Stinging Nettle (Urtica dioica): An Unusual Case of Galactorrhea

Laura Easton
ACDEF 3,4
Shalini Vaid
BDE 5
Angela K. Nagel
DEF 6
Jineane V. Venci
ABDEF 1,2,6
Robert J. Fortuna

Corresponding Author: Robert J. Fortuna, e-mail: Robert_Fortuna@urmc.rochester.edu

Financial support: None declared
Conflict of interest: None declared

Patient: Female, 30-year-old
Final Diagnosis: Galactorrhea • supplement side effect
Symptoms: Galactorrhea
Medication: —
Clinical Procedure: —
Specialty: General and Internal Medicine • Toxicology

Objective: Unusual or unexpected effect of treatment
Background: The increasing popularity and availability of herbal supplements among patients necessitates a better understanding of their mechanism of action and the effects they have on the body, both intended and unintended. Stinging nettle (Urtica dioica) is an herbaceous shrub found throughout the world that has been used for medicinal purposes for centuries.

Case Report: A 30-year-old woman with obesity and GERD presented to a primary care clinic with new-onset galactorrhea. A urine pregnancy test was negative. Prolactin, thyroid-stimulating hormone (TSH), and a metabolic panel were all within normal limits. A mammogram demonstrated scattered areas of fibroglandular density and benign-appearing calcifications in the left breast. The breast ultrasound showed no suspicious findings. Her medications included intermittent Echinacea, etonogestrel implant 68 mg subdermal, and the supplement stinging nettle 500 mg, which she had been taking over the past month for environmental allergies. After consultation with a clinical pharmacist, the stinging nettle was discontinued. No additional changes to her medications or supplements were made. One week after discontinuation, she returned to the clinic with complete resolution of the galactorrhea.

Conclusions: Stinging nettle (Urtica dioica) is a common supplement and has effects on (1) sex hormone-binding globulin, (2) histamine-induced prolactin release, and (3) serotonin-induced release of thyrotropin-releasing hormone. The local estrogen bioactivity in breast tissue may subsequently lead to gynecomastia and/or galactorrhea. Supplements are an often overlooked but a critical component of medication reconciliation and potential clinical adverse effects.

Keywords: Dietary Supplements • Galactorrhea • Herbal • Urtica dioica

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/933999
Background

Stinging nettle (*Urtica dioica*) is an herbaceous shrub found throughout the world that has been used for medicinal purposes for centuries (Figure 1) [1,2]. It has been used to treat arthritis, muscular strains, tendinitis, insect bites, eczema, hay fever, anemia, benign prostatic hyperplasia (BPH), and urinary tract infections [2]. Despite its widespread use throughout history, there have been limited scientific studies demonstrating the efficacy of stinging nettle for most conditions and even fewer studies documenting risks and adverse effects. Stinging nettle is widely available, both on store shelves and online, and is advertised as a helpful, soothing remedy. This report describes an unusual case of galactorrhea, in which the timing of the development and resolution of symptoms suggested a possible association between the supplement stinging nettle and galactorrhea.

Case Report

A 30-year-old woman with a past medical history significant for obesity, GERD, and several abnormal pap smears presented to a primary care clinic with new galactorrhea. Three days prior to presentation, she developed intermittent white discharge from both breasts. The discharge occurred in the morning after showering and appeared like colostrum, similar to that seen in a prior pregnancy. At that time, she was seen in an urgent care facility and was prescribed antibiotics for a presumed breast infection, but she never received or took the antibiotic.

On the day of presentation, the patient was evaluated in person and a detailed history was obtained. She had no concerns for pregnancy. She had an etonogestrel implant in place for the past 1.5 years and she had not been pregnant or been breastfeeding in the past 2 years. Additional history was negative for any abnormal menstrual bleeding, skin changes, breast masses, or history of breast stimulation. Her medications included an etonogestrel implant placed 1.5 years ago, intermittent Echinacea, and stinging nettle 500 mg, which she started taking approximately 1 month prior for environmental allergies. Other than the introduction of the stinging nettle, there had been no other recent changes to her medications or supplement use. Review of systems was only notable for weight gain in the past few months. She denied any headaches, vision changes, abdominal pain, nausea, or vomiting. She denied any tobacco use, alcohol use, or illicit drugs.

A physical exam was notable for an anxious, tearful patient. Vital signs were within normal limits and BMI was 42 kg/m². Her breast exam demonstrated fibrocystic changes in both breasts and a small 0.5-cm, firm, non-mobile nodule in the right breast in the 4:00 position. There were no abnormalities of the skin overlying the breast or the nipples. A neurologic exam demonstrated normal strength, symmetric sensation, and intact visual fields.

A urine pregnancy test was negative. Prolactin, thyroid-stimulating hormone (TSH), and a metabolic panel were obtained, and all were within normal limits. Given the nodule felt on the initial exam, she was sent for mammogram and targeted bilateral breast ultrasound. The mammogram showed scattered areas of fibroglandular density and benign-appearing calcifications in the left breast. The ultrasound showed no suspicious findings.

Etonogestrel and stinging nettle were both considered as possible causative agents of the galactorrhea [3]. Etonogestrel has galactorrhea listed in the package insert as a rare postmarketing reaction [4]. The etonogestrel implant was not removed based on the patient’s preference, long-term stability with the implant, and continued desire for contraception. The patient continued Echinacea since she had tolerated this medication, but did not continue stinging nettle. The supplement stinging nettle alone was discontinued. One week after discontinuation, the patient returned to the clinic with complete resolution of the galactorrhea.

Discussion

The differential diagnosis for galactorrhea is broad, including pregnancy, breast stimulation, hyperprolactinemia, thyroid disease, medications, or malignancy [5]. Multiple medications that block dopamine receptors (eg, phenothiazines, metoclopramide, tricyclic antidepressants), deplete dopamine (eg, methyldopa), inhibit dopamine release (eg, morphine), or block histamine receptors (eg, cimetidine) have been associated with galactorrhea. Etonogestrel has galactorrhea listed in the package insert as a rare postmarketing reaction [4]. The etonogestrel implant was not removed based on the patient’s preference, long-term stability with the implant, and continued desire for contraception. The patient continued Echinacea since she had tolerated this medication, but did not continue stinging nettle. The supplement stinging nettle alone was discontinued. One week after discontinuation, the patient returned to the clinic with complete resolution of the galactorrhea.

*Figure 1. Stinging Nettle (*Urtica dioica*) [17].*
Table 1. Proposed mechanisms of *Urtica dioica*-induced galactorrhea.

| Potential mechanism                              | Description                                                                 |
|-------------------------------------------------|-----------------------------------------------------------------------------|
| Inhibition of Sex-hormone binding globulin (SHBG) | Inhibition of SHBG may result in increased levels of unbound estrogen which produce hormonal actions, including galactorrhea [2] |
| Histamine mediated                               | Histamine contained in the hairs of *Urtica dioica* may stimulate prolactin release [8-10] |
| Serotonin mediated                               | Serotonin has been isolated in *Urtica dioica*. Serotonergic inhibition of dopamine may stimulate prolactin release. Additionally, serotonin may stimulate thyrotropin-releasing hormone (TRH) which in turn stimulates prolactin release [9,11-14] |

the package insert as a rare post-marketing reaction, but this is rarely clinically observed [4]. Similarly, Echinacea does not have known associations with galactorrhea. After a thorough work-up, the patient’s galactorrhea was attributed to the supplement stinging nettle (*Urtica dioica*). Urtica dioica has been identified as a galactagogue in the literature, and this is the second case report of stinging nettle associated with galactorrhea in a non-breastfeeding woman [1,6,7].

Although the mechanism is not completely understood, there are several potential mechanisms postulated for *Urtica dioica* to induce galactorrhea (*Table 1*). *Urtica dioica* is thought to bind to sex hormone-binding globulin (SHBG) via its polar extracts and cause elevated serum estrogen levels. The local estrogen bioactivity in breast tissue may subsequently lead to gynecomastia or galactorrhea [2].

In addition to directly binding to sex hormone-binding globulin, *Urtica dioica* contains elements of histamine and serotonin. Histamine has been identified in the hairs and leaves of *Urtica dioica* [8,9]. Histamine is known to promote the release of prolactin, leading to further potential galactorrhea [10]. Urtica dioica has also been found to contain serotonin [9,11]. Several prior case reports have documented slightly elevated prolactin levels in patients taking serotonergic agents, including fluoxetine, escitalopram, and venlafaxine [12-14]. In these cases, serotonergic inhibition of dopamine or stimulation of thyrotropin-releasing hormone were suggested as the potential causative mechanism [14]. It is possible that the serotonin found in *Urtica dioica* similarly contributed to galactorrhea. Typically, patients with galactorrhea present with elevated prolactin levels. While our patient’s prolactin was within normal limits, pulsatile hormone secretion may yield variations in laboratory findings that were not captured on lab testing [5].

Supplements are an overlooked but critical component of medication reconciliation. Patients often misperceive herbal products as natural and low risk and may neglect to mention their use to health care providers [15]. Thus, it is important that patients are asked specifically about supplement use during medication reconciliation and in evaluation for suspected drug-related problems.

Unlike prescription and over-the-counter medications, the Food and Drug Administration does not require herbal supplements to undergo rigorous safety and efficacy testing prior to sales. This paucity of literature complicates proactive identification of adverse effects and potential interactions. Incidences of harm are thus collected most often through case reports. Accordingly, health care providers should remain vigilant about reporting adverse effects to the Food and Drug Administration, through MedWatch Online Voluntary Reporting Form (https://www.safetyreporting.hhs.gov). To maintain the provider-patient relationship, providers must balance respecting patient beliefs regarding supplement use with the best available evidence regarding safety and efficacy. To the best of their ability, providers should provide patients with guidance regarding safe use of herbal products. We find that the Natural Medications database is the most comprehensive source of such data [16].

**Conclusions**

Stinging nettle (*Urtica dioica*) is a common supplement and has the potential to induce galactorrhea. The proposed mechanisms of this galactorrhea are through effects on sex hormone-binding globulin, histamine-induced prolactin release, and serotonin-induced release of thyrotropin-releasing hormone. Through meticulous medication reconciliation and diligent reporting of adverse effects, a better understanding of herbal supplements and their effects can be obtained. It is important to consider which supplements patients are taking, especially in clinical scenarios where a clear diagnosis or causative agent cannot be found.

**Declaration of Figures’ Authenticity**

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.
References:

1. Lust JB. The Herb Book: The Most Complete Catalog of Herbs Ever Published. Mineola, New York: Dover Publications, Inc., 2014;1-617
2. Urtica dioica; Urtica urens (nettle). Monograph. Altern Med Rev, 2007;12(3):280-84
3. Visconti F, Zullo F, Marra ML et al. A new long-term reversible contraception method: Sexual and metabolic impact. Transl Med UniSa. 2012;4:86-89
4. Nexplanon [package insert], M. Co, Editor. Whitehouse Station, NJ, 2015
5. Harrison’s Principles of Internal Medicine, 20e., ed. Jameson JL, et al. McGraw Hill, 2020
6. Zapantis A, Steinberg IG, Schilt L. Use of herbs as galactagogues. J Pharm Pract. 2012;25(2):222-31
7. Sahin M, Yilmaz H, Gursoy A et al. Gynaecomastia in a man and hyperoestrogenism in a woman due to ingestion of nettle (Urtica dioica). N Z Med J. 2007;120(1265):U2803
8. Emmelin N, Feldberg W. The mechanism of the sting of the common nettle (urtica urens). J Physiol. 1947;106(4):440-55
9. Upton R. Stinging nettles leaf (Urtica dioica L): Extraordinary vegetable medicine. Journal of Herbal Medicine. 2013;3(1):9-38
10. Müller EE, Locatelli V, Cella S et al. Prolactin-lowering and -releasing drugs. Mechanisms of action and therapeutic applications. Drugs. 1983;26(4):399-432
11. Collier HQ, Chesher GB. Identification of 5-hydroxytryptamine in the sting of the nettle (Urtica dioica). Br J Pharmacol Chemother. 1956;11(2):186-89
12. Aggarwal A, Kumar R, Sharma RC et al. Escitalopram induced galactorrhoea: A case report. Prog Neuropsychopharmacol Biol Psychiatry, 2010;34(3):557-58
13. Peterson MC. Reversible galactorrhea and prolactin elevation related to fluoxetine use. Mayo Clin Proc. 2001;76(2):215-16
14. Sternbach H. Venlafaxine-induced galactorrhea. J Clin Psychopharmacol. 2003;23(1):109-10
15. Lynch N, Berry D. Differences in perceived risks and benefits of herbal, over-the-counter conventional, and prescribed conventional, medicines, and the implications of this for the safe and effective use of herbal products. Complement Ther Med, 2007;15(2):84-91
16. Natural Medicines Comprehensive Database. 2021;9/14/2021]. Available from: https://naturalmedicines.therapeuticresearch.com/
17. “Stinging Nettle stingi ng bits” by John Tann is licensed with CC BY 2.0. To view a copy of this license, visit https://creativecommons.org/licenses/by/2.0/