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Synergism between bisphenol a exposure and overweight/obesity in increasing the malignancy risk in a cohort of patients with thyroid nodules

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Introduction: The plasticizer Bisphenol A (BPA) is an endocrine disruptor with thyroid interfering activity. Obesity is a recognized risk factor for thyroid cancer. A recent study showed that subjects with $BMI \ge 25$ are more prone to BPA-related thyroid disruption. To date, few and controversial experimental and epidemiological data provide weak evidence about a correlation between BPA exposure and thyroid cancer development. Aim of the present study was to assess a possible link between BPA, body fat excess, and thyroid cancer risk.

Patients and Methods: Multicentre, cross-sectional study including consecutive patients subjected to cytology for diagnostic definition of thyroid nodules. Blood samples were obtained for all enrolled patients. Serum BPA determination was performed by means of high performance liquid

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chromatography coupled in tandem with fluorescence and ultraviolet detection. Inclusion criteria: a) age \geq 18 years; b) clinical management performed in one of the involved centres. Exclusion criteria: a) inconclusive cytology (TIR -3A, -3B, -1 categories); b) clinical and/or cytological and/or histological features of autoimmune thyroiditis; c) clinical and/or cytological and/or histological features of medullary thyroid cancer; d) modifications in lifestyle and anthropometric variables occurred within the previous 5 years. BPA exposure was assessed by means of a qualitative approach, categorizing the subjects in exposed (detectable serum BPA levels) and not-exposed (undetectable BPA levels).

Results: Statistical analysis included 94 patients: 30 males and 64 females (median age 52 years); 54 benign nodules, 40 thyroid cancers; 28 normal weight patients (BMI < 25), 66 overweight/obese patients (BMI \ge 25 < 30 in 30 cases; BMI \ge 30 in 36 cases). Detectable BPA was found in 78 cases. In the overall study group and in the BMI < 25 group exposure to BPA was not significantly related to the risk of malignancy (*P*=0.119; OR 1.84 with 95% CI 0.76-4.45 and *P*=0.755; OR 0.83 with 95% CI 0.28-2.47, respectively). By contrast, in the BMI \ge 25 group, BPA-exposed subjects showed significantly higher risk of malignancy (*P*=0.046; OR 2.88 with 95% CI 0.79-10.54).

Conclusions: In our series, BPA exposure conferred higher risk of thyroid cancer only in case of concomitant overweight/obesity, therefore suggesting a synergistic action between BPA and the excess of adipose tissue in promoting thyroid carcinogenesis.

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