EFFECT ON OSTEOCLAST DIFFERENTIATION AND BONE RESORPTION OF BONE CEMENT CONTAINING TWO NEW RADIO-OPAQUE CONTRAST MEDIA

INTRODUCTION:

Aseptic loosening is the major long-term complication of total joint replacement. In the fibrous pseudomembrane surrounding a loose cemented implant there is a heavy foreign body macrophage and macrophage polykaryon response to polymethylmethacrylate (PMMA) and other implant biomaterial wear particles (1). Contrast agents, notably barium sulphate (BaSO₄) and zirconium dioxide (ZrO₂), are commonly added to the bone cement in order to confer radiopacity and thus aid in the radiological assessment of the implants. We have previously shown that macrophages responding to PMMA particles are able to differentiate into osteoclastic cells capable of resorbing bone (2). Moreover, we found that osteoclast formation is enhanced with PMMA particles containing the radio-opaque agent, BaSO₄ and ZrO₂ (3).

There is a need for alternative radiographic contrast media for use in orthopaedic surgery. The aim of the current study is to determine the effect on macrophage-osteoclast formation of two iodine-based X-ray contrast media [non-ionic dimer iodixanol (IDX) and non-ionic monomer iohexol (IHX)] which have been added to PMMA bone cement.

METHODS:

Four different samples of Palacos bone cement were prepared as instructed by the manufacturers. These were: (i) Palacos with no additives, (ii) Palacos containing 10% BaSO₄, (iii) Palacos containing 10% IDX and (iv) Palacos containing 10% IHX. Endotoxin-free particles of less than 5 µm (at concentrations of 5 µg/ml) were added to murine monocytes cultured on dentine slices and glass coverslips both in the presence and the absence of osteoblast-like UMR106 cells, 1,25 dihydroxyvitamin D₃ (1,25(OH)₂D₃) and dexamethasone. As a control group additional wells were prepared to which no particles were added. The cultures were maintained for 7 and 14 days, with the media containing 1,25(OH)₂D₃ and dexamethasone being replenished every 3 days. Osteoclast differentiation was assessed by the expression of the osteoclast-associated enzyme tartrate-resistant acid phosphatase (TRAP) on coverslips and lacunar resorption on dentine slices. The extent of lacunar resorption was measured using a computer image analysis system and expressed as percentage resorption pit area per total surface area on each dentine slice. The extent of lacunar resorption was measured using a computer image analysis system and expressed as percentage resorption pit area per total surface area on each dentine slice. The extent of lacunar resorption was measured using a computer image analysis system and expressed as percentage resorption pit area per total surface area on each dentine slice.

RESULTS:

Osteoclast differentiation, evidenced by the expression of TRAP and lacunar resorption, was noted in all co-cultures (Table 1). Relative to controls (i.e. those with no added particles and those containing pure Palacos bone cement with no additives), cultures containing cement particles with added BaSO₄ and 10% IDX showed a significant increase in osteoclast formation.

Table 1: Effect of various particles on macrophage-osteoclast differentiation

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean % Area Resorbed ± SEM</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>10.4 ± 1.8</td>
</tr>
<tr>
<td>Pure Palacos</td>
<td>12.8 ± 2.2</td>
</tr>
<tr>
<td>Palacos + BaSO₄</td>
<td>26.4 ± 3.1 *</td>
</tr>
<tr>
<td>Palacos + IDX</td>
<td>11.9 ± 1.6</td>
</tr>
<tr>
<td>Palacos + IHX</td>
<td>19.3 ± 2.5 *</td>
</tr>
</tbody>
</table>

Data expressed as mean % area resorbed per 3 dentine slice. * = p<0.01 comparing to control cultures (i.e. those with no added particles) and cultures containing Palacos particles with no additives.

In contrast, there was no significant difference between control cultures and cultures containing cement particles with 10% IHX. Moreover, cultures containing cement particles with added IHX showed considerably less osteoclast formation and bone resorption than cultures containing cement particles with added BaSO₄ or 10% IDX.

DISCUSSION:

These results indicate that radio-opaque agents in bone cement may contribute to the pathological bone resorption of aseptic loosening by enhancing macrophage-osteoclast differentiation. The present findings show that BaSO₄ and IDX-containing Palacos particles are likely to be associated with more osteolysis than particles of Palacos alone without additives. These findings indicate that measurement of the extent of macrophage-osteoclast differentiation in vitro should be used to assess the biocompatibility of radio-opaque agents in orthopaedic biomaterials.

ACKNOWLEDGEMENT:

This study was supported by the Wellcome Trust. Particle generation and size determination was performed by AEA Technology, Oxfordshire.

REFERENCES:


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