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Results of the International Scleroderma Renal Crisis Survey

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Data from a prospective study presented by Marie Hudson, MD, McGill University, Montreal, Quebec, Canada, showed results consistent with some, but not all, prior studies [Penn H and Denton CP. *Curr Opin Rheumatol* 2008; Guillevin L et al. *Rheumatology* 2012]. Compared with retrospective data, the findings suggested worse outcomes with exposure to angiotensin converting enzyme (ACE) inhibitors prior to the onset of scleroderma renal crisis (SRC).

SRC is an infrequent but life-threatening complication of systemic sclerosis (SSc) that typically presents as new, accelerated systemic hypertension and rapidly progressive renal failure. A steep decline in SRC-related mortality following the introduction of ACE inhibitors (1 year mortality of 76% pre-ACE inhibitors to <15% post ACE inhibitors) and some evidence of a reduction in the incidence of SRC over the same period has prompted an interest in the prophylactic use of ACE inhibitors in patients with SSc. However, by masking hypertension there is a concern that prophylactic ACE inhibitor use in SSc could delay the diagnosis of SRC and possibly lead to worse outcomes. Therefore, before undertaking a trial to determine the benefit of prophylactic ACE inhibitors in SSc, the investigators wanted to study the safety of ACE inhibitors prior to SRC. The objective of the International Scleroderma Renal Crisis Study was to determine whether SSc patients with incident SRC taking ACE inhibitors prior to the onset of SRC have worse outcomes than those not taking ACE inhibitors.

This was a prospective, international cohort study of incident SRC patients identified through an ongoing web-based survey. The primary outcome was death or dialysis at 1 year. The study comprised 75 patients. Mean age of subjects was 52 years and ~70% were women. Diffuse scleroderma was present in 75% of subjects and median disease duration was 1.5 years. Sixteen subjects (21%) had prior exposure to ACE inhibitors; 44% were on prednisone at the time of onset of their SRC. Mean daily prednisone dose for those with no ACE inhibitor exposure (18 mg QD) was significantly (p=0.035) higher than for those exposed to ACE inhibitors (9 mg QD). Mean systolic and diastolic blood pressure was higher in the group exposed to ACE inhibitor prior to the onset of SRC compared with the unexposed group (139/85 vs 124/75 mm Hg).

The rate of death was 50% among those exposed to ACE inhibitors and 32% for those not exposed; the rates of dialysis were similar for both groups. Kaplan-Meier survival analysis indicated a trend for lower survival probability in the group of patients exposed to ACE inhibitors prior to SRC (log-rank p=0.1284). The Cox proportional hazard ratio for risk of death adjusted for prednisone dose and systemic hypertension showed a 2-fold higher risk of death for patients previously exposed to ACE inhibitors (HR, 2.17; 95% CI, 0.88 to 5.33; p=0.09).

Overall, the 1-year outcomes of SRC were poor. Prior exposure to ACE inhibitors was associated with an increased risk of death after the onset of SRC, although there was uncertainty around the magnitude of the risk and the possibility of residual confounding could not be ruled out. Further studies will be needed to confirm these findings.

Independent Peer-Reviewed Highlights about the

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