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## DNA Integrity Is Compromised in Protamine-Deficient Human Sperm

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The objective of this study was to examine the relationship between DNA integrity and protamines in human sperm. One hundred forty-nine male infertility patients were included in an Institutional Review Board-approved study. Sperm were evaluated for DNA fragmentation using the DNA Integrity Assay, a test equivalent to the sperm chromatin structure assay (SCSA). Additionally, nuclear proteins were extracted and the protamine-1/protamine-2 ratio (P1/P2), protamine-1 (P1), protamine-2 (P2), and total protamine concentrations were evaluated. We identified 37 patients with abnormally low P1/P2 ratios, 99 patients with normal P1/P2 ratios, and 13 patients with abnormally high P1/P2 ratios. DNA fragmentation was significantly elevated in patients with low P1/P2 ratios ( $37.1 \pm 6.02$ ) vs those with normal and high P1/P2 ratios ( $26.7 \pm 1.9$  and  $23.8 \pm 3.2$ , respectively;  $P < .05$ ) and was inversely correlated with the P1/P2 ratio ( $R_s -0.18$ ,  $P < .05$ ), P1 concentration ( $R_s -0.29$ ,  $P < .001$ ), P2 concentration ( $R_s -0.24$ ,  $P < .005$ ), and total protamine concentration ( $R_s -0.28$ ,  $P < .001$ ). Furthermore,  $\chi^2$  analysis revealed a significant increase in the incidence of marked DNA fragmentation in patients with diminished levels of either P1 or P2. The present study is the first to report that human sperm protamine content is significantly related to DNA fragmentation. In particular, sperm P1 and P2 concentrations inversely correlate with DNA fragmentation, indicating a protective role of the protamines against sperm DNA damage. In light of recent studies highlighting the negative effect of sperm DNA damage on ART outcomes, these findings indicate a possible clinical significance for human sperm protamine levels.

Key words: Chromatin, DFI, DNA damage

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