In vivo inhibition of neutrophil activity by a FAS (CD95) stimulating module: arterial in-line application in a porcine cardiac surgery model.


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OBJECTIVE: Cardiac surgery with cardiopulmonary bypass is associated with aberrant neutrophil activation and potentially severe pathogenic sequelae. This experimental study was done to evaluate a leukocyte inhibition module that rapidly inactivates neutrophils through CD95 stimulation.

METHODS: German landrace pigs (4 groups, each n = 5) underwent cardiac surgery without cardiopulmonary bypass (group I), with cardiopulmonary bypass (group II), with cardiopulmonary bypass plus a leukocyte filter (group III), and with cardiopulmonary bypass plus a leukocyte inhibition module (group IV). The leukocyte filter or leukocyte inhibition module was introduced into the arterial line of the heart-lung machine.

RESULTS: Leukocyte counts were decreased by up to 43% in group IV compared with values in group II (P = .023). In group IV, but not in groups I to III, no delay in spontaneous neutrophil apoptosis was observed after annexin V-propidium iodide staining. Late apoptotic (11.7%) or necrotic neutrophils (9.3%) were detected in 2 animals (group IV). Tumor necrosis factor alpha serum levels increased over time in groups I to III (>2-fold) but remained at baseline levels in group IV (P < .05). Interleukin 8-mediated chemotactic neutrophil transmigration activity increased over time in groups I to III but was totally abrogated in group IV at any time point. The perioperative increase of creatine kinase and creatine kinase MB levels was lower in groups III (1.5-fold and 1.3-fold, respectively) and IV (1.2-fold and 1.5-fold, respectively) compared with values in group II (both 1.9-fold). CONCLUSIONS: The leukocyte inhibition module downregulated cardiopulmonary bypass-related neutrophil activity and thus might be beneficial in cardiac surgery and other clinical settings with unappreciated neutrophil activation.