J. Dent. Suppl. 2, 1994; **22**: S29-S32

Clinical testing of dental materials—general clinical aspects

P. Hörsted-Bindslev
Royal Dental College, Faculty of Health Sciences, University of Aarhus, Denmark

KEY WORDS: Dental materials, Biocompatibility, Clinical testing

Correspondence should be addressed to: Associate Professor Preben Hörsted-Bindslev, Department of Dental Pathology, Operative Dentistry and Endodontics, Royal Dental College, Faculty of Health Sciences, University of Aarhus, Vennelyst Boulevard, DK-8000 Aarhus C, Denmark.

INTRODUCTION

When a new restorative or endodontic material has passed the various preclinical levels of physical and biological testing, the ultimate test remains: the clinical assessment. This comprises the performance of the material under the conditions for which it has been developed.

For ethical reasons and because fewer teeth are extracted today for orthodontic and prosthetic reasons, testing of new materials on humans comprises a limited number of clinical studies and in most there is no possibility of obtaining histological analyses of the restored teeth. If teeth are available for histological examination some problems are encountered in the estimation of material toxicity. Thus, the pulp reactions studied are not solely a result of material toxicity but are the end result of multiple events. Among the factors involved are method of cavity preparation, condition of the dentine cavity wall, presence of bacteria, distance from cavity walls to the pulp, method of application and toxicity of the restorative material. *In vitro* studies and usage tests on animals have revealed that the relative importance of the above-mentioned factors may vary depending on the restorative methods and materials tested. Thus, the remaining dentine thickness may be of importance for the pulp reactions when some chemicals for dentine adhesion are evaluated[1], but it may be of minor importance when pulp reactions to bacteria are considered[2,3]. Different elements in the restorative procedure such as pretreatment of the cavity walls, physicochemical properties of the material and presence of bacteria may furthermore interact depending on the material in question. For example, use of acid on dentine may result in minor pulpal reactions and widening of the peripheral part of the dentinal tubules. However, if acid etching of dentine is a prerequisite for optimal adhesion of composites to dentine this treatment may be implemented in order to prevent later inflammatory reactions and secondary caries due to microbial invasion of the microspace. In this context the polymerization shrinkage and the following expansion of a composite due to water absorption should also be considered, because minimal shrinkage and maximal expansion will reduce microleakage.

What kind of information on biocompatibility can we obtain from clinical studies? The following will discuss some of the problems which may be encountered when attempting to identify the biological components in clinical studies on restorative and endodontic materials. Some prime elements which make up the clinical information available from restorative and endodontic treatments are histories of pain, oral mucosal reactions or symptoms, radiographic changes and generalized symptoms.

HISTORY OF PAIN

Information from human clinical studies is in one sense unique compared with biocompatibility studies at lower levels, as it is possible to obtain information about pain following treatment.

Pulpal pain following placement of composite restorations or the cementation of tooth-coloured inlays with resin-based materials have been described in the literature[4-8]. The frequency varies between 10% and 30% and in most cases the symptoms disappear within 2 weeks. The stimuli which provoke pain are different from those which cause pain following treatment with amalgam but

0300-5712/94/S020S29-32

the frequency seems comparable[4,7]. In one study it was observed that a quarter of the patients accounted for 60% of the complaints, whereas differences in experienced pain between different types of resin composite material were insignificant[7]. In another study, however, the frequency of pain was diminished by 50% by lining all dentine with a calcium hydroxide cement[6]. This finding could be interpreted as high toxicity of the resin composite material. However, in general, results from toxicity studies indicate that polymerized resin composite materials have low toxicity. Apparently the change in operative procedure accounts for the reduced pain experience. Thus, attention should be paid to a variety of factors when the reasons for postoperative pain are considered. Factors such as dentine permeability, filling technique employed, size, depth and design of preparation, the physicochemical properties of the resin composite material and especially the presence of bacteria and metabolic products on the dentinal wall or in the dentinal tubules may all be of importance.

It is interesting that toxicity of glass polyalkenoate (ionomer) cements has been claimed in some studies to be the reason for postoperative pain following cementation of crowns and bridges, whereas glass ionomer cements in other studies is recommended as a base for resin composite restorations in order to prevent postoperative pain, or as the material of choice for treatment of dentine hypersensitivity. This difference has been ascribed to the higher toxicity of the luting formulae because of differences in acid formulation and prolonged acidity of the luting materials (for review see ref. 9), but also dehydration of dentine prior to luting or rapid dissolution of the lute along the cavity margins giving easy access to microbiological invasion have been discussed as reasons for postoperative pain. It is furthermore interesting that the studies on pain following cementation were more frequently reported immediately after introduction of the luting formula. This may indicate that improper handling of the material is another factor of importance.

Finally, it should be noted that the correlation between clinical signs and symptoms, and histopathology of the pulp tissue is weak[10-13].

A history of pain following restorative treatment is an important component of the diagnostic puzzle. Pain is caused by an interaction of the various operative procedures and the original pulp status. Toxicity of the current materials is probably not of prime importance and it is hardly possible to point out clinical situations where low biocompatibility alone is the main cause of pain experience.

MUCOSAL REACTIONS

Chronic mucosal lesions following restorative treatment may be due to specific immunological or non-specific toxic reactions to products generated from the restorative materials. White, red or ulcerated mucosal lesions have been described to be present on rare occasions in relation to amalgam restorations. In these cases the differential diagnostic considerations should include toxic substances released from the restoration and hypersensitivity reactions especially towards mercury, but also lichen planus and leukoplakia should be considered[14]. Furthermore, it has been shown that such lesions may disappear following improved oral hygiene, indicating that accumulation of plaque on the restoration may be of importance[14]. Thus, it is difficult to assess the impact from the restorative material per se. This can be done more easily when acute reactions are considered. These reactions are observed directly in relation to or immediately following the operative procedure. Prolonged mucosal contact with materials used for enamel and dentine bonding has been shown to cause serious mucosal ulcerations in animal studies[15]. In clinical practice temporary and small white spot lesions and vague tingling sensations have been observed occasionally and reported from clinicians using these materials routinely, but only single case reports on side-effects have been published (e.g. ref. 16).

In general, local mucosal reactions to restorative materials are seldom reported and the prevalence seems to be very limited[9,17]. Most often the findings are not described in clinical studies of new restorative materials. This may be because the number of restorations studied is small, but it cannot be ruled out that mucosal reactions have not been given high priority in studies where the main objectives have been to evaluate abrasion, discoloration, marginal failures and secondary caries. A description of mucosal contact reactions is important from a biocompatibility point of view and should be included in clinical studies. By so doing relevant and important information on side-effects of various materials can be obtained. Due to the rare frequency of side-effects from at least the materials in current use a large number of case reports are necessary to form reliable data. Although the turnover of contemporary materials is rapid, data should still be collected.

RADIOGRAPHIC CHANGES

In vitro, cell culture tests and implantation and usage tests in animals of biocompatibility of root filling materials are numerous. The clinical significance of these tests may be difficult or sometimes impossible to assess. Apparently, it may even be difficult to compare results from different usage tests on monkeys as documented in two recent studies on virtually identical endodontic materials[18,19]. From one study it was concluded that the methods and criteria used were adequate for ranking the biocompatibility of the tested materials[18], whereas the other study concluded that the method applied did not provide sensitive discrimination among the endodontic materials[19]. Also clinical radiographic follow-up studies on root fillings are numerous, but comparisons of the prognoses of root filling materials, used and evaluated

Fig. 1. Serious swellings of the left half of the face following root filling with an epoxy resin root canal sealer. (Courtesy of J. K. Pedersen.)

Fig. 2. The symptoms disappeared following treatment with an antihistamine and removal of the root filling material. (Courtesy of J. K. Pedersen.)

under standardized conditions are very sparse. Introduction of a reproducible and objective periapical index may increase the possibility of comparing results obtained with different sealers[20]. Two prospective studies have been performed using this scoring system[21,22]. From the first study it was concluded that sealer A performed less well than sealer B. The second study, however, showed no difference between results with sealer A and B and it was concluded that when the sealer exerts a systematic effect on the prognosis, it is small and quickly overridden by other biological and technical factors associated with endodontic treatment. Well-known and accepted factors of importance are preoperative diagnostic and radiographical status, distance from root filling to apex and sealing quality of the root filling. Again, presence of bacteria plays a very important role for the result.

GENERALIZED CLINICAL SYMPTOMS

Generalized symptoms from use of restorative or endodontic materials are considered extremely rare (*Figs 1, 2*). Type IV mercury hypersensitivity reactions have been described (for review see ref. 14) and although few in published numbers, reactions to composite restorative materials (for review see ref. 9) are considered a problem of potentially increasing magnitude. Even if some root canal sealers contain highly allergenic compounds, the same case reports are constantly referred to in the literature when allergic side-effects of root filling materials are discussed[23].

Apparently, generalized adverse effects are few, but some cases may not come to light. The importance of reporting side-effects should be clarified and made compulsory for members of the dental profession.

A wide variety of symptoms which have been ascribed to the presence of amalgam restorations have until now not been scientifically verified (for review see ref. 24). But the entire discussion reminds the dental profession to be alert to the risk of long-term sequelae to operative treatment with materials containing toxic and allergenic constituents.

CONCLUSION

Many factors besides biocompatibility decide the success or failure of a material. Clinical and radiographic studies reveal only sparse information regarding the biocompatibility of dental materials. Therefore, as much information as possible should be built up from preclinical biocompatibility tests. This should be supplemented with reports from the clinic on verified side-effects collected by notified bodies appointed by national or international authorities.

References

1. Hörsted-Bindslev P. Monkey pulp reactions to cavities treated with Gluma Dentin Bond and restored with a microfilled composite. *Scand J Dent Res* 1987; **95**: 347–355.
2. Bergenholtz G. Effect of bacterial products on inflammatory reactions in the dental pulp. *Scand J Dent Res* 1977; **85**: 122–129.
3. Hörsted PB, Simonsen A-M and Larsen MJ. Monkey pulp reactions to restorative materials. *Scand J Dent Res* 1986; **94**: 154–163.
4. Johnson GH, Gordon GE and Bales DJ. Postoperative sensitivity associated with posterior composite and amalgam restorations. *Oper Dent* 1988; **13**: 66–73.
5. Lundin S-Å and Koch G. Class I and II composite resin restorations: a 4-year clinical follow up. *Swed Dent J* 1989; **13**: 217–227.
6. Qvist V and Thylstrup A. Pulpal reactions to resin restorations. In: Anusavice KJ, ed. *Quality Evaluation of Dental Restorations—Criteria for Placement and Replacement.* Chicago: Quintessence, 1989; pp 291–301.
7. Borgmeijer PM, Kreulen CM, van Amerongen WE, Akerboom HBM and Gruythuysen RJM. The prevalence of postoperative sensitivity in teeth restored with Class II composite resin restorations. *J Dent Child* 1991; **58**: 378–383.
8. Thordrup M, Isidor F and Hörsted-Bindslev P. A one-year clinical study of indirect and direct composite and ceramic inlays. *Scand J Dent Res* 1994; **102**: 186–192.
9. Stanley HR. Local and systemic responses to dental composites and glass ionomers. *Adv Dent Res* 1992; **6**: 55–64.
10. Lundy T and Stanley HR. Correlation of pulpal histopathology and clinical symptoms in human teeth subjected to experimental irritation. *Oral Surg Oral Med Oral Pathol* 1969; **27**: 187–201.
11. Hørsted P. Studies on the root filling cement Ri-oxol. A clinical, roentgenological and histological investigation. *Acta Odontol Scand* 1972; **30**: 187–199.
12. Dummer PMH, Hicks R and Huws D. Clinical signs and symptoms in pulp disease. *Int Endod J* 1980; **13**: 27–35.
13. Lin LM, Pascon EA, Skribner J, Gängler P and Langeland K. Clinical, radiographic, and histologic study of endodontic treatment failures. *Oral Surg Oral Med Oral Pathol* 1991; **71**: 603–611.
14. Holmstrup P. Oral mucosal reactions related to silver amalgam. In: Hörsted-Bindslev P, Magos L, Holmstrup P, Arenholt-Bindslev D, eds. *Dental Amalgam—A Health Hazard?* Copenhagen: Munksgaard, 1991; pp 62–82.
15. Arenholt-Bindslev D, Hörsted-Bindslev P and Philipsen HP. Toxic effects of two dental materials on human buccal epithelium *in vitro* and monkey buccal mucosa *in vivo*. *Scand J Dent Res* 1987; **95**: 467–474.
16. Gutteridge DL. Iatrogenic oral ulceration following restorative treatment with an acid-etch material. *Br Dent J* 1984; **156**: 403–404.
17. Kallus T and Mjör IA. Incidence of adverse effects of dental materials. *Scand J Dent Res* 1991; **99**: 236–240.
18. Pascon EA, Leonardo MR and Safavi K. Tissue reaction to endodontic materials: methods, criteria, assessment, and observations. *Oral Surg Oral Med Oral Pathol* 1991; **72**: 222–237.
19. Ørstavik D and Mjör IA. Usage test of four endodontic sealers in *Macaca fascicularis* monkeys. *Oral Surg Oral Med Oral Pathol* 1992; **73**: 337–344.
20. Ørstavik D, Kerekes K and Eriksen HM. The periapical index: a scoring system for radiographic assessment of apical periodontitis. *Endodont Dent Traumatol* 1986; **2**: 20–34.
21. Ørstavik D, Kerekes K and Eriksen HM. Clinical performance of three endodontic sealers. *Endod Dent Traumatol* 1987; **3**: 178–186.
22. Ørstavik D and Hörsted-Bindslev P. A comparison of endodontic treatment results at two dental schools. *Int Endodont J* 1993; **26**: 348–354.
23. Hensten-Pettersen A, Ørstavik D and Wennberg A. Allergenic potential of root canal sealers. *Endod Dent Traumatol* 1985; **1**: 61–65.
24. Hörsted-Bindslev P. Mercury and the dental patient. In: Hörsted-Bindslev P, Magos L. Holmstrup P, Arenholt-Bindslev D, eds. *Dental Amalgam—A Health Hazard?* Copenhagen: Munksgaard, 1991; pp 41–61.