

ORIGINAL RESEARCH—TRANSGENDER AND GENDER NONCONFORMANCE

Clinical Review: Breast Development in Trans Women Receiving Cross-Sex Hormones

Katrien Wierckx, MD,* Louis Gooren, MD, PhD,[†] and Guy T'Sjoen, MD, PhD*[‡]

*Department of Endocrinology, Ghent University Hospital, Ghent, Belgium; [†]AndroConsult, ChiangMai, Thailand;

[‡]Department of Sexology and Gender Problems, Ghent University Hospital, Ghent, Belgium

DOI: 10.1111/jsm.12487

ABSTRACT

Introduction. In trans women (male-to-female transsexual persons), cross-sex hormone therapy is administered to induce feminization. Breast development is an important part of feminization for most trans women.

Aim. The aim of this study is to assess the effect of cross-sex hormone therapy on breast development in adult trans women. Additionally, we aimed to investigate the benefit or harm of administration of progestogens on breast development.

Methods. A review of the literature in Embase, Medline, The Cochrane Library, PsycINFO databases, PubMed, and Web of Knowledge until January 2014.

Main Outcome Measures. Effects of cross-sex hormone therapy and progestogens on breast development in trans women.

Results. Only few studies with low quality of evidence addressed these topics. The available evidence suggests that breast development is insufficient for the majority of trans women and that type and dosage of hormonal therapy seem not to have an important role on final breast size.

Conclusions. Our knowledge concerning the natural history and effects of different cross-sex hormone therapies on breast development in trans women is extremely sparse and based on low quality of evidence. Current evidence does not provide evidence that progestogens enhance breast development in trans women. Neither do they prove the absence of such an effect. This prevents us from drawing any firm conclusion at this moment and demonstrates the need for further research to clarify these important clinical questions. **Wierckx K, Gooren L, and T'Sjoen G. Clinical review: Breast development in trans women receiving cross-sex hormones. J Sex Med 2014;11:1240–1247.**

Key Words. Transsexualism; Progesterone; Breast; Side Effects; Breast Cancer

Introduction

The current treatment regimens of most trans women (male-to-female trans persons) involve hormonal therapy as well as sex reassignment surgery (SRS). The aims of hormonal treatment are mainly to induce feminization which consists of breast formation, reduction of masculine hair growth, and a more female fat distribution [1]. In addition to inducing physical changes, the act of using cross-sex hormones is itself an affirmation of gender identity in many trans persons.

With regard to the hormonal impact on female breast development, the classic view is that estrogens induce proliferation, whereas progestins cause differentiation in female breast development [2,3]. It is widely assumed that progestins have no significant role in the formation of the volume of the breasts, the reason why it is not included in endocrine treatment of girls with Turner and juvenile trans women persons [1]. The first physical sign of puberty in girls is usually a firm, tender lump under the center of the areola of one or both breasts. By the widely used Tanner staging of

puberty, this is stage 2 of breast development (stage 1 is a flat, prepubertal breast). Within 6–12 months, the swelling has clearly begun in both sides, softened, and can be felt and seen extending beyond the edges of the areolae, described as stage 3 of breast development. By another 12 months (stage 4), the breasts are approaching mature size and shape, with areolae and nipples forming a secondary mound. In most young women, this mound disappears into the contour of the mature breast (stage 5), although there is so much variation in sizes and shapes of adult breasts that stages 4 and 5 are not always separately identifiable [2,4].

A number of studies have demonstrated the efficacy of several hormonal preparations to induce feminization in trans persons, but these observations are rather of a subjective than of an objective nature, in the sense that the feminization has not been quantified [5–8]. These treatment regimes mostly combine estrogen treatment with anti-androgen and/or gonadal axis suppressing medication. In Europe, cyproterone acetate, a progestational agent with androgen receptor-blocking properties, is commonly used before SRS, usually preceding or in combination with estrogens [8,9]. Thus, most trans women in Europe receive in fact a compound with progestational properties before SRS, though cyproterone acetate is not administered for its progestational properties but for its efficacy as an oral anti-androgen. As there is no FDA approval of cyproterone acetate, many centers in the United States use spironolactone, a diuretic with mainly anti-androgen but also a weak estrogenic [10] and progestational activity [11]. Other agents with anti-androgenic properties used are nonsteroidal androgen receptor blockers, such as flutamide and bicalutamide or 5-alpha reductase inhibitors such as finasteride and dutasteride. Several centers use gonadotropin-releasing hormone (GnRH) analogs to suppress androgen production [12,13], but the use of GnRH analogs is limited mainly because of its high costs [13]. Some clinicians also prescribe progestogens to decrease the doses of estrogens required for complete suppression of testosterone levels [14].

After SRS which involves orchidectomy, penectomy, and vaginoplasty, estrogen therapy is to be continued alone, and many centers discontinue agents blocking testosterone action or reducing testosterone levels and generally do not prescribe progestogens after SRS [8,9].

Postpubertal women show a large degree in size and shape of breast development [2]. Trans women are primarily interested in a sufficient degree of

breast development confirming the gender role of a woman to themselves and to the outside world. Although there is undeniably a role of progesterone in breast development and lactation, it is uncertain whether the treatment of progestogens adds much to the volume of the breasts, the concern of trans women.

This review will discuss the current knowledge on breast development during cross-sex hormone treatment. The second aim of this literature review is to investigate whether there is a specific role of progestogens relevant to breast development of trans women. In the medical profession and even more in the transsexual community, there has been an ongoing debate for many years on the potential benefit of adding progestogens to estrogen use in trans women's hormonal treatment, especially concerning its role in the volume/size breast development and maintenance. Progestagen treatment is also often requested by trans women themselves as it is their perception that their treatment should closely mimic hormonal treatment of hypogonadal women requiring hormone treatment. However, for the latter group, addition of progestogens has a different relevance, specifically the modifying estrogen effects on the uterus potentially inducing cancerous development.

Methods

We searched through the following electronic databases up to January 2014: Embase, Medline, The Cochrane Library, PsycINFO databases, PubMed, and Web of Knowledge. Search terms included “breast” and “trans,” and “transsexual” or “transgender.” We also searched on “cross-sex hormone therapy,” “hormone therapy,” “estrogen,” “progestins,” “progestogens,” “progesterone” and “trans,” and “transsexual” or “transgender” as some papers on endocrine treatment of trans persons included a section on breast development. English language articles in peer-reviewed medical journals concerning the effects of cross-sex hormone therapy and progestogens in adult trans women on breast size and breast growth were retrieved and reviewed for content. Also, the references of these papers were used to identify other literature of interest. Articles addressing surgical techniques or surgical complications and histological findings were excluded.

Results

The development of breasts in pubertal girls has been described in the Introduction highlighting

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