Aims: In this study, the effect of DNA damage in the course of sevoflurane anesthesia along with remifentanil and nitrous oxide, was investigated via Comet Assay technique. Materials and methods: The study included 52 patients. After approving informed consent form all participants, patients were randomly divided into three groups to provide different anesthesia maintenance. Anesthesia induction was carried out with propofol and vecuronium bromide in all groups. After intubation, Group SN (Sevoflurane-Nitrousoxide) received 50%O2+50% N2O and sevoflurane 2-4%. Group SR (Sevoflurane-Remifentanil) received remifentanil by infusion at rate of 0.2mcg/kg/min, sevoflurane 2-4%+100% O2. Group C (Control) sevoflurane 2-4% and 100% O2 for maintenance. Blood samples were obtained from all patients before induction, 120 th minute of operation, and on postoperative day one and five. Results: Genotoxic damage was observed in all groups. When the groups were compared, no statistically significant difference was observed between the groups. However, while the DNA damage regressed to preoperative values on the 5th postoperative day in Group SR, it did not regress to preoperative values in Groups SN and C. Conclusion: It has been demonstrated that nitrous oxide combined with sevoflurane for anesthesia administration is not an ideal agent, and that an alternative opioid with short-acting agent remifentanil, can be used. It has also been theorized, due to remifentanil’s contribution in Group SR’s anesthesia administration, that remifentanil can lead to using lower doses of sevoflurane and positively impact the recovery of genotoxic damage. Key words: Sevoflurane, Remifentanil, Nitrous Oxide, DNA damage, Genotoxicity, Comet assay. Received February 18, 2014; Accepted May 19, 2014