Duke University School of Medicine
PHYSICIAN ASSISTANT PROGRAM

Duke Endocrinology

Estrogen Monotherapy for Testosterone Suppression in Gender Diverse Patients

Christina Zhou, PA-S[1]; Quinnette Jones, MSW, MHS, PA-C[1]; Sarah Kokosa, PharmD, MHA[2]; Carly Kelley, MD, MPH, ECN[2]
1. Duke University Physician Assistant Program, Department of Family Medicine and Community Health
2. Duke Endocrinology, Duke University Health System

We take Pride in each other.

Background

Hormone therapy for gender diverse people assigned male at birth (AMAB) typically consists of estrogen in combination with anti-androgen medications.

- Exogenous estrogen use results in the development of feminine secondary sex characteristics while indirectly decreasing testosterone.[1]
- Anti-androgens such as spironolactone, leuprolide, finasteride, or dutasteride work to further suppress testosterone.[2]
- Use of anti-androgen can cause adverse side effects like hyperkalemia, polyuria, and orthostatic hypotension.

Anecdotally, estrogen monotherapy has been sufficient in reducing testosterone levels to goal in some patients, however there are no known studies which evaluate estrogen monotherapy and suppression of testosterone.

Purpose

The purpose of this chart review was to retrospectively identify estrogen formulations and dosages in patients with suppressed testosterone (<50 ng/dL) in the absence of anti-androgen medications.

Methods

The chart review was determined exempt by the Duke Health IRB committee and conducted in December 2023 at a single institution adult gender medicine endocrinology clinic housed within an academic medical center:

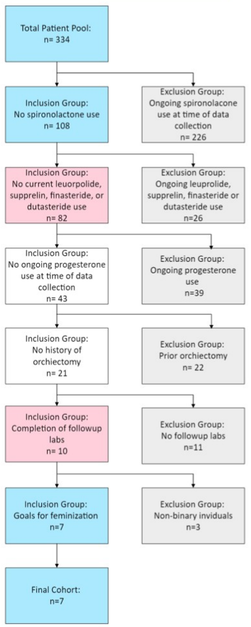
Inclusion criteria:

- Ages 18 - 84.99 years
- AMAB
- Estrogen use between Sept 2020 - Dec 2023

Exclusion criteria:

- Patients with ongoing use of anti-androgen medications at the time of data collection (including spironolactone, finasteride, dutasteride, bicalutamide, leuprolide, and supprelin implant)
- Progesterone use at time of data collection
- History of orchiectomy
- Missing labs for serum estradiol or total testosterone
- Treatment goals not consistent with full feminization

Estrogen formulations, dosages, and serum estradiol and testosterone values were recorded in addition to duration of hormone use and patient age.



Results

7 AMAB individuals met criteria from the original pool of 334 patients:

- Median age of individuals: 33 years
- Median duration on any hormone therapy: 3 years
- Median duration on estrogen monotherapy: 1 year
- Median estradiol level: 219 pg/mL
- Median testosterone level: 17 ng/dL

Estrogen formulations included injectable estradiol and transdermal patches:

- 4 patients (57%) utilized subcutaneous injections (4 mg or 5 mg weekly)
- 2 patients (29%) utilized intramuscular injections (6 mg or 8 mg weekly)
- 1 patient (14%) utilized transdermal patches (0.3 mg 3 times weekly)

Estradiol serum levels fell in 3 ranges:

- 3 of 7 (43%) patients had estradiol serum levels between 100-200 pg/mL
- 3 of 7 (43%) patients had mildly elevated levels between 201-250 pg/mL
- 1 patient (14%) had a marked elevation in estradiol level above 500 pg/mL

Successful testosterone suppression was achieved in most patients:

- 6 of 7 (86%) patients had serum testosterone levels <50 ng/dL
- 1 patient (14%) had serum testosterone levels at 74 ng/dL, though this is still within physiologic female range according to lab assay
- Patients that achieved testosterone suppression were able to maintain testosterone suppression on subsequent lab draws with continued therapy

Table 1: Age, medications, and resulting labwork of eligible patients

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age	64	57	36	33	31	30	21
Duration on any hormone therapy	3 years	1 year	4 years	3 years	7 years	1 year	2 years
Duration on estrogen monotherapy	2 years	1 year	0.75 year	3 years	3 years	0.5 year	1 year
Estrogen Formulation	Transdermal patches 0.3 mg 3x weekly	Estradiol Valerate 4 mg SC weekly	Estradiol Valerate 4 mg SC weekly	Estradiol Valerate 5 mg SC weekly	Estradiol Valerate 6 mg IM weekly	Estradiol Valerate 8 mg IM weekly	Estradiol Valerate 5 mg SC weekly
Last E2 Level (pg/mL)	239	200	246	219	140	678	127
Last T Level (ng/dL)	14	16	74	38	16	17	27

Conclusions

- Estrogen monotherapy may be adequate for suppressing testosterone without the need for anti-androgen medications.
- Injectable estrogen was the most common form of estrogen monotherapy in our patients and may be particularly effective in suppressing testosterone.
- Estrogen monotherapy may be a desirable option for feminizing hormone therapy for patients who wish to avoid anti-androgenic medications.
- Simplification of feminizing hormone therapy may reduce undesired side effects and decrease potential drug-drug interactions.

Limitations:

- Retrospective chart review model may omit potential confounding factors.
- Small sample size decreases ability to extrapolate data.

Future Areas of Research

Estrogen monotherapy considerations:

- Comparison of estrogen dosages and corresponding lab values between patients utilizing anti-androgen agents and patients avoiding anti-androgen agents to evaluate for differences required to achieve testosterone suppression with estrogen monotherapy.
- Comparison of patient reported outcomes for those completing estrogen monotherapy versus estrogen with anti-androgen treatment regimen.
- Further data collection on estrogen monotherapy with the use of patches or oral estradiol.

Dual estrogen and progesterone regimens:

- Progesterone has no current defined role in feminizing hormone regimens but is commonly utilized by transfeminine patients due to perception of assisting with breast development.
- Progesterone has been shown as effective for testosterone suppression in transfeminine individuals, and further studies using it as a substituted for other anti-androgens should be completed. [3]

References

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