

**P-442** Continuous injection of granulocyte - colony stimulating factor reduces neutrophil activation

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The use of granulocyte - colony stimulating factor (G - CSF) for the recovery from neutropenia has been established; however, acute lung injury due to G - CSF induced neutrophil activation is a serious complication. This study was designed to compare the activation of neutrophil with single bolus administration and continuous administration of G - CSF. Six healthy volunteers (age,  $33.8 \pm 1.4$  years,  $n=6$ ) received a single bolus injection of 50 mg/m<sup>2</sup> of G - CSF (SI;  $n=6$ ) or continuous subcutaneous injection of 50 mg/m<sup>2</sup> of G - CSF for 24 hrs (CI;  $n=6$ ), and were followed for 48 hrs. Circulating leukocyte counts, markers of activation on neutrophils, and circulating levels of G - CSF, IL - 6 and neutrophil elastase were measured. SI rapidly increased serum G - CSF levels that peaked at 4 hrs, whereas CI gradually increased G - CSF levels, which remained at a steady level from 8 to 24 hrs. SI caused a rapid decrease in neutrophil counts at 0.5 hr followed by sustained increase to peak at 12 hrs. CI gradually increased neutrophil counts, which peaked at 24 hrs, but the peak values were not significantly different between the groups. SI induced activation of neutrophils, which was characterized by increased expression of CD11b, decreased expression of L - selectin, and increased F - actin content, lead to increases in serum IL - 6 and neutrophil elastase level. Such changes were all attenuated with CI ( $p < 0.05$ ). Continuous subcutaneous injection of G - CSF resulted in a similar marrow response as a single injection but yielded reduced neutrophil activation.