Sepsis: management

A635 - Both the immediate and delayed inflammatory responses in all major organs are reduced by single dose 17α-estradiol following severe burn injury

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Introduction:
Severe burn injury can create a rapid-onset, sustained pro-inflammatory condition that can severely impair all major organs. This massive systemic response has been documented clinically by associated biomarker measurements including dramatic elevations in cytokines such as IL-6. The severity of multi-organ injury and subsequent development of other systemic complications in burn patients have been well-correlated with IL-6 levels, including the increased risk of sepsis/multi-organ failure and associated morbidity and mortality. Considering that estrogen is a powerful and easy to use anti-inflammatory agent, an experimental burn model was created to test the potential value of parenteral 17α-estradiol (E2) as a feasible and inexpensive early intervention to mitigate the the profound pro-inflammatory response associated with severe thermal injury.

Methods:
Male rats (n = 28) were assigned randomly into three groups: 1) controls/no burn (n = 4); 2) burn/placebo (n = 12); and 3) burn/E2 (n = 12). Burned rats received a 40% 3° TBSA dorsal burn, fluid resuscitation and one dose of E2 or placebo (0.5 mg/kg intra-peritoneal) 15 minutes post-burn. Eight animals from each of the two burn groups (burn/placebo and burn/E2) were sacrificed at 30 minutes (sham group at 7 days only), with four each of the two burn groups sacrificed at 45 days. Tissue samples from 9 major organs and serum were obtained and analyzed by ELISA for IL-6 at each of these intervals.

Results:
In the burned rats, 17α-estradiol decreased the organ levels of IL-6 significantly as measured at both early (30 min.) and late (45 day) phases post-burn. Also, sham animal levels were comparable to the estradiol group.

Conclusion:
Experimentally, a single, early post-burn dose of estrogen significantly mitigates the associated detrimental inflammatory response in all major organs up to 45 days. In turn, this may present a promising potential therapy to decrease the widespread multiple-organ dysfunction seen in severe burn injury patients.

Image 1:

30 minute post-burn IL-6 levels in all major organs

Image 2:
45 day post-burn IL-6 levels in all major organs