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Lupus low disease activity state is associated with lower adjusted mean SLEDAI and less lupus renal and haematological involvement

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Introduction: There is currently no agreed definition of a 'safe' state of systemic lupus erythematosus (SLE) despite the availability of various validated scales on its disease activity and damage. In 2013, the Asia Pacific Lupus Collaboration presented a definition of low disease activity of this condition, the Lupus Low Disease Activity State (LLDAS), which is conceptualised as "a state which, if sustained, is associated with a low likelihood of adverse outcome" and defined as:

1. SLE Disease activity Index (SLEDAI-2k) ≤4, with no SLEDAI activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, haemolytic anaemia, fever) and no gastro-intestinal activity;
2. No new features of lupus disease activity compared to the previous assessment;
3. SELENA-SLEDAI physician global assessment (Physician Global Assessment, scale 0-3) ≤1;
4. Current prednisolone (or equivalent) dose ≤7.5 mg daily; and
5. Well-tolerated standard maintenance doses of immunosuppressive drugs and / or approved biologic agents.

This study was a preliminary analysis of a LLDAS cohort validation study which examines prospectively whether sustained LLDAS is associated with lower disease activity, damage, and mortality.

Methods: A cross-sectional study was carried out to determine the frequency of and the factors associated with LLDAS. Consecutive patients with SLE as defined by the revised American College of Rheumatology criteria seen at the Queen Mary Hospital during the period August 2013 to October 2013 were enrolled in the study. SLEDAI scores and their components, and lupus organ manifestations between patients who achieved LLDAS or not were compared using a Wilcoxon rank-sum test.

Results: Of the 201 patients recruited, patients who achieved LLDAS had a significantly lower mean adjusted mean SLEDAI score (2.40 ± 2.33) over the past 4 years when compared with patients who failed to achieve LLDAS (adjusted mean SLEDAI = 3.86 ± 2.17; P<0.000005). Similarly, patients who achieved LLDAS had lower anti-dsDNA and higher complement levels (P = 0.0012), and lower renal (P = 0.0028) and haematological (P = 0.011) scores.

Conclusion: Preliminary analysis shows that LLDAS can discriminate patients with a relatively safe course of disease, as reflected by the association of LLDAS with lower adjusted mean SLEDAI for the past 4 years and less renal and haematological involvement. Further follow-up prospective studies may reveal whether a sustained LLDAS is associated with a better prognosis with less cumulative disease activity, damage, and lower mortality rate.

Intermittent hypoxia-induced endothelial activation in EA.hy926 cells in vitro

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Introduction: Obstructive sleep apnoea is characterised by repetitive episodes of complete or partial upper airway collapse during sleep, leading to recurrent drop in arterial oxygenation (intermittent hypoxia [IH]) and sleep fragmentation. Repetitive IH with rapid reversal to normoxia initiates a series of pathological events such as oxidative stress, inflammation, and sympathetic activation, all of which contributes to endothelial dysfunction (a predictor and precursor of atherosclerosis). The aim of the current study was to investigate the effect of IH on the activation of endothelial cells in a cellular model in vitro.

Methods: Cultured endothelial EA.hy926 cells were exposed to IH in the hypoxic chamber in which the O_2 levels were alternated between 1% for 10 minutes and 21% for 5 minutes. Cells in the control group were maintained in normoxic conditions (IN: 21% and 5% CO_2). Cells were exposed to IN or IH for 64 cycles. Expression of protein of interests in endothelial cells was analysed by Western blotting.

Results: Endothelial nitric oxide synthase (eNOS), a key enzyme regulating endothelial function, was downregulated after exposure to IH while inflammatory response proteins such as cyclooxygenase–2 and inducible NOS (iNOS) were upregulated. Increased phosphorylation of Akt [p-Akt (ser473)], Erk (p-Erk1/2), and p38 (p-p38) was observed in IH-treated cells compared to the control cells.

Conclusion: IH induces endothelial dysfunction with reduced eNOS protein expression. The expression of inflammatory proteins and activation of the specific signalling pathways suggest pathophysiological changes in response to IH in this in-vitro cellular model.

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