Clinical Abstract

Bone cement in the focus: Methyl methacrylate (MMA)

When bone cement is mixed a small part of the liquid component methyl methacrylate (MMA) is converted into gaseous form and is released into the room air. In high concentrations MMA can irritate lungs, eyes and skin.

Is there a health risk for the user?
This brochure provides information about MMA, its effects on humans and the situation in the operating room.

Summary

- The MMA concentrations reached short-term in the room air in bone cement mixing lie clearly below the permissible workplace limits.
- A health risk for operating room staff and patients appears to be largely excluded according to the present day state of knowledge.
- Vacuum systems reduce the MMA concentrations compared with manual mixing. The activated carbon filters frequently delivered in vacuum systems are decisive in this case.

Why is MMA necessary?

Bone cements are cold-curing resins that are based on a powder-liquid combination. In processing the powder consisting of polymethyl methacrylate (PMMA) is mixed to a dough with monomer methyl methacrylate (1). To largely avoid air inclusions, one today frequently uses systems in which the cement components are mixed under vacuum in a closed cartridge.

A small part of the liquid MMA can be converted during the application into the gaseous form and thus be released into the room air.

What happens with MMA in the body?

MMA (Fig. 1) is a colourless, easily flammable liquid that is used, for instance, in the manufacture of acrylic glass. The carbon-carbon double bond of the substance allows the polymerisation of MMA molecules to PMMA.

During the mixing and curing of the bone cement dough, small amounts of non-bonded monomer are released from the cement surface (2, 3). The share of the non-polymerised monomer remaining in the bone cement is around 2–6 % directly after application and curing and then drops to less than 0.5 % within 2–3 weeks.

MMA is rapidly absorbed in the blood through lungs, gastrointestinal tract and skin (5). It is then just a rapidly breathed out through the lungs, to a lesser extent secreted through the urine and faeces or oxidatively metabolised through the citrate cycle to carbon dioxide (CO_2) (4, 6–9). According to the present state of knowledge methacrylic acid-CoA arises in this case as intermediate product. This at the same time represents a product of decomposition of the natural amino acid valine (Fig. 2).

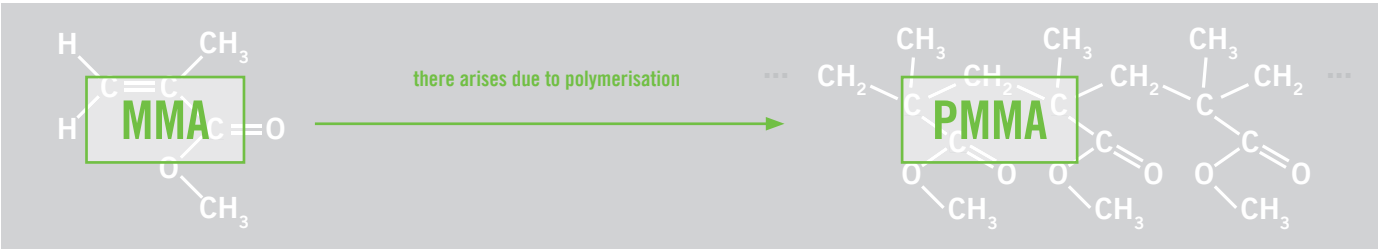

Fig. 1 Monomer methyl methacrylate (MMA) polymerised to polymethyl methacrylate (PMMA).

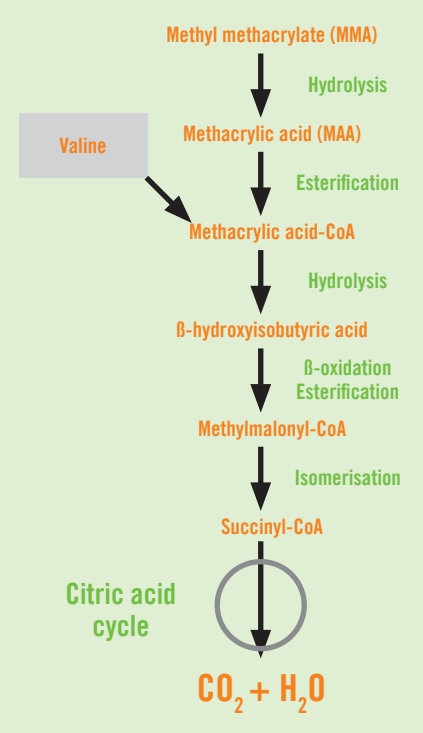

Fig. 2. Metabolism of MMA (4)

Can MMA have effects?

In high concentrations (cf. workplace limits) MMA can irritate the eyes and the mucosa of the respiratory system as well as the skin. Sensitization by skin contact with development of contact dermatitis is possible (10–14). The metabolite methacrylic acid is considered to be the actual irritating substance. Symptoms such as shortness of breath and coughing have been reported in connection with the inhalation of high concentrations of MMA (15–17).

A carcinogenic potential could not be proven (18). In a study with workers in acrylic glass manufacturing who were exposed on average for a duration of 7.6 years daily for 8 hours to concentrations of 13.2 ppm and partially up to 100 ppm MMA, there was no evidence of an increased risk of death (19).

Acute health disorders are not expected in short exposure and low MMA concentrations. MMA has a pronounced odour and can readily be perceived at room air concentrations of 0.2 ppm or more.

How can safety at the workplace be guaranteed?

The concentration of a substance in the air at the workplace at which generally the health of the employees is not impaired is designated as workplace limit (previously: maximum workplace concentration, MAC) (29). The workplace limit of MMA in Germany and other European countries such as Great Britain and Sweden lies at 210 mg/m³ or 50 ml/m³ (Note: 1 ml/m³ = 1 ppm) at an exposure of 8 hours per day and maximum 40 hours per week (21). The permissible value may be exceed by two-fold shortly for 5 minutes and then lies at 100 ppm (21). Injury to embryos does not have to be feared in compliance with the workplace limits (21).

How high can the MMA concentration be in the operating room?

The MMA concentrations released in the course of mixing bone cement lie far below the workplace limits from which an impairment of the health of the operating room staff can be expected. According to the results of a study by Schlegel et al., in which a typical situation in the operating room when mixing 40 g bone cement was simulated, the maximum MMA concentrations in the respiratory air for manual mixing over a period of 3 minutes lie at only approx. 8 ppm (2).

In most vacuum mixing systems the MMA concentration lies even at less than 4 ppm and thus only half as high in comparison with manual mixing (22) (Fig. 3). The MMA concentration when using proven vacuum mixing systems is accordingly very low. However, when bone cement is applied, release of not yet bonded monomers cannot be completely excluded.

Are there health consequence?

- Acute health disorders are not to be expected at low concentrations and short exposure.
- Long-term consequences of exposure to low MMA concentrations have not been proven.
- MMA can irritate the eyes, respiratory organs and skin only in high concentrations.
- Injury to embryos does not have to be feared in compliance with the workplace limits (21).

What does "ppm" mean?

The expression "parts per million" is shortened to "ppm".

It stands for the number 10 – 6 and is used in science for the millionth part, just as percent (%) stands for the hundredth part.

In the case of MMA 1 ppm corresponds to a volume of 1 millilitre per 1000 litres (= 1 cubic metre).

What can physicians and operating room personnel do?

- Preferably use vacuum mixing.
- Use mixing systems that generate a sufficiently large vacuum < 150 hPa (23).
- Comply with the working distance to the mixing system or bowl in manual mixing.
- Observe customary protective and hygienic measures.
- Modern clean room system in the operating room.

How much MMA is released depends not only on the mixing method used. In different phases of vacuum mixing MMA is released in concentrations of different levels. In the mixing phase the concentrations in the respiratory air are lower than in the filling phase, but it cannot be prevented that a part of the liquid monomer is converted further into gaseous form and thus escapes additionally into the room air (23). However, the MMA concentrations lie in all phases clearly below the workplace limits (Fig. 4).

What possibilities are there of avoiding contact with MMA in the operating room?

In some non-medical "indications" for MMA, e.g. coating the floor with MMA resins, it must be assumed basically that the air limits of MMA are exceeded. Workers are required here to adopt corresponding protective measures. In the operating room on the other hand, independently of the nature of the mixing method used, a health risk due to MMA vapours can be excluded on the basis of the available data. Further reasons contribute to this apart from clearly not reaching the workplace limits:

- General protection and hygienic measures in the operating room.
- Operating room gowns and gloves prevent MMA touching the skin, so that sensitisation is avoided.
- Modern ventilation system in the operating room.

Breathing protection is not required because of the low MMA concentrations in the use customary today of laminar airflow systems (24).

The activated carbon filters frequently also delivered in vacuum systems absorb MMA and thus reduce the release of the monomer into the room air. This filter effect plays a role above all during the generation of the vacuum and the mixing phase. Vacuum systems differ in their filter effect and according to the type of filter can absorb up to 55 % of the evaporated monomer (23). However, if this activated carbon filter is missing, then the monomer otherwise absorbed during evacuation is led back into the operating room through the vacuum pump.

DISCUSSION:

What importance does vacuum mixing have?

The use of vacuum mixing concentrates on

- Reducing the formation of micropores in the cement and thus improved fatigue strength of the cement
- Indication-optimised application possible
- Standardised initial mixing
- Reduction of the MMA concentration in the operating room compared with manual mixing

The choice of the mixing system should not dominate the choice of the cement, but the clinical result should stand in the centre. The use of vacuum mixing systems can improve the service lives of cemented dentures according to the arthroplasty registers. But cements not mixed under vacuum can also achieve good results.

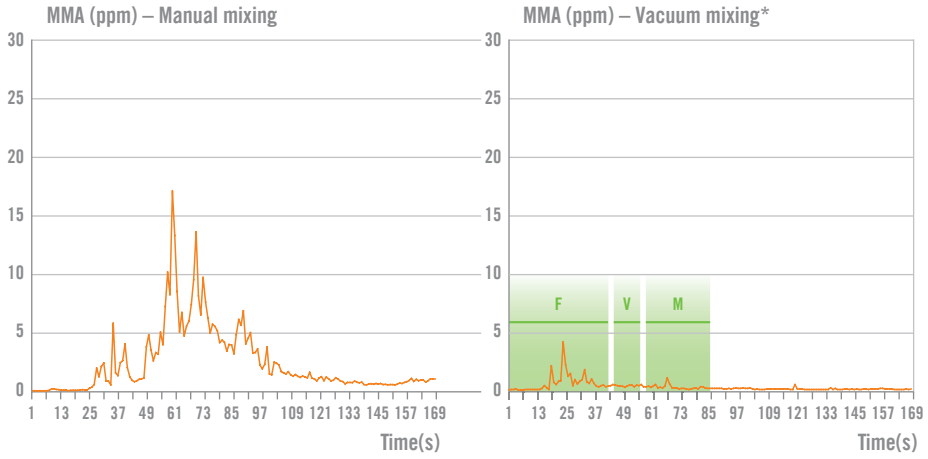

Fig. 3. Mean MMA concentrations from 10 mixings, calculated for each single second of the mixing procedure, modified according to (22). F = Filling phase, V = Applying the vacuum, M = Mixing phase (in vacuum mixing method).

* Vacuum mixing with the vacuum mixing system EASYMIX®

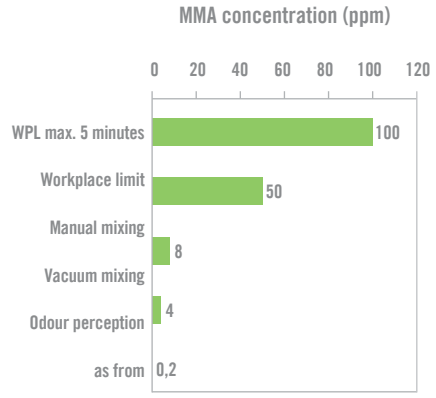

Fig. 4. Overview of workplace limits (WPL) for MMA in ppm in comparison with the average MMA concentrations reached in manual mixing and vacuum mixing (21, 22) as well as limit of odour perception.

Literature

1. Kühn KD. Bone Cements – up-to-date comparison of physical and chemical properties of commercial materials. Berlin Heidelberg New York, 2000.
2. Debrunner HU. Untersuchungen zur Porosität von Knochenzementen. Arch Orthop Unfallchir 1976; 86: 261–278.
3. Engesaeter LB, Espehaug B, Lie SA, Furnes O, Havelin LI. Does cement increase the risk of infection in primary total hip arthroplasty? Revision rates in 56,275 cemented and uncemented primary THAs followed for 0–16 years in the Norwegian Arthroplasty Register. Acta Orthop 2006; 77: 351–358.
4. Crout DH, Lloyd EJ, Singh J. Metabolism of methyl methacrylate: evidence for metabolism by the valine pathway of catabolism in rat and in man. Xenobiotica 1982; 12: 821–829.
5. Eggert A, Huland H, Ruhnke J, Seidel H. [Penetration of methylmethacrylate-monomer in blood circulation following hip joint prosthesis surgery in man]. Chirurg 1974; 45: 236–242.
6. Eggert A, Eckert W, Seidel H. Zur Ausscheidung von Knochenzementmonomer in der Atemluft. Arch Orthop Trauma Surg 1980; 97: 221–224.
7. Raje RR, Ahmad S, Weisbroth SH. Methylmethacrylate: tissue distribution and pulmonary damage in rats following acute inhalation. Res Commun Chem Pathol Pharmacol 1985; 50: 151–154.
8. Bratt H, Hathway DE. Fate of methyl methacrylate in rats. Br J Cancer 1977; 36: 114–119.
9. Wenzel H, Garbe A, Nowak H. Untersuchungen zur Pharmakokinetik von Monomethylmethacrylat. 1973; 1. Internationaler Kongress für Prothesentechnologie und funktionelle Rehabilitation.
10. Gift JS. Toxicological review of methyl methacrylate. In support of summary information on the integrated risk information system (IRIS): U.S. Environmental Protection Agency, 1998.
11. Daunderer M. Klinische Toxikologie. Loseblattausgabe 58. Ergänzungslieferung. Landsberg: ecomed, 1990.
12. Scolnick B, Collins J. Systemic reaction to methylmethacrylate in an operating room nurse. J Occup Med 1986; 28: 196–198.
13. Kassis V, Vedel P, Darre E. Contact dermatitis to methyl methacrylate. Contact Dermatitis 1984; 11: 26–28.
14. Marshall M, Guill A, Odom RB. Hearing aid dermatitis. Arch Dermatol 1978; 114: 1050–1051.
15. Lozewicz S, Davison AG, Hopkirk A, et al. Occupational asthma due to methyl methacrylate and cyanoacrylates. Thorax 1985; 40: 836–839.
16. Pickering CAC, Niven R, Simpson J. A study of occupational asthma at the IOI acrylics site at Darwen, Lancashire. ICI Acrylics, Darwen, Lancashire 1993.
17. Savonius B, Keskinen H, Tuppurainen M, Kanerva L. Occupational respiratory disease caused by acrylates. Clin Exp Allergy 1993; 23: 416–424.
18. Tomenson JA, Carpenter AV, Pemberton MA. Critical review of the epidemiology literature on the potential cancer risks of methyl methacrylate. Int Arch Occup Environ Health 2005; 78: 603–612.
19. Tomenson JA, Bonner SM, Edwards JC, Pemberton MA, Cummings TF, Paddle GM. Study of two cohorts of workers exposed to methyl methacrylate in acrylic sheet production. Occup Environ Med 2000; 57: 810–817.
20. Verordnung zum Schutz vor Gefahrstoffen (Gefahrstoffverordnung – GefStoffV). 2004.
21. Ausschuss für Gefahrstoffe (AGS), Bundesministerium für Arbeit und Soziales. Arbeitsplatzgrenzwerte. Technische Regeln für Gefahrstoffe. TRGS 900. 2006.
22. Schlegel UJ, Sturm M, Ewerbeck V, Breusch SJ. Efficacy of vacuum bone cement mixing systems in reducing methylmethacrylate fume exposure: comparison of 7 different mixing devices and handmixing. Acta Orthop Scand 2004; 75: 559–566.
23. Horas U, Seidel P, Heiss C, Kilian O, Dingeldein E, Schnettler R. Vakuummischsysteme zur Knochenzementfertigstellung – Ein Vergleich unterschiedlicher Systeme. Z Orthop Ihre Grenzgeb 2002; 140: 603–610.
24. Heraeus Medical GmbH. Sicherheitsdatenblatt gemäß 91/155/EWG incl. 2001/58/EG.

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