

**Effect of nut consumption on semen quality and functionality in healthy males: a randomized controlled trial**

*A. Salas-Huetos<sup>1,2</sup>, R. Moraleda<sup>1</sup>, S. Giardina<sup>1,2</sup>, E. Anton<sup>3</sup>, J. Blanco<sup>3</sup>, J. Salas-Salvadó<sup>1,2</sup>, M. Bulló<sup>1,2</sup>*

*<sup>1</sup>Universitat Rovira i Virgili, Human Nutrition Unit, Reus 43201, Spain*

*<sup>2</sup>Consorcio CIBER- M.P.- Physiopathology of Obesity and Nutrition CIBERObn, Instituto de Salud Carlos III ISCIII, Madrid 28029, Spain*

*<sup>3</sup>Genetics of Male Fertility Group,*

*Cell Biology Unit- Department of Cellular Biology- Physiology and Immunology- Faculty of Biosciences- Uiversitat Autònoma de Barcelona UAB, Bellaterra Cerdanyola del Vallès 08193, Spain*

**Study question:**

Can a chronic consumption of a mixture of nuts improve the semen quality parameters and the sperm functionality in healthy individuals?

**Summary answer:**

Including nuts in a regular diet significantly improved the sperm count, vitality, motility, and morphology, partly explained by a reduction of the DNA fragmentation.

**What is known already:**

Human semen quality has declined in industrialized nations where pollution, smoking, and trends toward a western-style diet are hypothesized as potential causes. Recently, some studies described that healthy diets rich in omega-3, antioxidants (e.g. vitamin C and E, selenium and zinc), carnitines and folate could improve semen quality. Because nuts are nutrient dense foods containing some of the above-mentioned nutrients, we hypothesize that, added to a western-style diet, would beneficially affect semen quality and functionality.

**Study design, size, duration:**

The study was designed as a 14-week randomized, controlled, parallel two-group trial. 119 healthy male aged 18-35 were allocated to either following their usual western-style diet supplemented with 60 g/day of a mix of almonds, hazelnuts and walnuts or to follow with their usual western-style diet free of nuts.

**Participants/materials, setting, methods:**

Sperm and blood samples were collected at baseline and after 14 weeks of intervention. Dietary information was recorded in four visits distributed along the trial. Conventional semen parameters (WHO, 2010) were determined as primary outcome. To elucidate at the molecular level the effects of nuts consumption, sperm DNA fragmentation (TUNEL assay), sperm ROS (chemiluminescence using Luminol), sperm chromosome stability (FISH for chromosomes X, Y and 18) and total sperm DNA methylation (ELISA assay) were measured.

**Main results and the role of chance:**

A total of 98 participants completed the study. General characteristics of the study population (age, weight, height, BMI, waist circumference, and systolic and diastolic blood pressure) did not differ between interventions. No significant differences were observed in conventional blood biochemical parameters (fasting plasma glucose, total cholesterol, HDL, LDL and VLDL cholesterol, triglycerides, fasting plasma

insulin, C-reactive protein and folate). In nuts group, we found a significant increased intake of total lipids, MUFA, PUFA, magnesium, vitamin E, omega-3, ALA, and omega-6. We found an improvement of sperm count (P-value=0.0043), vitality (P-value=0.0027), total motility (P-value=0.0093), progressive motility (P-value=0.0207), and morphology (P-value=0.0073) in the nut group compared to the control. Participants in the nuts group shown a significant reduction of the sperm DNA fragmentation (SDF) (P-value=0.0018) a parameter closely related with male infertility. Negative correlations between sperm vitality and SDF ( $\rho=-0.2252$ ; P-value=0.0266), and between total spermatozoa and SDF ( $\rho=-0.3170$ ; P-value=0.0015) were detected. No changes between interventions were found in ROS (P-value=0.1996), sperm chromosome (X, Y and 18) anomalies (P-value disomies=0.3336, P-value nullisomies=0.9386, and P-value diploidies=0.0674), and DNA methylation (P-value=0.8652).

**Limitations, reasons for caution:**

By design, a limitation of this trial is that it focuses on health, apparently fertile and with western-style diet subjects, and the results cannot be extrapolated to the general population.

**Wider implications of the findings:**

Our findings support a beneficial role of chronic nut consumption in sperm quality and explore the molecular mechanism that could explain our results. Additional efforts to identify male-specific dietary recommendations that optimize sperm quality and fertility should be encouraged.

**Trial registration number:**

The trial was registered in ISRCTN registry with identifier ISRCTN12857940 (DOI: 10.1186/ISRCTN12857940).

Yes

Funding by commercial/corporate company(ies)