Letter to the Editor (Correspondence) on the Article Entitled "Gastric Emptying Patterns in Type 2 Diabetes Mellitus Patients with Symptoms of Gastroparesis and the Impact of Levosulpiride on These Patterns"

Nitin Chintaman Gawari[1], Sujata Prakash Shingare[2], AV Tilak[3], Krupa H Vasani[4]

[1,2]Assistant Professor, [3]Professor and HOD, [4]Junior Resident, Department of Pharmacology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India

Dear Editor,

We read with interest the expert consensus by Kant et al. on levosulpiride for the management of symptoms of gastroparesis in type 2 diabetes mellitus (T2DM) patients. The article is timely and informative, particularly in view of the increasing complexity of treatment in Indian diabetes care. The debate around the novel mechanism of levosulpiride—addressing the relationship both gastric motility patterns and therapeutic outcomes—is well articulated and is in line with the increasing emphasis on both.[1]

The recommendation on the use of levosulpiride in patients with symptoms of gastroparesis in T2DM is practical and relevant. Levosulpiride, in particular, has been shown to effectively alleviate symptoms such as nausea, vomiting, and early satiety, likely due to its action on the chemoreceptor trigger zone.[2]

However, we would like to make a few comments:

- The authors have clearly established the global and Indian burden of diabetes, which is strong. However, the introduction could flow more smoothly from general (diabetes mellitus burden) to specific (gastroparesis) to research gap. The research gap ("limited research on the correlation between scintigraphic patterns and symptoms") is mentioned at the end but could be more explicit and earlier in the text. The rationale for using levosulpiride is stated but not linked directly to the research gap.[3]
- Data transparency: A flow diagram of participant recruitment and attrition was not provided. Adding a participant flow diagram showing numbers at each stage will be better (screened, eligible, included, followed up, analyzed). There is no accounting for missing data, and it is unclear whether all 27 participants completed follow-up. The number of participants who did not improve or who worsened was not mentioned.
- Confounding variables (glycemic control, concomitant medications, and diet) are not discussed. The article does not connect to the local (North India) study context, which is important for external validity. There is also a lack of discussion on generalizability to other populations.

Orcid

Nitin Chintaman Gawari https://orcid.org/0009-0006-4241-8909
Sujata Prakash Shingare https://orcid.org/0009-0002-5260-364X

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Gonadotropin-releasing Hormone Agonist-induced Autoimmune Thyroiditis in a 49-year-old Woman

Sruthi Yalamanchili[1], Nikhil Gupta[2], Tanvi Batra[3], Atul Kakar[4]

[1,2]DNB trainee; [3]Associate Consultant; [4]Chairman and Senior Consultant, Department of Internal Medicine, Sir Ganga Ram Hospital, New Delhi, India

Dear Editor,

Goserelin is a synthetic gonadotropin-releasing hormone (GnRH) agonist that initially stimulates and then profoundly suppresses pituitary gonadotropin secretion through receptor desensitization. It is commonly prescribed in the management of hormone-dependent conditions such as prostate cancer, breast cancer, endometriosis, and adenomyosis.[1] Typical side effects of goserelin are attributable to the resulting hormonal deprivation, including vasomotor symptoms, bone mineral loss, mood disturbances, and injection site reactions. However, rare endocrine complications beyond expected hypoestrogenism, such as thyroid dysfunction, have also been described.[2,3] Here we discuss the case of a 49-year-old woman, a known case of prediabetes (glycosylated hemoglobin: 6.2%), hypertension, and dyslipidemia, who presented to the gynecology outpatient department with complaints of menorrhagia and infertility. Laboratory investigations revealed normal blood counts and normal kidney and liver functions, with a standard thyroid function test [free T4/thyroid-stimulating hormone (TSH): 11.1 pmol/L and 2.10 mU/L, respectively]. Hormonal workup, including luteinizing hormone, follicle-stimulating hormone, and serum anti-Mullerian hormone, was normal. CA-125 was normal. A Pap smear showed no evidence of malignancy, and mammography showed breast imaging-reporting and data system (BI-RADS) 1. Ultrasound of the pelvis revealed a markedly bulky uterus (172 mL) and no significant fibroids. Evaluation revealed abnormal uterine bleeding associated with adenomyosis (AUB-A). Considering this to be a mechanical barrier to successful embryo implantation, she was initiated on GnRH agonist therapy. She was administered a monthly dose of goserelin (Zoladex) 3.6 mg subcutaneously for a total of 6 months. Treatment successfully induced a hypoestrogenic menopausal-like state, leading to amenorrhea. A follow-up pelvic ultrasound after completion of therapy showed a significant reduction in uterine volume from 172 to 93.4 mL, confirming a good anatomical response to GnRH therapy. No thyroid-related symptoms were reported during the treatment course. Six weeks after her last dose of GnRH agonist, she presented to us with complaints of palpitations, episodic tremors, heat intolerance, anxiety, and insomnia. There was no history of neck pain or visual disturbances. On examination, she had fine tremors with tachycardia (pulse rate: 102/minute, regular). The rest of the hemodynamic and systemic examination was normal. Physical examination of the eyes and thyroid gland revealed no abnormalities. Initial investigations revealed a normal complete blood count and liver and kidney function tests. Thyroid function tests revealed overt thyrotoxicosis [Low TSH (0.004 µIU/mL), low fT3 (1.098 pg/dL) and high fT4 (3.6 ng/dL)]. Thyroid antibody testing revealed markedly elevated antithyroid peroxidase (anti-TPO) and antithyroglobulin (anti-Tg) levels, 764

and 142 IU/mL, respectively. TSH receptor antibody (TRAb) was mildly positive (3.51 IU/L). Fasting glucose and lipid profiles were normal. To differentiate thyroiditis from Graves' disease, a technetium-99m pertechnetate thyroid scan was performed, which showed normal thyroid morphology with a total uptake of 0.6% (normal range: 0.2–3%), without any evidence of nodules. This normal uptake despite suppressed TSH strongly favored a diagnosis of painless autoimmune thyroiditis. Other causes of thyrotoxicosis, such as toxic multinodular goiter, iodine-induced hyperthyroidism, or medication-induced thyroid dysfunction, were ruled out. Symptomatic treatment with propranolol for palpitations and tremors was initiated. Serial monitoring after 8 weeks showed gradual normalization of thyroid function (T3: 3.1 pg/mL, T4: 1.01 ng/dL, TSH: 2.21 µIU/mL), indicating a return to a euthyroid state. She continues to be on regular follow-up with no clinical features of hypothyroidism. Her menstrual symptoms and metabolic parameters are well-controlled.

Though uncommon, there is emerging evidence linking GnRH agonist therapy to disturbances in thyroid function, particularly autoimmune thyroiditis and transient thyrotoxicosis.[2–4] The precise pathophysiological mechanism remains unclear but is hypothesized to involve immune dysregulation secondary to abrupt withdrawal of estrogen, which typically exerts protective, immunosuppressive effects. This disruption may unmask subclinical autoimmune thyroid disease or trigger *de novo* thyroiditis in genetically susceptible individuals, paralleling the pathogenesis observed in postpartum thyroiditis.[5–7] Several features in our patient support a diagnosis of goserelin-induced painless autoimmune thyroiditis. The delayed onset of thyrotoxic symptoms 6 weeks after the final goserelin dose is consistent with the time course observed in immune-mediated thyroid dysfunction. Laboratory investigations revealed markedly elevated thyroid peroxidase (TPO) and thyroglobulin antibodies, suggesting an autoimmune basis. Furthermore, the technetium thyroid scan demonstrated normal uptake, differentiating the condition from Graves' disease, which typically exhibits increased tracer uptake. There was no thyroid tenderness, nodularity, or orbitopathy, making other differentials such as subacute thyroiditis unlikely. Nakashima et al. reported two women with endometriosis developing transient thyrotoxicosis following prolonged GnRH-agonist therapy, hypothesizing that hypoestrogenism-related immune shifts contributed to the thyroid dysfunction.[4] Similarly, Van Bon and Wiersinga described transient thyrotoxicosis in a hypothyroid woman undergoing goserelin therapy, highlighting a rare but plausible immune-mediated mechanism.[2] In contrast to some cases where radionuclide scans showed low uptake, our patient's imaging revealed normal thyroidal activity, possibly reflecting early or mild autoimmune involvement rather than destructive thyroiditis. Importantly, spontaneous normalization of thyroid function over several weeks without antithyroid therapy mirrored the self-limiting course observed in autoimmune thyroiditis.

The management of GnRH-induced thyroid dysfunction is typically conservative. Since the hyperthyroid phase results from the release of preformed thyroid hormones rather than active synthesis, beta-blockers suffice for symptomatic control, and antithyroid medications are unnecessary. Regular monitoring of thyroid function is advised to detect potential progression to hypothyroidism during recovery.

This case illustrates a rare occurrence of GnRH agonist-induced thyrotoxicosis, likely triggered by an autoimmune mechanism analogous to postpartum thyroiditis. It emphasizes high vigilance for thyroid dysfunction, even several weeks after completion of GnRH agonist therapy, particularly in individuals with a potential autoimmune predisposition. Early recognition and patient counseling regarding the benign, self-limited nature of this complication play a crucial role in the management of this disease.

Author's Contributions

Sruthi Yalamanchili: Data curation, formal analysis, investigation, methodology, resources, writing—original draft, visualization; Nikhil Gupta: Methodology, resources, writing—original draft; Tanvi Batra: Conceptualization, software, writing—review and editing; Atul Kakar: Project administration, funding acquisition, supervision.

Sources of Support

None.

Conflict of Interest

There is no conflict of interest.

Patient Consent Statement

Participant's consent has been obtained.

Orcid

Sruthi Yalamanchili https://orcid.org/0009-0005-2243-6299
Nikhil Gupta https://orcid.org/0009-0007-4784-6184
Tanvi Batra https://orcid.org/0009-0007-8215-5792
Atul Kakar https://orcid.org/0000-0001-5643-4658

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