

The biological effect of intrapleural tissue plasminogen (tPA) activator and DNase delivery in pleural infection patients.

Background

Pleural infection (PI) is a major global disease with an increasing incidence. Pleural fluid (PF) drainage is essential for the successful treatment of PI. The MIST2 RCT showed that the intrapleural administration of tPA and DNase, or tPA alone increases the volume of drained PF. A mouse study suggested that this volume increase is due to the interaction of the pleura with the tPA via the MCP-1 pathway.

Aim

To test the hypothesis that PF volume induction is mediated by the MCP-1 pathway.

Methods

210 PI patients were randomised to receive for 3 days either: tPA and DNase, tPA and placebo, DNase and placebo or double placebo. Daily PF drainage was recorded and samples of PF were stored. PF MCP-1 levels were measured by ELISA.

Results

During treatment (days 1-3) tPA+DNase and tPA+placebo significantly increased (ANOVA $p < 0.001$) the volume of drained PF compared to DNase+placebo or double placebo groups. There was no significant difference (ANOVA $p > 0.05$) between any of the groups during the post-treatment period (days 5-7). tPA+DNase and tPA groups triggered significantly higher (ANOVA $p < 0.001$) PF volumes during treatment compared to post-treatment. PF MPC-1 levels were not correlated to the drug given nor the volume of drained PF.

Conclusions

Intrapleural administration of tPA+/-DNase stimulated a statistically significant rise of the volume of drained PF and did not promote MCP-1 pathway activation. The PF volume increase did not occur via the activation of the MCP-1 pathway.

Funding

National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC).