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LETTER TO THE EDITOR

Use of anti-thyroid drugs in patients with hyperthyroidism: a case for shared decision-making

Luca Giovanella [1,2] · Frederik A. Verburg [3]

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Dear Sir,

Struja and Schuetz [1] took a recently paper by Kitahara et al. [2] as a "sic et simpliciter" demonstration of the "association of radioiodine exposure and later risk of cancer in Graves' Disease (GD) patients" and asked for a revision of current guidelines such as from the American Thyroid Association [3]; furthermore, they called for a wider use of anti-thyroid drugs (ATDs). In addition, a multidisciplinary shared decision-making approach is strongly advocated, in which the risks and benefits of each treatment for Graves' disease should be outlined.

It is hard to see how any physician would not support the process of shared decision-making between specialists and patients wherever the clinical situation offers the slightest possibility of doing so. Of course, this process does require proper evaluation of reported data, well beyond titles, and abstracts, in order to prevent ideologies from gaining the upper hand over scientific reason.

Certainly, the paper by Kitahara et al. may on the surface insinuate a causal relationship between a moderate cancer mortality risk excess and radioiodine therapy of benign thyroid disease. However, an objective assessment of this paper inevitably leads to the conclusion that a multitude of limitations precludes the assumption offered when assessed with the necessary scientific rigor.

Briefly,

1. The role of thyroid hormones (TH) excess in promoting cancerogenesis was completely ignored despite the well-known positive relationship between hyperthyroidism and the risk of breast, prostate, lung, and colon neoplasia [4]. In fact, the Kitahara team previously demonstrated a significant breast cancer-related mortality excess in hyperthyroid women over 60 years old but no impact of radioiodine therapy on this association was found [5].
2. In an earlier comparison of cancer mortality by treatment in the same sample studied by the Kitahara team, a 1.31 cancer-related standardized mortality ratio (SMR) was found in patients given ATDs. However, the subgroup receiving radioiodine had an SMR of 1.02, not statistically different from expected cause-specific mortality in the general population. For breast cancer, SMR was 1.69 for patients given ATDs and 1.08 for patients receiving radioiodine, respectively [6].
3. Only patients treated with radioiodine were enrolled by Kitahara et al. and, in addition, no correction for any of the typical cancer risk factors (e.g., smoke, diabetes, alcohol) was applied. Considering that the group of patients with the highest radioiodine activity also had the highest rate of coronary heart disease does make one suspect, however, that this group likely also had the highest rate of smokers, thus more than sufficiently explaining any excess cancer rate.
4. To properly analyze the role of radioiodine, the authors should have included a suitable control group such as hyperthyroid patients treated only with surgery, ATDs, or both. Ryödi and colleagues [7] compared surgery and radioiodine in a large scale, long-term follow-up study and concluded that "the increased cancer risk in hyperthyroid patients is attributable to hyperthyroidism and shared risk factors, not the treatment modality" (in spite of the fact that the paper is included into the list of references, this statement is otherwise neglected by Kitahara et al.).

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✉ Luca Giovanella
Luca.Giovanella@eoc.ch

[1] Clinic for Nuclear Medicine and Thyroid Competence Centre, Imaging Institute of Southern Switzerland, Via Ospedale 6, CH-6500 Bellinzona, Switzerland

[2] Clinic for Nuclear Medicine, University Hospital and University of Zurich, Zurich, Switzerland

[3] Department of Nuclear Medicine, University Hospital Marburg, Marburg, Germany

Frankly speaking, considering these points, one must question whether the study by Kitahara et al. even supports a hypothesis of a relationship between radioiodine therapy and cancer mortality in GD's patients. Rather, the scope of the study's interpretation of the evidence generated goes well beyond any data presented and is, on critical methodological reflection, wholly unjustified. Therefore, it must be questioned whether the strong wording is not motivated by other factors than the mere generation of scientific evidence. In fact, as in spite of nearly 8 decades of radioiodine therapy, no study has yet been able to prove the latter hypothesis [8]; this therapeutic modality still remains one of the safest ones known in all of medicine.

In conclusion, while a multidisciplinary shared decision-making approach is certainly useful in managing Graves' disease, it should be based on proper consideration of the available evidence. In this setting, it should be considered that there are data supporting a higher risk of cancer-related mortality in patients treated with ATDs than radioiodine, as well as a higher risk of cancer-related mortality due to hyperthyroidism per se, and patients should be informed adequately.

Compliance with ethical standards

Conflict of interest L.G. is a member of Roche Diagnostics advisory board and has received research grants and speaker honoraria from Roche Diagnostics, IBSA, and Sanofi-Genzyme. F.A.V. has received research grants from Sanofi-Genzyme and speaker honoraria from Sanofi-Genzyme, Diasorin, and Jubilant Draximage.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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