass-ionomers, polyacid-modified resin composites ('compomers'), giomers, amalgam and silicate cement[5]. Although there are differences between brands, the release of fluoride from C-GIC and RM-GIC is broadly similar in amount and pattern. Moreover, in laboratory studies, the amount released is dependent on the eluant, e.g., whether it is distilled water, artificial saliva or saline[5]. It is also evident that the amount of fluoride released is inversely associated with the acidity of the eluant, and this may be of clinical importance. However, from a clinical perspective, the amount of fluoride release required for inhibition of secondary caries, or for remineralisation of demineralised enamel adjacent to a restoration, is not known. Thus, estimating the anti-caries activity of glass-ionomers from laboratory data remains problematic. That these considerations are equally valid for both C-GIC and RM-GIC explains the lack of clinical differences between both types of materials with regard to caries.

This review identified a lack of high-quality trials on the review topic (Table 1). Therefore, further high quality randomized control trials are needed to confirm the observed results. Reporting of such trials should follow the CONSORT statement[27] and, particularly, include a clear description of how the randomized allocation of study subjects was conducted, report on details of any restrictions and state who generated the allocation sequence, who enrolled the subjects and who assigned subjects to their groups. Reporting should further include information about whether such allocation was concealed from the clinical operators until interventions were assigned and if it was, about how this was done, as well as whether or not participants, clinical operators and evaluators of the study results were aware of group assignment and if not, how the success of such masking was assessed.

CONCLUSIONS

The systematic literature search identified four randomized/quasi-randomized control trials including 22 separate datasets with relevance to the review question. None of the datasets found one material to be superior to the other in terms of caries absence. The answer to the review question was that in comparison to conventional GIC of the same size, type of dentition and follow-up period, the margins on restorations with resin-modified GIC appear to remain as free of secondary caries as conventional GIC restorations. However, these findings have to be regarded with caution, as all the included studies had limited internal validity due to unclear randomized sequence allocation and/or allocation concealment, as well as patient, operator and evaluator masking. Further high quality randomized control trials are therefore needed. It is recommended that reporting of such future trials should follow the CONSORT statement.

ADDRESS FOR CORRESPONDENCE

Dr S Mickenautsch, Division of Public Oral Health, University of the Witwatersrand, 7 York Rd, 2193 Parktown/Johannesburg, South Africa. Email: neem@global.co.za

REFERENCES

1. Mjör, I.A. and Toffenetti, F. Secondary caries: A literature review with case reports. *Quintessence Int.,* 2000;**31**:165-179.
2. McDonagh, M.S., Whiting, P.F., Wilson, P.M. *et al.* Systematic review of water fluoridation. *BMJ,* 2000;**321**:855-859.
3. Twetman, S., Axelsson, S., Dahlgren, H, *et al.* Caries-preventive effect of fluoride toothpaste: a systematic review. *Acta Odontol. Scand.,* 2003;**61**:347-355.
4. Ewoldsen, N. and Herwig, L. Decay-inhibiting restorative materials: past and present. *Compend. Contin. Educ. Dent.,* 1998;**19**:981-984.
5. Wiegand, A., Buchalla, W. and Attin, T. Review on fluoride-releasing restorative materials--fluoride release and uptake characteristics, antibacterial activity and influence on caries formation. *Dent. Mater.,* 2007;**23**:343-362.
6. Kent, B.E., Lewis, B.G. and Wilson, A.D. Glass ionomer cement formulations: I. The preparation of novel fluoroaluminosilicate glasses high in fluorine. *J. Dent. Res.,* 1979;**58**:1607-1619.
7. Ikeda, K., Fujishima, A., Suzuki, M., Inoue, M., Sasa, R. and Miyazaki, T. Resin content in cement liquids of resin-modified glass ionomers. *Dent. Mater. J.,* 1999;**18**:248-258.
8. Mount, G.J. Longevity of glass ionomer cements. *J. Prosthet. Dent.,* 1986;**55**:682-685.
9. Mjör, I.A. Glass ionomer cement restorations and secondary caries: A preliminary report. *Quintessence Int.*, 1996;**27**:171-174.
10. Randall, R.C. and Wilson, N.H.F. Glass-ionomer restoratives: A systematic review of a secondary caries treatment effect. *J. Dent. Res.,* 1999;**78**:628-637.
11. Mickenautsch, S., Yengopal, V., Leal, S.C., Oliveira, L.B., Bezerra, A.C. and Bönecker M. Absence of carious lesions at margins of glass-ionomer and amalgam restorations: a meta-analysis. *Eur. J. Paediatr. Dent.,* 2009;**10**:41-46.
12. Higgins, J.P.T. and Green, S. *Cochrane handbook for systematic reviews of interventions 4.2.6*, Issue 4. J. Wiley & Sons. Chichester, 2006;97-99.
13. Sutherland, S.E. Evidence-based dentistry: Part V. Critical appraisal of the dental literature: papers about therapy. *J. Can. Dent. Assoc.,* 2001;**67**:442-445.
14. Ahovuo-Saloranta, A., Hiiri, A., Nordblad, A., Worthington, H. and Mäkelä M. *Pit and fissure sealants for preventing dental decay in the permanent teeth of children and adolescents*. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD001830. DOI: 10.1002/14651858.CD001830.pub2.
15. Higgins, J.P.T. and Green, S. *Cochrane handbook for systematic reviews of interventions 4.2.6*, Issue 4. J. Wiley & Sons. Chichester, 2006;79-89.
16. Higgins, J.P.T. and Green, S. *Cochrane handbook for systematic reviews of interventions 4.2.6*, Issue 4. J. Wiley & Sons. Chichester, 2006;136-145.
17. Thompson, S.G. Why sources of heterogeneity in meta-analysis should be investigated. *BMJ,* 1994;**309**:1351-1355.
18. Qvist, V., Manascher, E. and Teglers, P.T. resin-modified and conventional glass ionomer restorations in primary teeth: 8-year results. *J. Dent.,* 2004;**32**:285-294.

19. McComb, D., Erickson, R.L., Maxymiw, W.G. and Wood, R.E. A clinical comparison of glass ionomer, resin-modified glass ionomer and resin composite restorations in the treatment of cervical caries in xerostomic head and neck radiation patients. *Oper. Dent.,* 2002;**27**:430-437.
20. Brackett, W.W., Gilpatrick, R.O., Browning, W.D. and Gregory, P.N. Two-year clinical performance of a resin-modified glass-ionomer restorative material. *Oper. Dent.,* 1999;**24**:9-13.
21. Hübel, S. and Mejáre, I. Conventional versus resin-modified glass-ionomer cement for Class II restorations in primary molars. A 3-year clinical study. *Int. J. Paediatr. Dent.*, 2003;**12**:2-8.
22. Mejáre, I., Lingström, P., Petersson, L.G. *et al*. Caries-preventive effect of fissure sealants: a systematic review. *Acta Odontol. Scand.*, 2003;**61**:321-330.
23. Egger, M., Zellweger-Zähner, T., Schneider, M. *et al*. Language bias in randomised controlled trials published in English and German. *Lancet*,1997;**350**:326-329.
24. Jüni, P., Holenstein, F., Sterne, J. *et al*. Direction and impact of language bias in meta-analyses of controlled trials: empirical study. *Int. J. Epidemiol.*, 2002;**31**:115-123.
25. Chalmers, T.C., Matta, R.J., Smith, H. Jr. and Kunzler, A.M. Evidence favoring the use of anticoagulants in the hospital phase of acute myocardial infarction. *N. Engl. J. Med.,* 1977;**297**:1091-1096.
26. Schulz, K.F., Chalmers, I., Hayes, R.J. and Altman, D.G. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *J. Am. Med. Assoc.,* 1995;**273**:408-412.
27. Moher, D., Schulz, K.F. and Altman, D.G. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet*, 2001;**357**:1191-1194.