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Reduced inflammatory potential of Antioxidant Ultra High Molecular Weight Polyethylene containing Vitamin E May Lead to Improved Longevity in Total Joint Replacement Prostheses

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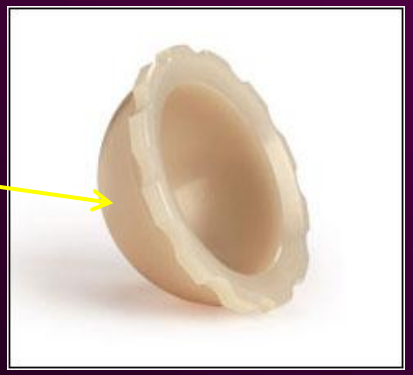
BACKGROUND

- Vitamin E (VE) has been added to UHMWPE acetabular cups and tibial trays to reduce oxidative damage to the polymer.

- Wear rates of VE containing UHMWPE shown to be reduced in the hip and the knee.

- Biological response to VE-containing UHMWPE particles in peripheral blood mononuclear cells (PBMNCs) - the production of osteolytic mediators, TNF-α, IL-β, IL-6 and IL-8 was significantly reduced in PBMNCs stimulated with UHMWPE + VE (PVE) particles compared to virgin UHMWPE particles.

VE acetabular cup



VE tibial tray

BACKGROUND

- The wear particles generated by UHMWPE with and without VE were not significantly different in size distribution.

- This study confirmed that VE modulated the response of LPS-stimulated PBMNCs to produce lower levels of TNF-α compared to control LPS-stimulated PBMNCs.

- True - VE was added additionally as a liquid to UHMWPE particle stimulated PBMNCs or when PBMNCs were exposed to wear particles generated from UHMWPE containing 1000ppm VE (PVE).

BACKGROUND

- The exact mechanism of how VE affects the release of inflammatory mediators from particle-stimulated macrophages is not yet understood.

- It is likely to involve the anti-inflammatory and/or antioxidant effects of VE.

- This reduced biological response to the wear particles containing VE may lead to increased longevity *in vivo* for total joint replacement components comprised of this material.

AIM

- The aim of this study was to investigate the anti-inflammatory effects of vitamin E in LPS and UHMWPE particle stimulated human peripheral blood mononuclear cells (PBMNCs).

- The effects of UHMWPE containing different concentrations of vitamin E (1000 ppm, the current clinical material; and experimental materials with 3000 ppm (used clinically in Japan), and 30,000 ppm VE) on the production of the inflammatory cytokine, TNF- α, IL-1β, IL-6, and IL-8 was investigated.

RESULTS

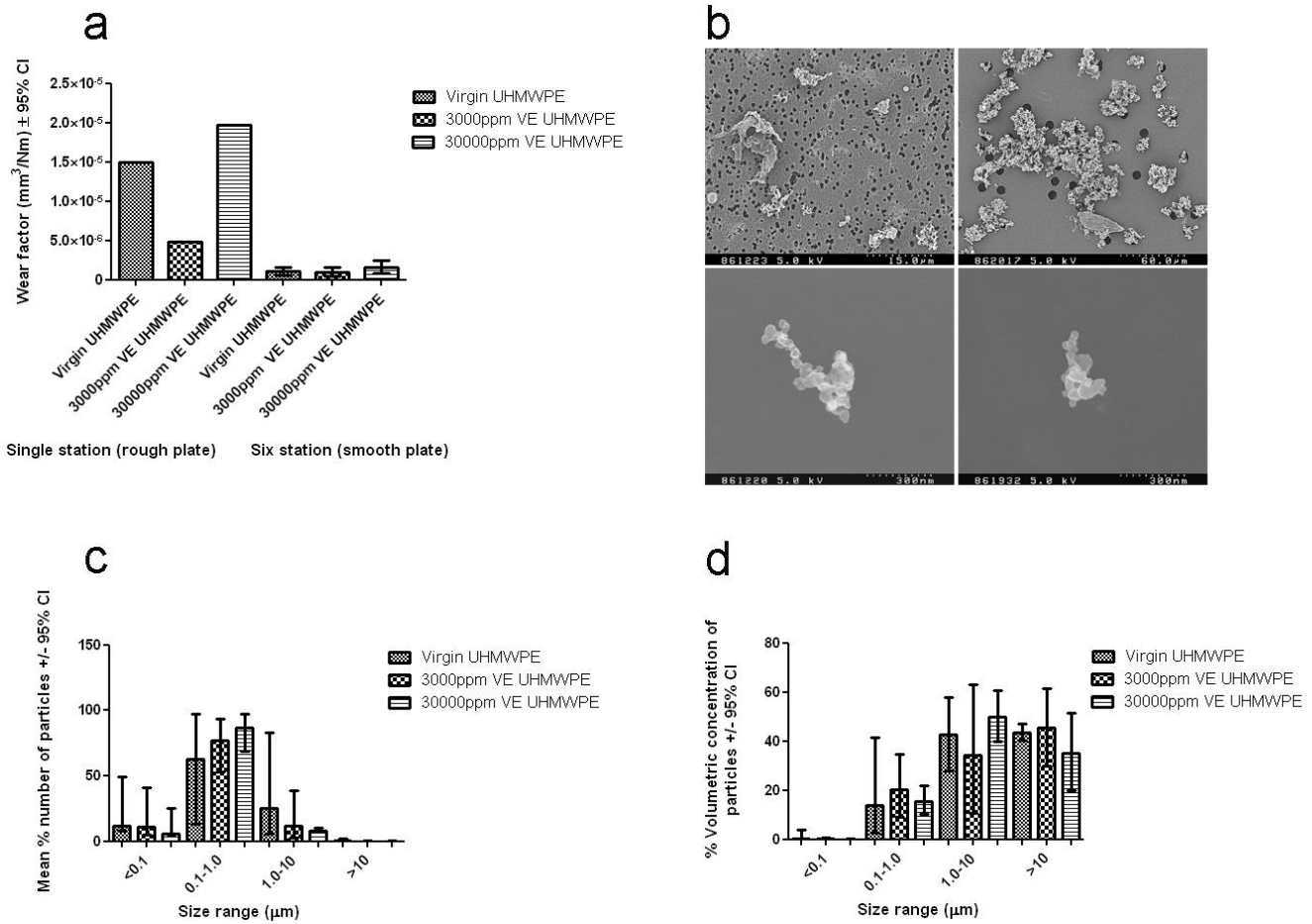


Figure 1. Wear and wear particle analysis of UHMWPE with and without Vitamin E.

RESULTS

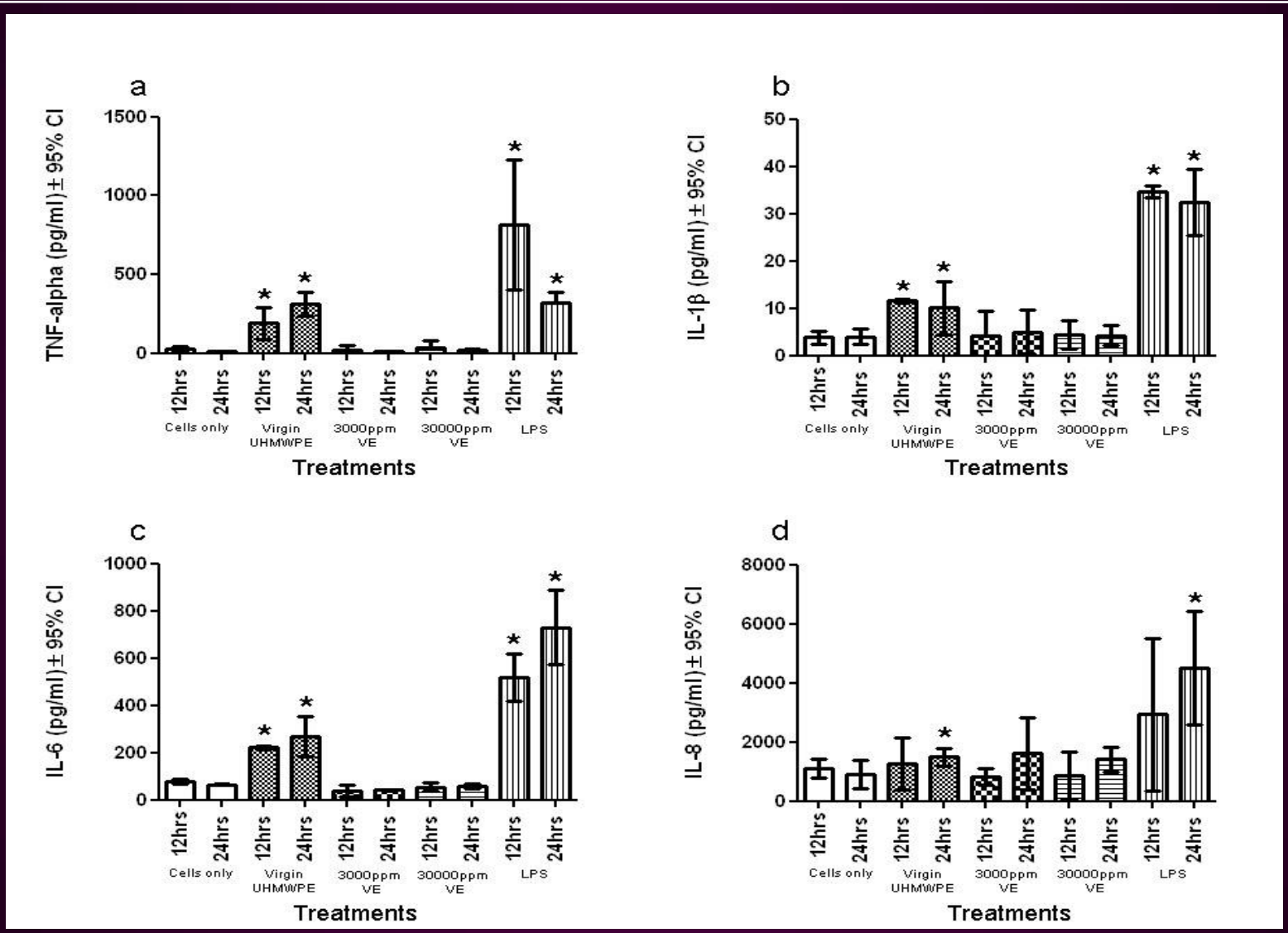


Figure 2. Cytokine production from human PBMNCs cultured with UHMWPE particles with and without Vitamin E.

RESULTS

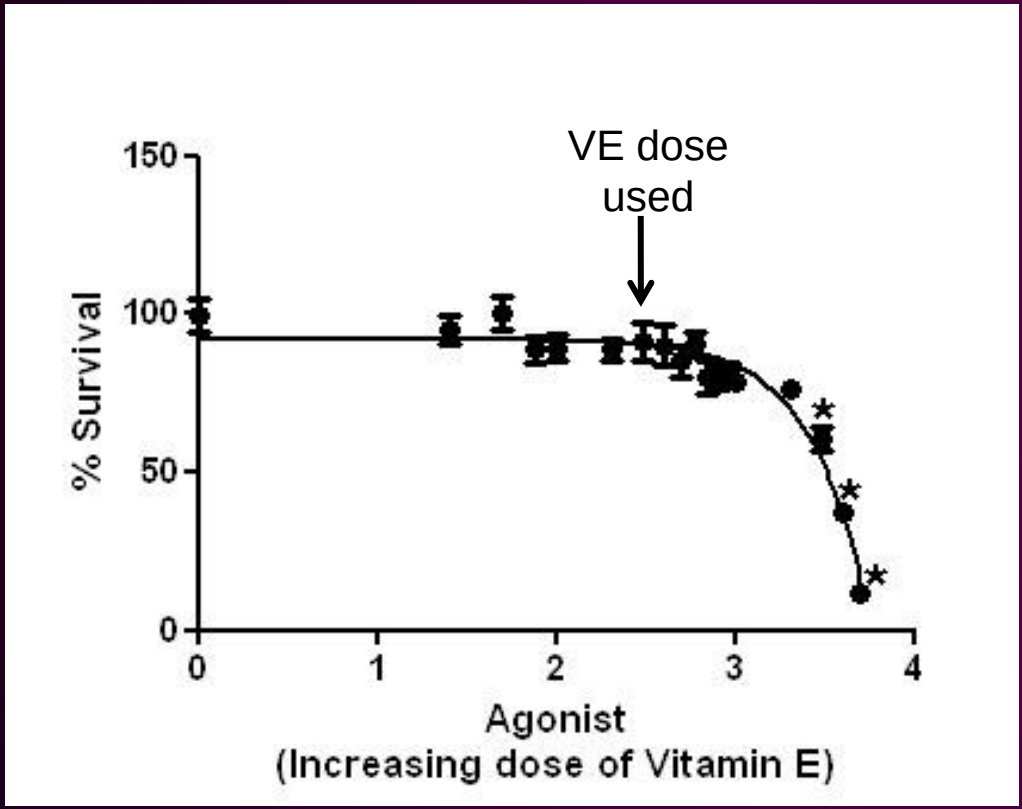


Figure 3. Vitamin E dose response curve.

Prior to experiments with the clinical material (1000 ppm VE), the cytotoxicity of Vitamin E was assessed in PBMNCs using the ATPlite™ assay and adverse effects were only observed at relatively high doses (Fig 3, >3 mM).

It was established that Vitamin E at a dose of 800 µM was optimal for use in the *in vitro* experiments, and that this dose was not cytotoxic.

RESULTS

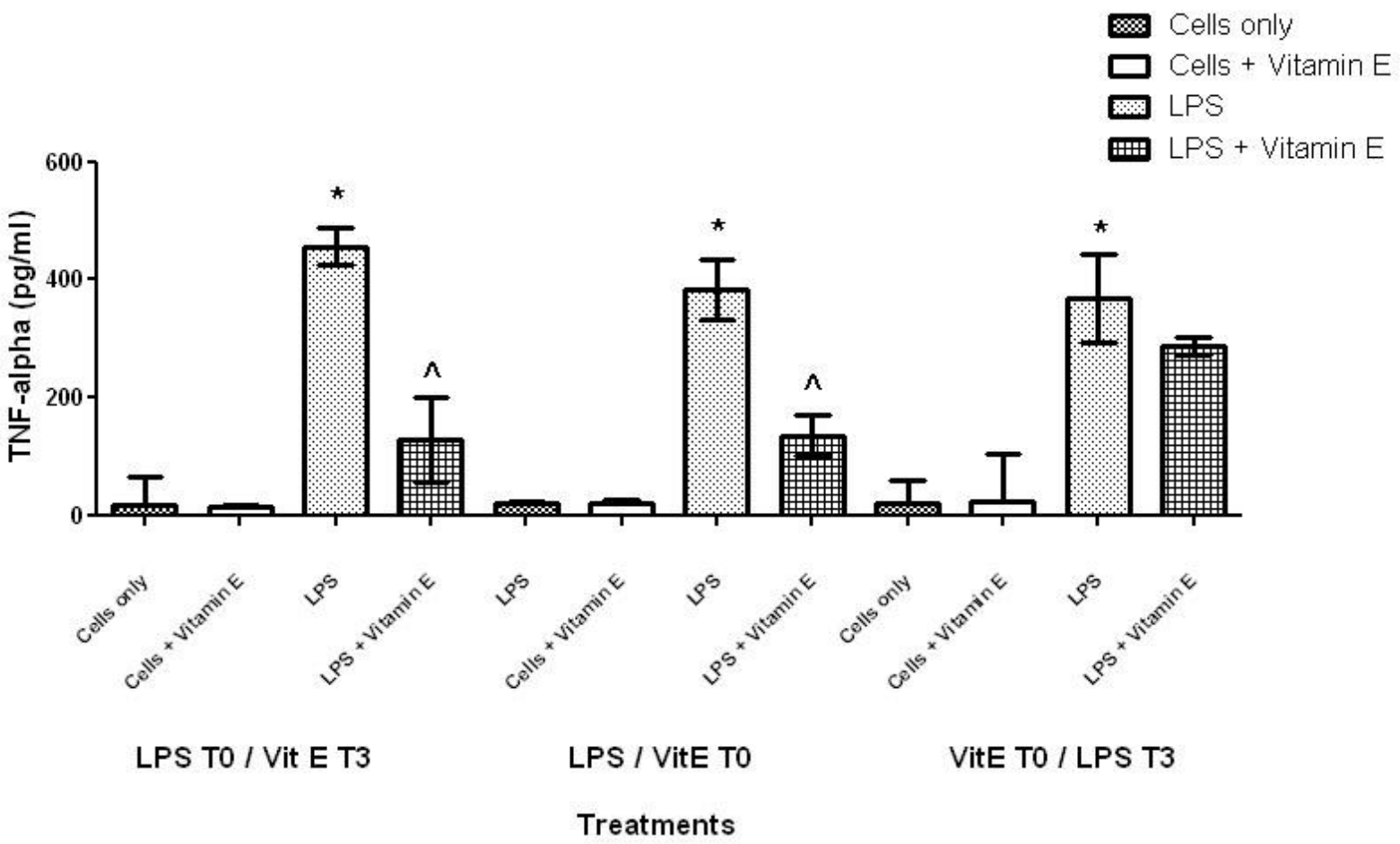


Figure 4. Moderation of TNF-α production by vitamin E in PBMNCs stimulated with LPS (Lipopolysaccharide; 200ng.ml^{-1}).

RESULTS

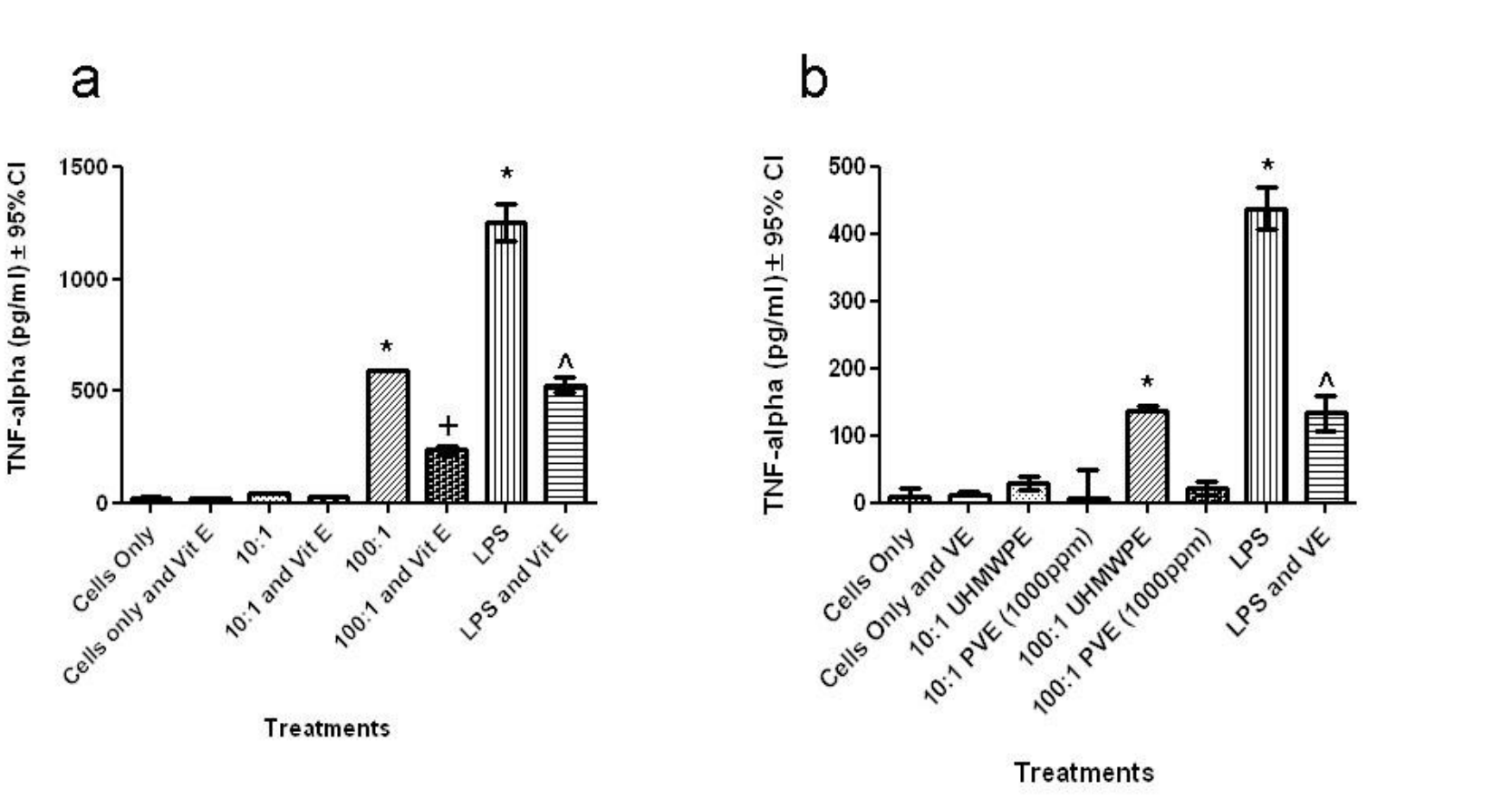


Figure 5. TNF-a production in PBMNCs after stimulation with UHMWPE particles from the clinical material (1000ppm VE).

CONCLUSION

- In conclusion the virgin UHMWPE and UHMWPEs containing VE had comparable wear rates when evaluated using a multidirectional pin on plate wear simulator.

- Primary human mononuclear cells cultured with wear debris generated from UHMWPE containing 3000 ppm and 30000 ppm VE secreted very low levels of osteolytic cytokines, including TNF-α, comparable to the cell only negative control group.

- Particles from the virgin material caused the release of significantly higher levels of osteolytic cytokines at comparable volume doses.

- These results were confirmed when particles from the clinical material, GUR1050 containing 1000 ppm vitamin E were cultured with PBMNCs.

- Vitamin E UHMWPE has a lower osteolytic potential compared to conventional UHMWPE, which may lead to longer lasting total joint replacement components that may be suitable for younger and more active patients.

ACKNOWLEDGEMENTS

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Thank You