**Survivin and NAIP in Human Benign Prostatic Hyperplasia: Protective Role of the Association of Serenoa repens, Lycopene and Selenium from the Randomized Clinical Study.**

1)Minutoli L. 2)Morgia G. 3)Micali A. 4)Rinaldi M. 5)Irrera N. 6)Marini H. 7)Puzzolo D. 8)Russo GI. 9)Cimino S. 10)Bitto A. 11)Pizzino G. 12)Pallio G. 13)Altavilla D. 14)Squadrito F.

*University of Messina, AOU Policlinico "G. Martino"*

Benign prostatic hyperplasia (BPH) treatment includes the apoptosis machinery modulation through the direct inhibition of caspase cascade. We previously demonstrated that Serenoa repens (Ser) with lycopene (Ly) and selenium (Se) reawakened apoptosis by reducing survivin and neuronal apoptosis inhibitory protein (NAIP) levels in rats. The aim of this study was to evaluate the effectiveness of Ser-Se-Ly association on survivin and NAIP expression in BPH patients. Ninety patients with lower urinary tract symptoms (LUTS) due to clinical BPH were included in this randomized, double-blind, placebo-controlled trial. Participants were randomly assigned to receive placebo (Group BPH + placebo, n = 45) or Ser-Se-Ly association (Group BPH + Ser-Se-Ly; n = 45) for 3 months. At time 0, all patients underwent prostatic biopsies. After 3 months of treatment, they underwent prostatic re-biopsy and specimens were collected for molecular, morphological, and immunohistochemical analysis. After 3 months, survivin and NAIP were significantly decreased, while caspase-3 was significantly increased in BPH patients treated with Ser-Se-Ly when compared with the other group. In BPH patients treated with Ser-Se-Ly for 3 months, the glandular epithelium was formed by a single layer of cuboidal cells. PSA showed high immunoexpression in all BPH patients and a focal positivity in Ser-Se-Ly treated patients after 3 months. Evident prostate specific membrane antigen (PSMA) immunoexpression was shown in all BPH patients, while no positivity was present after Ser-Se-Ly administration. Ser-Se-Ly proved to be effective in promoting apoptosis in BPH patients.