Pre-Packed Vacuum Bone Cement Mixing Systems. A Further Step in Reducing Methylmethacrylate Exposure in Surgery

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Objectives: Polymethylmethacrylate bone cements are widely used in orthopaedic and trauma surgery as well as in dentistry. The toxic side effects of inhaled methylmethacrylate (MMA) fumes generated during mixing have been well studied. Vacuum cement mixing systems have been shown to reduce the risk of airborne MMA significantly compared to handmixing. In an effort to further reduce MMA exposure, the latest generation of mixing devices are pre-packed with the ingredients and thus allow preparation in nearly closed circuits. Until now, there has been no study proofing the efficacy of those systems in protecting theatre staff from MMA vapours.

Methods: A pre-packed vacuum mixing system (Optipac®) was compared with two standard systems (Palamix® and Easymix®) regarding MMA emission. The latter systems require loading with the bone cement compounds prior to mixing. Following a standardized procedure, 10 mixes were performed with each system and the emission of MMA vapours in the breathing zone was recorded using photoionization detection over a period of 3 min.

Results: The mean MMA exposure was reduced when using the pre-packed system compared to the devices that require filling with the components. The highest emission peaks were recorded during the mixing and preparation steps in all systems.

Conclusions: Modern pre-packed vacuum mixing systems further help to reduce the occupational hazards created by bone cement preparation. However, MMA fumes can still be detected using this technique. Although this is an important step in reducing MMA exposure in the operating theatre, further technical effort has to be taken to eliminate the continuous leakage of monomer from the devices while mixing and to minimize necessary manipulation for final delivery.

Keywords: bone cement; methylmethacrylate; MMA; photoionization detection; pre-packed; surgery; vacuum mixing

INTRODUCTION

Methylmethacrylate (MMA) monomeric fumes, which are emitted during preparation of polymethylmethacrylate bone cement have been shown to have toxic side effects ranging from allergic reactions (Betts et al., 2006; Liljelind et al., 2009) to neurological disorders (Christiansen et al., 1986; Sadoh et al., 1999). Although there is no evidence for potential carcinogenicity of the substance, all efforts should be made to reduce the exposure towards MMA
fumes during mixing in the operating theatre (Tomenson et al., 2005). Vacuum mixing has been shown to improve tensile strength and fatigue life of bone cement, which is essential for implant fixation (Lidgren et al., 1984, 1987; Wixson et al., 1987; Davies and Harris 1990; Geiger et al., 2001; Mau et al., 2004). Hence, the method became widely accepted as a part of modern cementing technique in orthopaedic surgery: In a national survey in the UK representing 587 surgeons, 94% stated that they use vacuum mixing systems for bone cement preparation (Nedungayil et al., 2006). Besides increasing cement quality, vacuum bone cement mixing systems have been shown to reduce MMA fume exposure significantly when directly compared to handmixing in an open bowl, as we were able to demonstrate in a previous study (Schlegel et al., 2004). This finding was also confirmed by other authors (Bettencourt et al., 2001; Ungers et al., 2007). Especially, the filling of the system with the compounds and the mixing process itself has shown to be critical working steps, leading to high MMA emission (Schlegel et al., 2004).

In a further effort to reduce the emission of MMA vapours, the latest generation of vacuum mixing systems feature pre-packed, all-in-one designs in a nearly closed circuit. Theoretically, exposure towards MMA fumes should be reduced to a minimum when using these novel systems. However, no studies have yet been carried out to evaluate the effectiveness of this technical modification. We therefore compared the MMA concentration in the breathing zone of two commercially available vacuum mixing systems to a pre-packed closed system. The measurements were carried out using photoionization detection (PID) as single recording method (Schlegel et al., 2009).

METHODS

Mixing systems

The Optipac® system. (Biomet, Berlin, Germany) is a novel bone cement vacuum mixing device, in which both monomer fluid and polymer powder are pre-packed in an enclosed system (Fig. 1). To begin with, the upper lid of the system has to be replaced by the mixing lid with the stirring paddle. After this step, there is no need to open the device again. The powder monomer is already pre-filled within the mixing cartridge. The liquid monomer component is contained in an aluminium pouch, which is already connected to the system, so that it can be injected/sucked in during the mixing process under vacuum. After the mixing procedure, the bottom lid is released and the collection of the cement under vacuum is completed. In the last step, the mixing rod has to be broken off and the corresponding nozzle can be attached to the mixing cartridge, ready for cement delivery. Transfer into the application gun is the last working step.

Easymix®. (Zimmer, Freiburg, Germany) is an established vacuum mixing device that requires filling with the bone cement compounds as the first working step (Fig. 2). After this, a mixing lid with the integrated mixing rod is applied to close the system. Similarly, the rod can be broken off after mixing and the plunger is pushed up mechanically. A cement nozzle then has to be secured to the bottom of the cylinder before transfer into the application gun.

Palamix®. (Heraeus Medical, Wertheim, Germany) also has to be filled with the liquid and powder components (Fig. 3). A special lid with the mixing paddle is applied to close the cylinder. After mixing under vacuum, the inner part of the mixing staff has to be pulled out and the remaining tube now serves as the application nozzle. The plunger is pushed up mechanically and the cylinder is ready for transfer into the gun.

Bone cement

For all systems and mixing procedures, identical cement was used. We used 40 g of Refobacin® Bone...
Cement R (Biomet), which was stored at ambient temperature, for filling in the Palamix® and Easy-Mix® systems. The Optipac® system is already pre-packed with the identical amount and type of bone cement.

Mixing procedure

The first author performed 10 mixes with each of the studied vacuum mixing systems. Devices for repeats were randomly selected from the three available systems to avoid systematic errors. The measurements were started before any of the cement components were opened. Preparation was done according to the instructions of the manufacturer. The required time for every working step was standardized and measured to minimize interference. The following times have been defined: filling of the mixing systems (30 s), initializing the vacuum pump (10 s), mixing (30 s), and transfer into the application gun. In the next step, the plunger of the gun was pressed until bone cement was visible at the tip of the nozzle. For the remaining time of the reading, the gun was laid on the table with the tip pointing at the place where the mixing system was mounted before. A purpose built vacuum pump creating a vacuum of 0.5 bar (Biomet) was attached to all systems in all cases. All materials and remnants of mixed bone cement were removed from the theatre right after the measurement to eliminate residual MMA in the air. A 15-min interval between measurements was used to eliminate air contamination prior to the next experiment.

Set-up for fume concentration measurements

We performed the measurements in a standard operating theatre with a total volume of 140 m³ (2.7 m high × 6.3 m wide × 8.3 m long). Laminar airflow was present throughout the measurements. Incoming air volume was 3750 m³ h⁻¹ and exhaust air was 3360 m³ h⁻¹, leading to a total exchange rate of 26 times per h. We recorded air humidity and temperature in the theatre every 2 h: mean humidity was 17.2% (range 16.6–18.4) and the average temperature was 21.6°C (range 20.1–21.8). Detection was carried out using a hand-held PID with a suction rate of 0.5 l min⁻¹ (MiniRae 3000®; RAE-Systems, San Jose, CA, USA). The lower detection limit was 0.1 ppm and the estimation was carried out after calibration to isobutylene (correction factor = 1.5). Background measurements with PID were carried out regularly after five mixing experiments to rule out background contamination.

The mixing systems were mounted on an instrument table (80 cm high) next to the operating table.
On a second table, the PID was situated at a height of 140 cm, which corresponds to the breathing zone of the nurse during bone cement preparation. The horizontal distance of the detection tip from the upper opening of the systems was 15 cm.

**Statistical analysis**

Continuous data are described by mean and standard deviation (SD). Mean concentrations were determined for every measurement over a period of 3 min. Additionally, mean MMA exposure was calculated for every second of the preparation process and plotted for the particular system. To compare the MMA exposure (ppm) among systems, the results were tested in a univariate analysis and post hoc tests (Tukey) were calculated. A $P$-value $\leq 0.05$ was considered significant. Data analysis was performed with Graph Pad Prism 5 for OS X (GraphPad Software, La Jolla, CA, USA).

**RESULTS**

The mean exposure to MMA for 10 mixes was 2.7 (SD 1.56) ppm for the Optipac®, 3.5 (SD 1.44) ppm for the Easymix®, and 7.4 (SD 2.74) ppm for the Palamix® system, as visualized in a boxplot in Fig. 4. The statistical analysis showed that the concentrations differences were significant between systems except for Optipac® versus Easymix (Table 1). As the PID allows continuous data collection, we were able to plot mean MMA concentrations per second of 10 mixes for every mixing device. Apart from determining the mean time for each working step, this method also allows (bottom lines in Figs. 5–7) the identification of high exposure steps in the workflow.

For the Optipac® system, the highest emission peaks (7.6 and 11.9 ppm) were measured during the preparation for application, while there were none during the initial arrangement (Fig. 5). A concentration $<12.7$ ppm of MMA vapours was present throughout the process in the Easymix® system (Fig. 6). Highest exposure was found here during the filling, mixing, and preparation phase. The Palamix® system (Fig. 7) resulted in two high MMA concentration peaks (37.1 and 13.7 ppm) in the breathing zone during the mixing and the preparation step. Interestingly, working steps that are associated with the final preparation of the cylinder as breaking the mixing rod or attaching of the delivery nozzle are also phases that are associated with high emission peaks. Apparently, any handling of the cylinder creates MMA vapours that can easily ascend to the breathing zone by the ongoing manipulation. Overall, the retrieved analysis indicates that pre-packed vacuum mixing systems can further reduce the MMA exposure, when compared to standard mixing devices.

**DISCUSSION**

As we already demonstrated in a preceding study, MMA fumes evaporate continuously from the mixing systems, although the procedure is performed under vacuum (Schlegel et al., 2004). This finding is not surprising in standard mixing systems as the filling with the compounds already leads to first emission peaks. But even in the pre-packed Optipac® system, we could detect MMA vapours during mixing and preparation. This phenomenon is due to the fact that a mixing device cannot be perfectly sealed as the upper lid of the systems has to be combined with the stirring staff. The minimal gap between mixing paddle and upper lid is a point of minor resistance so that forced mixing action results in high loss of monomer from inside the system. The Palamix® system resulted in a high overall exposure during mixing and preparation. When compared to the two other systems, the difference was significant. This is probably due to the combined mixing rod in the upper lid, which also serves as an application nozzle later in the workflow. When manipulating the paddle during mixing, more fumes escape here via the gap between lid and stirring bar than in other systems. The highest single MMA peak $\text{sec}^{-1}$ in this series was 105 ppm recorded right after the mixing step at 94 s with a Palamix® system. This could be observed very regularly, when removing the inner
part of the nozzle (stirring staff). The generated negative pressure evacuates contaminated air out of the device and brings it directly up to the breathing zone. The Easymix/C210 system showed continuous loss of monomer throughout the entire mixing procedure, but the overall exposure was surprisingly low, which is probably due to the fact that the nozzle is applied to the downside end of the cylinder and there is not too much manipulation necessary to get it ready.

The mean MMA exposure when using the Optipac/C210 system was lower when directly compared with the other devices. Although not significant, the mean MMA exposure was 0.9 ppm lower than in the Easymix/C210 system. Obviously, this is due to the lack of fume exposure during the filling step. Still, there is a certain amount of leakage in the pre-packed system especially during mixing and preparation as the mixing rod has to be broken away and a cap has to be taken off to secure the nozzle.

The lowest European exposure limits for MMA (50 ppm) are now mostly interpreted as time-weighted averages over an 8-h workday or as short-term exposure limits over a period of 15 min (100 ppm). Following those standards, all mixing systems would have been within the legal limits. Even repeated mixing or processing 120 mg of bone cement (required for revision in total hip arthroplasty) simultaneously with those systems would not exceed the cited range.

The PID measurement method used here relies on a corrected calibration on isobutylene and thus measures MMA in an indirect method. The validity of the direct-reading PID detector has been questioned (Ungers et al., 2007). However, this technique is very common in many technical applications and in our opinion does not affect the accuracy or outcome of the study. This is especially important as the technique was identical in all cases and hence allowed comparability of the presented data. Although PID tends to underestimate the actual concentration, we could demonstrate in our last series good correlation of gas chromatography (GC) and PID values as

Table 1. Comparison of mean MMA exposure for a 3-min mixing procedure in three mixing systems. One-way analysis of variance $F = 16$, $P < 0.0001$, $R^2 = 0.54$

<table>
<thead>
<tr>
<th>Tukey’s multiple comparison test</th>
<th>Mean difference</th>
<th>$q$</th>
<th>Significant? $P &lt; 0.05$?</th>
<th>95% confidence interval of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optipac versus EasyMix</td>
<td>-0.8780</td>
<td>1.388</td>
<td>No</td>
<td>-3.098 to 1.342</td>
</tr>
<tr>
<td>Optipac versus Palamix</td>
<td>-4.753</td>
<td>7.512</td>
<td>Yes</td>
<td>-6.973 to -2.533</td>
</tr>
<tr>
<td>EasyMix versus Palamix</td>
<td>-3.875</td>
<td>6.124</td>
<td>Yes</td>
<td>-6.095 to -1.655</td>
</tr>
</tbody>
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Fig. 5. Mean concentrations of MMA exposure for 10 mixes (PID) calculated for every second of a 3-min workflow using the Optipac® system (Vac, Vacuum; Fill, Filling).
we used both simultaneously for MMA detection (Schlegel et al., 2009). Furthermore, our data compares well with the results in the cited study, which used GC and flame ionization detection as measuring method in 50 cm above the mixing systems. The authors reported mean MMA fume concentrations of 5.2 and 1.9 ppm when using vacuum mixing systems over a period of 3 min (Ungers et al., 2007).

As the main focus of the study was a comparison of three different mixing systems, we decided to have all procedures done by one experienced operator. This allows easy comparability of the measurements, but it is well known that exposure varies among individual users. Hence, no conclusions can be drawn from this investigation regarding exposure variability among different operators. However, as the
workflows for any of the included devices are highly standardized, the variance should be minimal when following the manufacturers’ instructions. Set-up for measurements was designed to replicate the clinical situation. However, it should be considered that more than two individuals are usually present in the operating theatre. As each of them creates additional air turbulence, exposure concentrations might differ from the results found in our scenario.

As outlined at the beginning, vacuum mixing of bone cement is clinically beneficial (Geiger et al., 2001) and reduces exposure towards toxic MMA fumes at the same time. There is not sufficient proof for the carcinogenicity of MMA (Tomenson et al., 2005), but the direct contact with the cement can cause skin irritation as vinyl and latex gloves are permeable to the agent (Liljelind et al., 2009; Thomas and Padmanabhan 2009). Moreover, neurological and cardiovascular symptoms have been attributed to MMA (Sadoh et al., 1999; Leggat et al., 2009). Likewise, the effects of MMA inhalation on the respiratory tract have been studied in an animal model and disorders like pneumonia, hemorrhage, and epithelial hyperplasia have been reported (Aydin et al., 2002). Altogether, direct contact with MMA should generally be avoided and MMA vapours created during the preparation should be reduced to a minimum (Leggat et al., 2009).

CONCLUSIONS

Modern pre-packed vacuum mixing systems further help to reduce the occupational hazards created by bone cement preparation. However, MMA fumes can still be detected using this technique. Although an important step in reducing MMA exposure in the operating theatre, further technical effort has to be taken to eliminate the continuous leakage of monomer from the systems devices while mixing and to minimize necessary manipulation for final delivery.

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REFERENCES


