
Abstract
This study was designed to examine the effect of 500 to 5,000 mg of ascorbic acid on DNA adducts, natural killer (NK) cell activity, programmed cell death, and cell cycle analysis of human peripheral blood leukocytes. According to our hypothesis, if ascorbic acid is a pro-oxidant, doses between 500 and 5,000 mg should enhance DNA adduct formation, decrease immune function, change the cell cycle progression, and increase the rate of apoptosis. Twenty healthy volunteers were divided into four groups and given either placebo or daily doses of 500, 1,000 or 5,000 mg of ascorbic acid for a period of 2 weeks. On days 0, 1, 7, 15, and 21, blood was drawn from them, and the leukocytes were separated and examined for intracellular levels of ascorbic acid, the level of 8-hydroxyguanosine, NK cell activity, cell cycle progression, and apoptosis. Depending on the subjects, between a 0% and a 40% increase in cellular absorption of ascorbic acid was observed when daily doses of 500 mg were used. At doses greater than 500 mg, this cellular absorption was not increased further, and all doses produced equivalent increases in ascorbic acid on days 1 to 15. This increase in cellular concentration of ascorbic acid resulted in no statistically meaningful changes in the level of 8-hydroxyguanosine, increased NK cytotoxic activity, a reduced percentage of cells undergoing apoptosis, and switched cell cycle phases from S and G2/M to G0/G1. After a period of 1 week, with no placebo or vitamin washout, ascorbic acid levels along with functional assays returned to the baseline and became equivalent to placebos. In comparison with baseline values, no change (not more than daily assays variation) was seen in ascorbate concentrations or other assays during oral placebo treatment. We concluded that ascorbic acid is an antioxidant and that doses up to 5,000 mg neither induce mutagenic lesions nor have negative effects on NK cell activity, apoptosis, or cell cycle.