

Markers of Inflammation: data from the MOSAIC randomised trial of CPAP for minimally symptomatic OSA.

Online repository.

*Stradling JR, *Craig SE, *, #Kohler M, *Nicoll D, †Ayers L, ‡Nunn A, ‡Bratton DJ.

*Oxford Centre for Respiratory Medicine and Oxford Biomedical Research Centre
Churchill Hospital Campus
Oxford University Hospitals NHS Trust
Oxford, OX3 7LJ, UK

†Department of Clinical Immunology,
Churchill Hospital Campus
Oxford University Hospitals NHS Trust
Oxford, OX3 7LJ, UK

‡MRC Clinical Trials Unit at UCL
Aviation House
125 Kingsway
London, WC2B 6NH, UK

#Sleep Disorders Centre and Pulmonary Division
University Hospital of Zurich
Raemistrasse 100
8091 Zurich, Switzerland

All correspondence to:

John R Stradling
Oxford Centre for Respiratory Medicine and Oxford Biomedical Research Centre
Churchill Hospital Campus
Oxford University
OX3 7LJ
UK

Email: john.stradling@orh.nhs.uk

Phone: +44 1865 225698

Fax: +44 1865 225221

Key words: Sleep apnoea, inflammation, interleukin 6, interleukin 10, C-reactive protein, tumour necrosis factor alpha.

Word count:

134

Methods

Study design

The MOSAIC, randomised, parallel, six-month, controlled trial (Multicentre Obstructive Sleep Apnoea Interventional Cardiovascular trial) was conducted between May 2006 and February 2010. The trial was approved by all the centres' ethics committees (REC No: 05/Q1604/159) and registered (ISRCTN 34164388). Patients were randomised 1:1 to standard care plus an auto-adjusting CPAP machine (Autoset S8, ResMed, Abingdon, UK), versus just standard care alone. The joint primary outcomes at 6 months were: change in ESS, and change in a composite five-year vascular risk score. Secondary outcomes at 6 months were change in objective sleepiness, self-assessed health status, blood pressure, lipids, glucose metabolism, obesity measures, and sleep apnoea severity (ODI). These have been reported previously.[1]

Entry criteria

All patients were diagnosed with OSA using overnight respiratory polygraphy as standard in the participating centres. Eligibility included: 45 to 75 years, proven OSA with a >4% oxygen desaturation index (ODI) on the original diagnostic study of >7.5 per hour, and any sleepiness present considered by both patient and sleep physician as insufficient to warrant CPAP.

Blood markers of systemic inflammation

The exploratory endpoints for this research letter, measurements of IL-6, IL-10, TNF and hsCRP, were performed using plasma samples which were immediately frozen and stored at -80 °C. IL-6, IL-10 and TNF were measured by high-sensitivity ELISA with commercially available kits (BMS213HS, BMSF0004 and BMS223HS, Bender MedSystems GmbH, Vienna, Austria). The lower limit of detection for IL-6, IL-10

and TNF were 0.03 pg/ml, 0.05 pg/ml and 0.13 pg/ml, respectively. The intra- and inter-assay coefficients of variation were 4.9 % and 6.0 %, respectively for IL-6 and 6.8 % and 7.5 % for IL-10, and 8.5 % and 9.8 % for TNF. All cytokines were measured in duplicate and in the same batch. The Dade Behring BN method (particle-enhanced immunonephelometry), which has a range 0.18-1150 mg/L, was used to measure hsCRP as previously described and validated.[2]

Statistics

All outcomes were analyzed using multivariable regression models, with adjustment for the minimisation variables and baseline value of the corresponding variable being analyzed. This produces a treatment effect, with 95% confidence interval (CI), due to being in the CPAP arm relative to standard care.

Results

The table shows the effect of CPAP compliance on hsCRP, IL-6, IL-10 and TNF.

There is no suggestion that higher compliance produced an improvement in any of these markers of inflammation.

Outcome	Treatment effect (95% CI)		p-value for difference
	<4 hrs/night vs control n=81	>4 hrs/night vs control n=44	
Highly sensitive C-reactive protein (mg/l)	-0.19 (-0.62 to +0.25)	-0.23 (-0.76 to +0.29)	0.57
Inter leikin-6 (pg/ml)	-0.06 (-0.22 to +0.09)	0.02 (-0.17 to +0.20)	0.65
Inter leikin-10 (pg/ml)	0.45 (-0.08 to +0.98)	0.18 (-0.46 to +0.83)	0.25
Tumour necrosis factor (pg/ml)	0.06 (-0.05 to +0.17)	0.02 (-0.12 to +0.16)	0.59

Reference List

- 1) Craig SE, Kohler M, Nicoll D et al. Continuous positive airway pressure improves sleepiness but not calculated vascular risk in patients with minimally symptomatic obstructive sleep apnoea: the MOSAIC randomised controlled trial. *Thorax* 2012;67:1090-6.
- 2) Roberts WL, Moulton L, Law TC et al. Evaluation of nine automated high-sensitivity C-reactive protein methods: implications for clinical and epidemiological applications. Part 2. *ClinChem* 2001;47:418-25.