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Annex. PICNIT Study Group

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References


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Statin therapy does not influence in the form onset of differentiated thyroid carcinoma

El tratamiento con estatinas no influye en la forma de presentación del carcinoma diferenciado de tiroides

Dear Editor:

Statin treatment may result in a reduction of certain types of neoplasia. In thyroid, statins have shown their ability to induce anaplastic carcinomas cell line redifferentiation. It has also been described that these drugs reduce both the incidence and size of thyroid nodules. In this work we shall analyse whether the use of statins is associated with a different profile of differentiated thyroid cancer (DTC) presentation. A total of 192 cases were included retrospectively. The sample was divided in 2 groups. Group 1: Patients receiving on going statin treatment for at least a whole year before the intervention, and who continued to receive statins by the time the thyroidectomy was performed. Group 2: Patients who did not take the drug during the 3 years prior to the surgery. Both groups were compared in terms of demographics, presence of diabetes mellitus, smoking habits, pre-surgical levels of thyrotropin (TSH), and the characteristics of the tumour at the time of the intervention: histological type (papillary carcinoma [PTC] and follicular carcinoma [FTC]), size, percentage, percentage of microcarcinoma, multifocal quality, nodal metastasis, associated thyroidiy and distant metastasis. The statistical analysis was made according to the chi-square and Mann–Whitney U tests.

Group 1 included 36 cases (29 females and 7 males, average age 63.7 [12.5] years). In group 2 there were 156 subjects (121 females and 35 males, average age 49.3 [15.6] years). Differences were not significant in terms of gender but in terms of age, with a majority of subjects treated with hypolipidemic agents (p < 0.001). Likewise, group 1 presented a larger number of patients with diabetes mellitus type 2 (18 [50%] as opposed to 14 [9%]; p < 0.001). No differences were observed in terms of pre-surgical THS levels, tumour size, tumour multicentricity, and presence of lymph-nodes or distant metastasis. The incidence of FTC was higher among patients who received statin treatment. Thus, 8 of 36 cases (22%) from group 1 were FTC, while only 13 of 156 patients (8.3%) from group 2 presented this histological variant (p = 0.02). However, patients with FTC were older than those affected with PTC (p > 0.01), therefore differences disappeared age-wise.

Different works have displayed a possible relation between statins and the thyroid gland. Gullu et al. have shown that the drug reduces TSH and increases thyroid hormones in patients with hypothyroidism. Yandell et al. suggested that statins might show blood reduction of false negative TSH result. On the other hand, some studies have revealed the protective effect of statins in the development of certain types of cancers, even though a recent meta-analysis concluded that drugs offer a neutral effect in relation to cancer incidence and death risk. In some cases, the DTC suffers a tumour non-differentiation process, making it refractory to conventional treatments. Loss of differentiation entails a deterioration in the patient’s prognosis. Different strategies have been implemented for years to try and revert the process (redifferentiation process). Among many of the drugs used, statins have shown, in vitro experiments, that they can induce differentiation and apoptosis, and they can inhibit the invasive component in cell lines in thyroid non-differentiated and anaplastic cancer.

In view of these findings, statins have been proposed as an adjuvant therapy to treat advanced DTC. The non-proliferative effect of statins has been corroborated not just in experimental studies and in relation to thyroid cancer, but also in clinical studies...
and in relation to benign thyroid diseases. In their published work, Capelli et al. showed that dyslipidemic patients treated with statins for at least 5 years presented a lower prevalence of thyroid nodular disease and a reduction in the number and volume of thyroid nodules, in comparison to the control group. The reduction in nodular number and size is related to the daily drug dose administered. Chon et al. have verified the same results in elderly patients with diabetes mellitus type 2. In spite of the aforementioned evidence, there is no study, to date, that has analysed the relation between statin treatment and the TDC presentation form. In this study we have assessed the influence of hypolipidemic treatment over variables widely used as bad prognosis markers for this type of cancer. In our sample we have not been able to associate the treatment with a less aggressive profile of tumour, according to the meta-analysis result published by Dale et al. Thus, unlike the findings published in relation to benign thyroid disease, statin treatment is not associated with a different TDC profile presentation.

References


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