



Methyl Methacrylate Levels in Orthopedic Surgery: Comparison of Two Conventional Vacuum Mixing Systems

Jasmin Jelecevic^{1*}, Stanislaw Maidanjud², Andreas Leithner³,
Kai Loewe³ and Klaus-Dieter Kuehn³

1.Department of Traumatology, Hospital Wels-Grieskirchen, Grieskirchner Straße 42, 4600 Wels, Austria

2.Department of Product Management, Heraeus Medical GmbH, Philipp-Reis-Str. 8-13, 61273 Wehrheim, Germany

3.Department of Orthopedic Surgery, Medical University of Graz, Auenbruggerplatz 2, 8036 Graz, Austria

*Author to whom correspondence should be addressed. Tel: +43-676-711-9953; E-mail: jasmin.jelecevic@gmail.com

Submitted 5 December 2012; revised 12 November 2013; revised version accepted 20 December 2013.

ABSTRACT

Poly-methyl methacrylate bone cements contain methyl methacrylate (MMA), which is known for its sensitizing and toxic properties. Therefore, in most European countries and in the USA, guidelines or regulations exist for occupational exposures. The use of vacuum mixing systems can significantly reduce airborne MMA concentrations during bone setting. Our goal was to test two commonly used vacuum mixing systems (Palamix® and Optivac®) using Palacos® R bone cement for their effectiveness at preventing MMA vapor release in a series of standardized trials in a laboratory as well as in an operating theatre. MMA was quantified every second over a period of 3 min using a photoionization detector (MiniRAE® 3000) device positioned in the breathing area of the user. Significant differences in MMA mean vapor concentrations over 180 s were observed in the two experimental spaces, with the highest mean concentrations (7.61 and 7.98 ppm for Palamix® and Optivac®, respectively) observed in a laboratory with nine air changes per hour and the lowest average concentrations (1.06 and 1.12 ppm for Palamix® and Optivac®, respectively) in an operating theatre with laminar flow ventilation and 22 air changes per hour. No significant differences in overall MMA concentrations were found between the two vacuum mixing systems in either location. Though, differences were found between both systems during single mixing phases. Thus, typical handling of MMA in orthopedic procedures must be seen as not harmful as concentrations do not reach the short-term exposure limit of 100 ppm. Additionally, laminar airflow seems to have an influence on lowering MMA concentrations in operation theatres.

KEYWORDS: bone cement; mean exposure level; methyl methacrylate; poly-methyl methacrylate

INTRODUCTION

Methyl methacrylate (MMA) is widely used in production of acrylic glass, glues, and paints; in dentistry for dental casts and dental implants; and as the main

component of the liquids of poly-methyl methacrylate (PMMA) bone cements for the fixation of implants in joint replacement surgery. MMA is a colorless, clear, flammable liquid of intense odor. The concentration

of MMA in the immediate breathing zone can vary significantly in an operating theatre (Buchhorn *et al.*, 1992).

No persuasive evidence has been provided that exposure to MMA is carcinogenic to human beings (Tomenson *et al.*, 2005). Allergic reaction to the MMA may occur through direct contact of the MMA liquid with the skin, as well as through inhalation. In high concentrations, MMA is known to irritate the eyes and the respiratory system mucosa or to possibly cause contact dermatitis (Marshall *et al.*, 1978; Kassiss *et al.*, 1984; Scolnick and Collins, 1986; Gift, 1998). It has been reported that when inhaled in high concentration, MMA may cause symptoms such as shortness of breath or coughing (Lozewicz *et al.*, 1985; Savonius *et al.*, 1993).

Reports also exist of MMA diffusion from polymer and sensitization with dental prosthesis carrier, followed by mucosal inflammation (Bradford, 1948; Fisher, 1954). Isolated cases of sensitization caused by a surgeon's hand manipulating the PMMA bone cement have also been reported (Pegum and Medhurst, 1971; Fries *et al.*, 1975).

For protection of workers from chemical risks, the European Commission has listed indicative occupational exposure limit values (IOELVs) with MMA being one of the substances mentioned. IOELVs are defined in accordance with scientific data and 'set threshold levels of exposure below which, in general, no detrimental effects are expected for any given substance after short-term or daily exposure' (Official Journal of the European Union, 2009). According to IOELV for MMA, the time-weighted average (TWA) must not exceed 50 ppm per 8 h and must not exceed the short-term exposure limit (STEL) of 100 ppm per 15 min.

Several studies have shown that vacuum mixing systems can significantly reduce MMA vapor concentrations in the operating theatre compared to the traditional open bowl hand mixing (Bettencourt *et al.*, 2001; Schlegel *et al.*, 2004; Ungers *et al.*, 2007). However, the vacuum mixing system cartridges are never completely sealed as the bone cement components must be poured in and therefore some MMA vapor escapes during the preparation and mixing phases and during application.

The goal of our study was to examine the MMA vapor concentration reached when vacuum mixing of

bone cement. Two different settings with two different vacuum mixing systems were compared.

MATERIALS AND METHODS

We tested two vacuum mixing systems, the Palamix® (Heraeus Medical, Wehrheim, Germany) and Optivac® systems (Biomet, Berlin, Germany) using Palacos® R PMMA bone cement. Both vacuum mixing systems mainly consist of a cartridge, which is to be connected to a vacuum pump. Bone cement components are mixed then at low pressure. By forwarding the bottom, the mixed bone cement is applied through the nozzle, which is placed on top of the cartridge. Thereby, the bottom of Optivac® cartridge precollects the bone cement as it moves up to the top due to being released at the low pressure—the vacuum collection mechanism, whereas Palamix® has a conventional mechanical collection. Mixing was performed according to the manufacturers' instructions.

Each of the vacuum mixing systems was used five times in a laboratory and five times in an operating theatre. The experiments were done in a random order within each of the settings.

Laboratory testing

The total volume of the laboratory room was 150 m³ (*L*: 10 m; *W*: 5 m; *H*: 3 m). The laboratory was equipped with a standard nonlaminar flow ventilation system set to operate at nine air changes per hour. Temperature and relative humidity were noted in the beginning of every mixing cycle. The measured temperature ranged from 17.9 to 22.0°C, with an average of 19.9°C; relative humidity ranged from 63.0 to 68.3%, with an average of 64.6%. All necessary materials were placed on the working table (*L*: 2.5 m; *W*: 1 m; *H*: 0.9 m). The photoionization detector (PID) was positioned 50 cm above the working surface of the table and 140 cm above the floor to approximate the user's breathing zone. Thereby, it was guaranteed that all mixings took place 15–20 cm beneath the PID sensor tip.

Operating theatre testing

The operating theatre had a total volume of 135 m³ (dimensions *L*: 7.3 m; *W*: 6.15 m; *H*: 3 m). All mixing took place under the laminar airflow ventilating system. The air exchange rate was 22 times per hour. Temperature and relative humidity were noted at the

beginning of each mixing cycle. Temperature measured in the operating theatre was constant at 23°C and relative humidity ranged from 44.6 to 48.2%, with an average of 46.0%. All necessary materials were placed on the working table (*L*: 1.2 m; *W*: 0.7 m; *H*: 0.9 m). The PID was positioned in the same way as described above.

An experienced user of both tested vacuum mixing systems performed the mixing procedure for a total of ten times for each system.

MMA measurement was started with breakage of the MMA ampoule, thereupon the experiments were divided into three stages:

Stage 1: the cartridge was filled and sealed and vacuum was then allowed to build up (30 s).

Stage 2: the bone cement is then mixed.

With the Optivac® system, bone cement collection occurs under vacuum and the cartridge is then loaded into an application gun. With the Palamix® system, the cartridge is loaded into the application gun and the cement is collected mechanically (60 s).

Stage 3: the bone cement is evacuated onto the working plate (90 s). Total time for the process is 3 min (180 s).

Prior to each experiment, all materials containing bone cement were removed and the laboratory/operating theatre was ventilated for at least 15 min, until no residual airborne MMA was measurable with the PID.

For MMA measurements, a PID device MiniRAE® 3000 (Rae Systems, San Jose, CA, USA) was used with an extended range of 0–15 000 ppm and response time of 3 s (sampling pump with air flow rate of 0.5 l per minute). The energy of the detection lamp used in this study was 10.6 eV. For MMA detection, it was calibrated using isobutylene gas with a correction factor of 1.5.

Temperature and humidity were measured using a GFTH 95 and GTH 175/Pt (Greisinger Electronic, Regenstauf, Germany) digital hygrometer/thermometer. The thermometer had a measuring range of –199.9 to +199.9°C and measuring resolution of 0.1°C. The hygrometer had a measuring range of 10–95% relative humidity and a measuring resolution of 0.1%.

MMA evaporation occurs during both mixing and curing of the PMMA bone cement. MMA

concentrations in the air might differ with the amount expelled from the vacuum mixing system. To compare the two vacuum mixing systems against the residual amounts of bone cement, which remain in the cartridge, residual bone cement was measured by weighing all relevant system components before the filling stage and after the total evacuation of the bone cement. The residual bone cement weight was then computed simply by subtracting the weight of the empty system from the weight of the system after the mixing procedure.

Data were collected continuously at a rate of 1 s, over a period of 3 min. For each recording period, we manually noted the starting time. Data were analyzed using Microsoft® Office Excel 2007 (Microsoft® Corporation, Redmond, WA, USA). We used the mean value and standard deviation to describe the collected data.

Mean concentrations were determined for every stage of each mixing cycle. Additionally, the mean level was calculated and graphically presented to show measured MMA concentrations over the whole measuring period for each system.

For statistical analysis, we used the IBM® SPSS® Statistics 20.0.0 (International Business Machines Corporation, Armonk, NY, USA). For the comparison of two systems, results were tested in a univariate analysis and *post hoc* tests were calculated. A *P* value of ≤0.05 was considered significant.

RESULTS

In the laboratory setting, the overall mean MMA vapor concentration for five complete mixing cycles was 7.61 ppm (SD 4.28) for the Palamix® system and 7.98 ppm (SD 3.39) when using Optivac®. Statistical data analysis showed no significant difference in overall mean concentrations generated by the two systems. See the results summarized in Table 1.

During Stage 1 (filling and vacuum buildup), the highest concentration peaks were 27.4 and 10.7 ppm for the Optivac® and Palamix® systems, respectively. During Stage 2 (mixing and collecting), Optivac® had its highest peak at 12.6 ppm, whereas MMA vapor concentration with Palamix® was not >3.1 ppm. At Stage 3 (loading of the cement gun and evacuating), each system produced multiple peaks in concentration. With Optivac®, the peaks were 12.6 ppm at 120 s and 18.2 ppm at 160 s and with Palamix®, the peak

concentrations occurred at 120 s (19.7 ppm) and 170 s (24.7 ppm). These values each are average across all five experiments performed with each system.

The timeline of mean MMA vapor concentration over all stages of the mixing procedure is shown in Fig. 1.

In the operating theatre testing, the total mean MMA vapor concentration for five mixing cycles over 3 min with Palamix® was 1.06 ppm (SD 0.36) and 1.12 ppm (SD 0.11) when using Optivac®. Statistical data analysis showed no significant difference in total concentration between the two systems. However, a significant difference between the highest peaks of the two systems ($P \leq 0.05$) was found in Stage 1. See the results summarized in Table 2.

During Stage 1 (filling and vacuum buildup), the highest concentration peaks were 1.86 and 0.8 ppm for Optivac® and Palamix®, respectively. In Stage 2 (mixing and collecting), Optivac® had its highest peak at 2.24 ppm, whereas MMA vapor concentration with Palamix® was not >1.57 ppm. During the last stage, for Optivac®, the peak was 1.61 ppm at 120 s and for Palamix®, there again were two peaks: 1.74 ppm at 140 s and 1.63 ppm at 160 s. These values each

are average across all five experiments performed with each system.

The mean MMA vapor concentration timeline over all stages of the mixing procedure is shown in Fig. 2 for both mixing systems. Notice that there is a difference in scale between Figs 1 and 2.

The values of mean total MMA exposure from both experiment settings for both vacuum mixing systems (Fig. 3) are summarized below. MMA concentrations reach much higher levels in the laboratory experiments than in experiments conducted in the operation theatre. During none of the experiments did MMA concentrations exceed the 15-min STEL of 100 ppm.

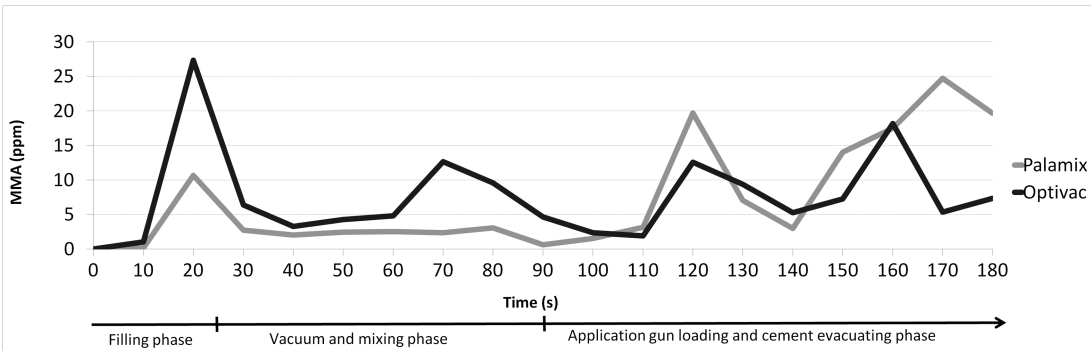
Mean residual bone cement quantity when using Palamix® was 9.4 g (SD 0.64) or 15.6% of the bone cement mixed, whereas the mean residual quantity was 16.9 g (SD 0.75) or 28.1% for the Optivac®. Statistical analysis indicates there is a significantly higher residual quantity of bone cement with the Optivac® system ($P \leq 0.05$).

DISCUSSION

Use of PMMA bone cements during vacuum mixing in orthopedic procedures using experimental

Table 1. Summary of MMA vapor concentrations in laboratory setting in ppm

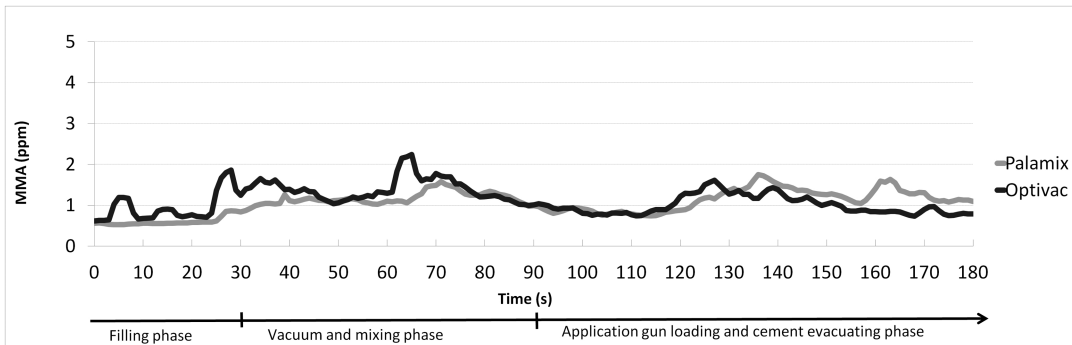
Vacuum mixing system	Palamix®	Optivac®
Mean total exposure (0–180 s)	7.61 (SD 4.28)	7.98 (SD 3.39)
Mean exposure, Stage 1 (0–30 s)	4.52 (SD 5.22)	11.59 (SD 12.18)
Mean exposure, Stage 2 (30–90 s)	2.18 (SD 1.73)	6.55 (SD 3.77)
Mean exposure, Stage 3 (90–180 s)	12.26 (SD 7.57)	7.73 (SD 4.08)



1 MMA mean concentration for both systems over a period of 3 min—laboratory with 9 air changes per hour (five experiments per mixing system).

Table 2. Summary of MMA vapor concentrations in operating theatre setting in ppm

Vacuum mixing system	Palamix®	Optivac®
Mean total exposure (0–180 s)	1.06 (SD 0.36)	1.12 (SD 0.11)
Mean exposure, Stage 1 (0–30 s)	0.60 (SD 0.11)	0.96 (SD 0.31)
Mean exposure, Stage 2 (30–90 s)	1.17 (SD 0.30)	1.38 (SD 0.45)
Mean exposure, Stage 3 (90–180 s)	1.14 (SD 0.51)	1.00 (SD 0.25)



2 MMA mean concentration for both systems over a period of 3 min—operating theater with laminar flow at 22 air changes per hour (five experiments per mixing system).

conditions similar to those encountered in workplace settings resulted in MMA vapor concentrations well below the IOELVs (TWA and STEL). However, over 3 min, both of the tested systems produced measurable amounts of MMA, ranging at an average from 7.61 to 7.98 ppm in the laboratory and from 1.06 to 1.12 ppm in an operating theater for Palamix® and Optivac®, respectively.

We have identified three main causes for MMA vapor leakage into the environment while using vacuum mixing systems for PMMA bone cements in orthopedic procedures: (i) filling the cartridge with monomer liquid; (ii) mixing the bone cement, which allows small amounts of MMA vapor to escape through narrow openings; and (iii) evacuation of bone cement out of the mixing cartridge and handling as the polymerization reaction progresses. The latter is not dependent on the vacuum mixing system.

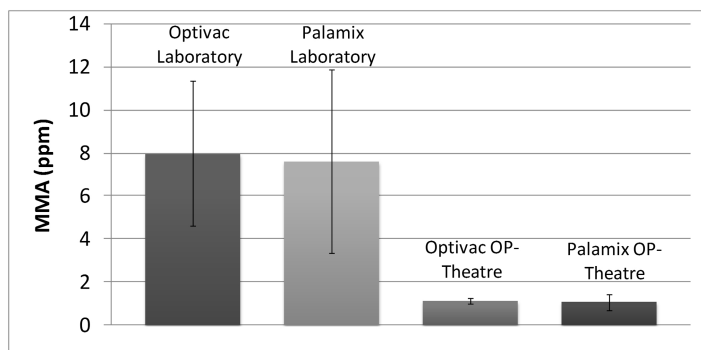
It has been suggested that vacuum mixing systems using mechanical collection of bone cement contribute to higher MMA evaporation (Wang and Breusch, 2005). Our data do not support this, as MMA vapor concentrations during the mixing and bone cement-collecting phase were significantly lower for the

Palamix® vacuum mixing system with mechanical collection compared to the Optivac®, which is equipped with a vacuum collection mechanism.

Laboratory testing

The two vacuum mixing systems showed no significant difference in MMA vapor release across the full measuring period in the laboratory environment.

We observed peaks during the filling and vacuum stage when using both systems. To explain the occurrence of occasional peaks during the filling and vacuum stage, we suspect that the cause is most probably some random movement of the user of which we were not aware; however, based on our results, we hypothesize that such random movement is less likely to produce higher peaks when using Palamix®. As part of the Palamix® vacuum mixing system, there is a filling funnel with two sections, for the bone cement powder pouch and the MMA liquid ampoule. The open ampoule empties automatically upon being placed there. Thus, no additional manipulation is needed. This results in reduced chance of accidentally created peaks of MMA vapor concentrations during the filling process.



3 Mean total MMA concentrations over 3 min with SD measured with the PID.

Peaks were also measured after evacuation of the bone cement. As this stage is not system dependent, it is difficult to clarify if the peaks correlate directly with vacuum mixing systems. However, we hypothesize that it is due to the significantly larger quantity of the bone cement that is evacuated out of the Palamix® vacuum mixing system. On average, the Palamix® system emits 6.2 g (~10%) more of the total mixed bone cement than the Optivac® system. We were not able to exclude other possible causes for this, such as movement of the user or the staff or other environmental factors.

Operating theatre testing

Operating theatre results show much lower concentrations of MMA in the breathing area of the user than in the laboratory. This was true for both vacuum mixing systems and all stages of their use.

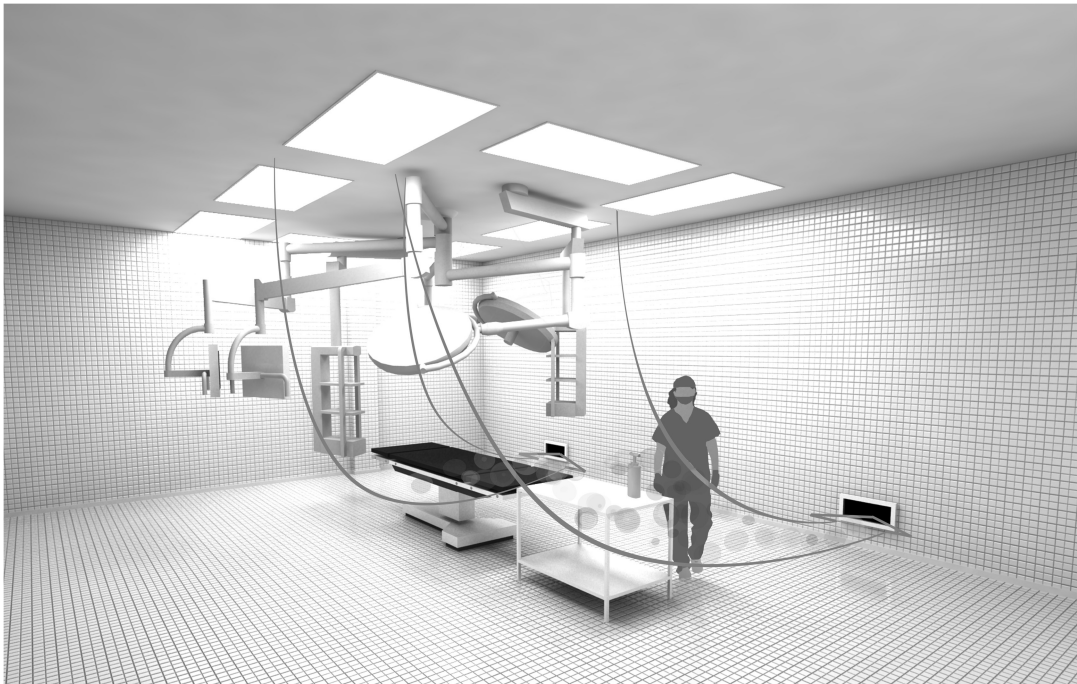
We hypothesize that the laminar airflow ventilating systems with higher air exchange rates typically used in operating theatres are likely to contribute to lower levels of MMA. While average temperature or relative humidity differed slightly between the two experimental settings, it is unlikely that these would account for the significant differences in airborne concentrations.

The reason might be that air exhaustion is normally placed at the bottom of operating theatre walls, which is part of laminar airflow ventilation systems. Thus, a certain airflow pathway occurs. Handling PMMA bone cements inside this air pathway might result in sensing higher MMA vapor concentrations (Fig. 4). Therefore, we assume that in the operating theatre, the mixing system–operating nurse should be placed outside the airflow pathway so MMA vapors can be

exhausted prior to being sensed by the user (Fig. 5). The position of the exhaustion as well as the air exchange rate can vary between operating theatres, causing variations in MMA concentration as well. It is therefore important for the user to familiarize himself or herself with the airflow patterns and take position in described manner. As a result, similar MMA concentration to the ones we measured can be expected.

During operating theatre trials over the whole measuring period, no significant differences were found between the Palamix® and Optivac® vacuum mixing systems in respect to the mean MMA vapor concentration in the breathing area of the user. This correlates with the results from the laboratory setting as for comparison of the two systems.

In the third stage of the mixing procedure, which involved evacuation of the bone cement out of the vacuum mixing cartridge onto a working plate, there was no significant difference in MMA concentrations between the systems. Our MMA concentration values measured with Optivac® in the operating theatre correlate with Schlegel *et al.* (2004), where it was tested for MMA fumes using two detection methods (GC and PID); however, we were not able to confirm the results of another study of Schlegel *et al.* (2010) who tested also Palamix®. In that study, Palamix® averaged 7.4 ppm (SD 2.74) under similar positioning of the measuring device against the mixing as in our operating theatre trials. We obtained a comparable result of 7.61 ppm (SD 4.28) in our laboratory trials, while the MMA concentration in our operating theatre trials was significantly lower at 1.06 ppm (SD 0.36). However, this may be referred to the difference in air exchange rates and/or



4 Mixing while staying within the air pathway.



5 Mixing while staying out of the air pathway.

humidity levels between our settings and those from Schlegel *et al.* (2010).

Our results disagree with those of Wang and Breusch (2005) who found that collection under vacuum leads to lower MMA emission into the environment when compared to vacuum mixing systems with mechanical collection. Again, this might refer to the difference in our study settings.

It should be stated that this study was performed in a controlled environment. There are several major factors—such as ventilation rates, room volume, and larger quantities of PMMA bone cement used—that can influence the MMA concentration in the clinical working environment, thus eventually leading to higher exposure of the personnel. Therefore, it is important to implement sampling methods within the working environment, to assess personnel exposures, and consequently provide protection steps to keep personnel exposures below the 15-min STEL value of 100 ppm.

Our results suggest that under similar environmental conditions, MMA concentrations during orthopedic procedures are unlikely to exceed the IOELV 8-h TWA of 50 ppm.

FUNDING

Heraeus Medical GmbH; Medical University of Graz.

ACKNOWLEDGEMENT

S.M. and K.D.K. are both employees of Heraeus Medical, the company which produces one of the products that have been tested, the Palamix mixing system.

REFERENCES

- Bettencourt A, Calado A, Amaral J *et al.* (2001) The influence of vacuum mixing on methylmethacrylate liberation from acrylic cement powder. *Int J Pharm*; **219**: 89–93.
- Bradford EW. (1948) Case of allergy to methylmethacrylate. *Br Dent J*; **84**: 195.
- Buchhorn GH, Streicher RM, Willert HG. (1992) Exposure of surgical/orthopedic operating room personnel to monomer vapors during the use of bone cements—review of the literature and report of experiences. *Biomed Tech (Berl)*; **37**: 293–302.
- Fisher AA. (1954) Allergic sensitization of the skin and oral mucosa to acrylic denture materials. *J Am Med Assoc*; **156**: 238–42.
- Fries IB, Fisher AA, Salvati EA. (1975) Contact dermatitis in surgeons from methylmethacrylate bone cement. *J Bone Joint Surg Am*; **57**: 547–9.
- Gift JS. (1998) *Toxicological review of methyl methacrylate (CAS No. 80-62-6) in support of summary information on the Integrated Risk Information System (IRIS)*. Washington, D.C., U.S. Environmental Protection Agency. Available at <http://www.epa.gov/ncea/iris/toxreviews/1000tr.pdf>. Accessed 1 October 2012.
- Kassis V, Vedel P, Darre E. (1984) Contact dermatitis to methyl methacrylate. *Contact Dermatitis*; **11**: 26–8.
- Lozewicz S, Davison AG, Hopkirk A *et al.* (1985) Occupational asthma due to methyl methacrylate and cyanoacrylates. *Thorax*; **40**: 836–9.
- Marshall M, Guill A, Odom RB. (1978) Hearing aid dermatitis. *Arch Dermatol*; **114**: 1050–1.
- Official Journal of the European Union. (2009) L338: Commission Directive 2009/161/EU of 17 December 2009 establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Commission Directive 2000/39/EC. pp. 87–9. ISSN 1725–2555.
- Pegum JS, Medhurst FA. (1971) Contact dermatitis from penetration of rubber gloves by acrylic monomer. *Br Med J*; **2**: 141–3.
- Savonius B, Keskinen H, Tuppurainen M *et al.* (1993) Occupational respiratory disease caused by acrylates. *Clin Exp Allergy*; **23**: 416–24.
- Schlegel UJ, Sturm M, Ewerbeck V *et al.* (2004) Efficacy of vacuum bone cement mixing systems in reducing methylmethacrylate fume exposure: comparison of 7 different mixing devices and handmixing. *Acta Orthop Scand*; **75**: 559–66.
- Schlegel UJ, Sturm M, Eysel P *et al.* (2010) Pre-packed vacuum bone cement mixing systems. A further step in reducing methylmethacrylate exposure in surgery. *Ann Occup Hyg*; **54**: 955–61.
- Scolnick B, Collins J. (1986) Systemic reaction to methylmethacrylate in an operating room nurse. *J Occup Med*; **28**: 196–8.
- Tomenson JA, Carpenter AV, Pemberton MA. (2005) Critical review of the epidemiology literature on the potential cancer risks of methyl methacrylate. *Int Arch Occup Environ Health*; **78**: 603–12.
- Ungers LJ, Vendrely TG, Barnes CL. (2007) Control of methyl methacrylate during the preparation of orthopedic bone cements. *J Occup Environ Hyg*; **4**: 272–80.
- Wang J, Breusch SJ. (2005) Choice of mixing system. In Breusch SJ, Malchau H, editors. *The well-cemented total hip arthroplasty. Theory and practice*. Berlin, Germany: Springer. pp. 113–8. ISBN 978 3 540 28924 1.