

LITERATURE REVIEW

HARMFUL EFFECTS OF METHYLMETHACRYLATE AND FORMALDEHYDE FROM ACRYLIC RESIN DENTURE BASE MATERIALS

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استعمل مركب الميثيل ميتاكريليت بشكل واسع كتعويض صناعي وكبديل لعظم القحف . يعتبر مركب الميثيل ميتاكريليت والفورمالدهايد من نواتج أكسدة الميثيل ميتاكريليت الأحادي وتعتبر هذه المركبات عوامل محسسة مسؤولة عن بعض الأذيات المخاطية . يؤدي الميثيل ميتاكريليت الأحادي إلى التهاب الغم التحسسي والتهاب الجلد . إن تعرض الرئتين والرغامى لأبخرة الميثيل ميتاكريليت الأحادي أمر مؤذي يمكن أن يؤدي هذا التعرض إلى تبدلات مرضية في الأجرية اللمفاوية حول القصبة ، كما يمكن أن يؤدي إلى احتقان دموي في الشعيرات التنفسية . عند استعمال هذا المركب كبديل لعظم القحف فإنه يدخل الدوران الجهازى والتنفسى مما يؤدي إلى تشكل آفات وإلى تغيرات مرضية مميزة تتمثل في فقدان أهداب الرغامى والبشرة التنفسية القصبية وفرط نزفية من أنسجة الرئتين وهبوط حاد في ضغط الدم وبالتالي توقف القلب وانهيار الجهاز القلبي الوعائى . على كل حال من المعروف ويشكل واسع أن التأثيرات القلبية الوعائية التالية لإدخال إسمنت الراتنج العظمي خلال الإجراءات العظمية معتدلة الشدة وعابرة .

Methylmethacrylate has been extensively used as a dental prosthetic and as a cranial-bone substitute for years. Methylmethacrylate and formaldehyde which is formed as oxidation products of the residual methylmethacrylate monomer are allergic agents responsible for mucosal injuries. Methylmethacrylate monomer also causes allergic stomatitis and dermatitis. Exposure of lungs and trachea to methylmethacrylate vapor is harmful. Significant pathologic changes as loss of cilia of tracheas and bronchial respiratory epithelism, hyperplasia of peribronchiolar lymphoid follicles, and respiratory capillary hyperemia may result. When used as a cranial-bone substitute, the monomer enters the systemic and pulmonary circulation. Hemorrhagic lesions of the lung parenchyma, acute hypotension leading to cardiac arrest and cardiovascular collapse may occur. Cardiovascular effects following insertion of bone resin cement during orthopedic procedures are widely believed to be only mild and transient, however.

Introduction

Methylmethacrylate has been extensively used as a dental prosthetic and as a cranial-bone substitute for over two decades.

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Acrylic resin dentures contain methylmethacrylate (MMA) as residual monomer. MMA has the potential to elicit irritation, inflammation and allergic response of the oral mucosa.^{1,5} Further, residual monomer is capable of producing both stomatitis and an angular cheilitis.⁶

Formaldehyde is another allergic agent in acrylic dentures responsible for mucosal injuries. Formaldehyde is formed as an oxidation product of the residual MMA monomer in inhibition layers and poorly polymerized resins.^{8,10} Formaldehyde formation was suggested to occur through the decomposition of the oxygen-methylmethacrylate copolymer or by the oxidation of MMA.

In 1993, Tsuchiya et al⁸ demonstrated that formaldehyde leached from acrylic resins was remarkably reduced by removing the unpolymerized surface layers.

Formaldehyde is proved to be cytotoxic at much lower concentrations than methylmethacrylate.¹² Formaldehyde is also a strong irritant to the mucous membranes even at concentrations as low as 0.63 to 1.25 mg/cubic meter¹¹.

The allergic reaction occurs within a few to several hours after the mucosa is exposed to the resin. When allergic reactions were noted, they were described as white, necrotic lesions on the mucosa; either as small, multiple lesions or as large ulcers mimicking aphthous stomatitis.

Acrylic denture base materials may either contain self-polymerizing or heat polymerizing resin. There are few documented cases of allergic contact stomatitis to self-polymerizing resin.^{16,13,16} Although allergic responses to the methacrylates in general are rare, those reactions that do occur are caused most often by the self-polymerizing (cold-cure) resins rather than by the heat-cured ones.¹³ A heat polymerized resin is more biocompatible than the autopolymerized material since significant amounts of methylmethacrylate remains in the

autopolymerized resins.^{8,17}

Axelsson's¹⁸ study showed that dentures initially containing 2% to 3% residual methylmethacrylate monomer contained 1% to 2% after 3 years in the oral cavity. A slow monomer release has been demonstrated in clinical investigations.^{9,18,19}

In many studies, a good correlation has been demonstrated between the amount of methylmethacrylate monomer remaining in acrylic resins after polymerization and the methylmethacrylate concentration leached from acrylic resins.^{17,20,22}

Leaching of formaldehyde appears to correlate to the difference in allergic potential between auto-and-heat-polymerized resins possibly indicating the etiological significance of formaldehyde in the allergic inflammation of denture wearers.⁸

Allergic contact stomatitis is a delayed type of hypersensitivity characterized by the following:^{6,7,23}

1. The patient has had previous exposure to the allergen or sensitizing material.
2. The reaction conforms to known allergic pattern, such as redness, necrosis or ulceration.
3. The reaction resolves when the allergen is removed.
4. The reaction recurs when the tissues are re-exposed to the allergens at the same site.
5. A patch test is positive.

Allergic contact stomatitis is usually associated with an allergic hypersensitivity of the skin. There may be sensitization of the skin only, sensitization of both the skin and mucous membrane, or sensitization of the mucous membrane only and not the skin.

In 1956, Fisher identified methylmethacrylate monomer as the cause of allergic

dermatitis of four dentists and dental laboratory technicians who had come in repeated contact with acrylic denture materials, and one orthopedic surgeon handling bone cement.²⁴

Adverse effects caused by the chemotoxic activity of dental polymers have been investigated by cell culture techniques *in vitro*, animal studies *in vivo*, and by clinical observations on patients treated with removable dentures and fixed partial dentures.^{1,18,25,34} The immunological contribution to the severe tissue response was indicated histologically by the presence of excessive plasma cells and immunologically activated lymphocytes."

In Tsuchiya⁸ study, subcutaneous implantation of acrylic resin caused more severe inflammation in guinea pigs previously sensitized to formaldehyde. These findings suggest that the tissue responses are induced by formaldehyde leached from the resin.

There are many reports about side effects of MMA when used in Medicine. Contact dermatitis,^{36,38} allergic stomatitis,¹³ respiratory distress,³⁹ and cardiovascular pathology⁴⁰ are among those described in these reports. Cardiovascular effects range from hypotension to cardiac arrhythmia,^{40,41} coronal embolus and cardiac arrest.^{42,13}

An animal study showed a pronounced vasodilator) action of the monomer without myocardial depression.⁴³ When methylmethacrylate is placed in direct contact with cancellous bone, prior to polymerizing, small amounts of the monomer enter the systemic and pulmonary circulation. Intravenous injection of large amounts of acrylic monomer in dogs caused hemorrhagic lesions of the lung parenchyma.

Charnley postulates that the transient circulatory changes result from absorption of methylmethacrylate monomer into the vascular compartment. This pattern closely resembles the

hypotension following intravenous injection of the liquid monomer in dogs.⁴⁶

Episodes of acute hypotension and cardiovascular collapse at the time of intraosseous implantation of the resin cement have been reported.^{40,43,4} Absorption of the cement monomer may have been responsible for acute hypotension leading to cardiac arrest. A fall in blood pressure in association with the use of bone cement is also known to occur.⁴³

Thomas et al.⁴⁸ investigated the possible causes of, and contributing factors to death under anaesthesia, during an operation for hip joint replacement with a prosthesis, using methylmethacrylate monomer bone cement. Changes of the central venous pressure and electrocardiogram were recorded following the insertion of cold curing acrylic bone cement. The author stated that great care should be taken to limit absorption of monomer.

The frequency and magnitude of circulatory changes following methylmethacrylate implantation were determined by Schuh⁴⁹. In his patients, intraosseous application of methylmethacrylate was followed in almost every instance by alteration of arterial pressure or heart rate. The mechanism of action underlying the cardiovascular side-effects has not been identified. However, these results suggest, as do responses in experimental animals, that methacrylate monomer exerts its effects through a vasodilator) action. The mechanism of action underlying the cardiovascular side-effects has not been identified. The occasional increase in heart rate together with an increase in blood pressure might be explained as a compensatory mechanism.^{40,49,50}

Sokmen and Oktemer⁵¹ showed that when rats were exposed to low concentrations (0.45ppm) of methylmethacrylate monomer vapor, histopathological manifestations of lungs and trachea were observed. They exposed 60 male Swiss Albino rats to methylmethacrylate monomer vapor

in air for periods of 4.8 and 12 weeks, 5 days per week and 1 hour per day. At the end of four and eight week periods, statistically significant pathologic changes were: loss of cilia of trachea and bronchial respiratory epithelium, hyperplasia of peribronchial lymphoid follicles, and respiratory capillary hyperemia. In conclusion, methylmethacrylate monomer vapor was found to have an irritating effect on lungs and trachea. These results demonstrate the importance of ventilation in working places for people who use methylmethacrylate.

In 1974, Tansy et al.⁵² observed an inhibition of gastrointestinal motility by breathing the methylmethacrylate monomer. They assumed that this effect might be occurring due to the cardiopulmonary mechanism.

Blanchet et al.⁵³ also noticed peribronchiolar lymphadenopathy, edema, emphysema, and peri-vascular lymphocyte infiltration by a histo-pathologic study in 1980 but they were not able to indicate the amount of methylmethacrylate vapor used in the procedure.

Although most studies have focused on the cytotoxicity of leached methylmethacrylate,^{12,13,54,5} more attention should be given to formaldehyde leachable from acrylic resins as a chemical agent that can cause damage to the oral mucosa in patients wearing acrylic resin dentures.^{9,12,19}

To minimize the possible risk of sensitization or allergic reactions by acrylic resin dentures, immersion of acrylic resin dentures in hot water (50°C) for one hour before insertion is recommended.^{12, 56} This procedure is particularly important with the autopolymerized resins used either for rebasing or as a denture base materials. The residual monomer content in heat-cured acrylic appears to be resistant to removal by immersion in water, however.²⁰

While the cytotoxic properties of methylmethacrylate monomer are well known and in spite of the toxicity of this monomer, the cardiovascular effects following insertion of bone cement during orthopedic procedures are widely believed to be only mild and transient in nature.⁴⁸

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