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Influence of Postoperative Finasteride Therapy on Recurrence of Gynecomastia After Mastectomy in Men Taking Finasteride for Alopecia

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Abstract

Finasteride is commonly used for treatment of alopecia. Because finasteride is a cause of gynecomastia, there is concern regarding the continuation of finasteride therapy after mastectomy. No studies have been performed to determine whether finasteride should be continued after mastectomy when gynecomastia occurs in patients taking finasteride for the treatment of alopecia. The researchers studied the effects of finasteride on gynecomastia recurrence after mastectomy in men with gynecomastia taking finasteride for alopecia. The researchers retrospectively evaluated 1,673 patients with gynecomastia who underwent subcutaneous mastectomy with liposuction at Damsoyu Hospital from January 2014 to December 2016. In total, 52 of the patients were taking finasteride for alopecia before surgery and continued to use it in the same manner after mastectomy. Ultrasonography was performed 1 year after mastectomy. The patients' median age was 26.5 (24.75–30) years. All 52 patients had bilateral gynecomastia. The median duration of finasteride therapy before and after surgery was 12 (5–25.75) and 33 (27.5–40.5) months, respectively. There were no statistically significant differences between the groups with and without the use of finasteride in relation to postoperative complications and recurrence rates. Taking finasteride seems to have little effect on recurrence in patients with alopecia who have undergone surgical treatment of gynecomastia. Surgeons may recommend continuous finasteride therapy in patients with alopecia who wish to take finasteride after mastectomy.

Keywords

gynecomastia, alopecia, mastectomy, finasteride

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Gynecomastia develops in 30% to 70% in men after adolescence (Carlson, 1980; Niewoehner & Nuttall, 1984; Nuttall, 1979). There are many causes of gynecomastia, including finasteride therapy (Narula & Carlson, 2014; Traish, Hassani, Guay, Zitzmann, & Hansen, 2011). Finasteride is a 5-alpha reductase inhibitor that is mainly used for the treatment of benign prostatic hyperplasia and alopecia (Traish et al., 2011). Finasteride may inhibit the production of 5-alpha dihydrotestosterone (5α-DHT), 5-alpha dihydroprogesterone (5α-DHP), and 5-alpha dihydrodeoxycorticosterone (5α-DHDOC) in the body and induce various adverse effects collectively termed post-finasteride syndrome (erectile dysfunction, ejaculatory dysfunction, change in libido, gynecomastia, memory and attentional disturbances, increased anxiety, depressed

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mood, and others, some of which may be reversible and some irreversible; Ganzer, Jacobs, & Iqbal, 2015; Traish et al., 2011). The inhibition of 5a-DHT increases estradiol levels, which are thought to stimulate mammary tissue growth resulting in the development of the gynecomastia (Dimitrakakis, Zhou, & Bondy, 2002; Traish et al., 2011).

Alopecia is a common disease with a prevalence of about 30% and 50% among White men aged 30 and 50 years, respectively (Alfonso, Richter-Appelt, Tosti, Viera, & Garcia 2005). Alopecia is effectively treated with finasteride (Mella, Perret, Manzotti, Catalano, & Guyatt, 2010). Usually, 1 mg of finasteride is used for the treatment of alopecia, and a complication of this dose is gynecomastia (Ramot, Czarnowicki, & Zlotogorski, 2009). Gynecomastia can require treatment when symptoms such as breast pain, tenderness, sensitivity, and emotional and psychological stress are present (Fruhstorfer & Malata, 2003; Narula & Carlson, 2014). Among the patients who require treatment for gynecomastia, some are taking or planning to take finasteride for treatment of alopecia. Deciding whether finasteride should be continued or discontinued after mastectomy for treatment of gynecomastia in patients taking finasteride is a very difficult problem for surgeons. Based on the principle of finasteride's effect on gynecomastia, removal of the mammary tissue during the operation seems to have little effect on the recurrence. Also, to the best of the authors' knowledge, no reports have described the effect of continuous administration of finasteride on the recurrence of gynecomastia after mastectomy. Therefore, the purpose of this study is to investigate the effect of finasteride on the recurrence of gynecomastia after mastectomy in men.

Materials and Methods

The researchers retrospectively evaluated 1,673 patients with gynecomastia who underwent subcutaneous mastectomy with liposuction at Damsoyu Hospital from January 2014 to December 2016. The inclusion criterion for patients with gynecomastia who were candidates for surgical treatment was a 3-year history of either (a) persistent breast enlargement or symptoms including mastalgia or (b) persistent breast enlargement and related psychosocial/emotional distress. This study included patients who had gynecomastia prior to taking finasteride and those who took the medication before undergoing mastectomy and continued to take even after the surgery. Of the 1,673 patients, 52 were taking finasteride and 1,621 were not taking finasteride.

Before the surgery, a detailed medical history was obtained and physical examination was performed to detect secondary causes of gynecomastia. Patients taking finasteride were included in the study, and those patients taking medications that could cause secondary gynecomastia such as anabolic steroids, androgen, and ranitidine were excluded from the study. The grade of gynecomastia was determined according to Simon's classification (Simon, Hoffman, & Kahn, 1973). All patients underwent breast ultrasonography prior to surgery to confirm the presence of the mammary gland tissue. Patients without glandular tissue on breast ultrasonography were excluded. After the operation, all resected tissues were weighed and histopathologically examined. The volume of fat obtained by liposuction was measured.

Surgical Technique and Follow-Up

All patients underwent surgery with general anesthesia. A 2-cm-long inferior periareolar semicircular incision was made and tumescent solution (1,000 ml of 0.9% normal saline, 20 ml of 2% lidocaine, 20 ml of 8.4% sodium bicarbonate, and 1 ml of 1:1,000 epinephrine) was evenly injected into the breast tissue through the incision. Liposuction was performed using a power-assisted liposuction device (Liposlim®; Nanum Medical Inc., Seoul, Korea). The mammary glands were completely excised (Figure 1), and the supramammary fatty layer was addressed with liposuction. The incision was closed using absorbable suture material in a subcuticular manner (Vicryl 4-0; Ethicon Inc., Somerville, NJ, USA). The wound was then covered with Steri-Strips™ (3M, Maplewood, MN, USA).

The patients were followed up for 1, 3, and 6 months postoperatively to evaluate the shape of the breast and the development of any complications (Figure 2). Recurrence of symptoms and the use of finasteride were investigated once a year or more frequently according to the patients' needs; after an operation for benign disease, many patients choose to discontinue follow-up if no uncomfortable symptoms are present or when the surgical outcome is satisfactory. If the patient did not respond to the follow-up or was unable to visit the hospital for any reason, the investigation was achieved through telephone counseling. Breast ultrasonography was performed in all patients 1 year postoperatively and in patients with recurrence of pain, tenderness, or breast enlargement. If proliferation of the mammary gland tissue was confirmed by ultrasonography, patients were diagnosed with recurrence.

Satisfaction Assessment Methods

Postoperative satisfaction surveys regarding breast symmetry and cosmetic outcomes were conducted 3 months postoperatively. Patient satisfaction was measured with pain and cosmesis separately using a 5-point Likert scale (1: *continuous pain, very unsatisfactory appearance*; 2: *some pain, unsatisfactory appearance*;

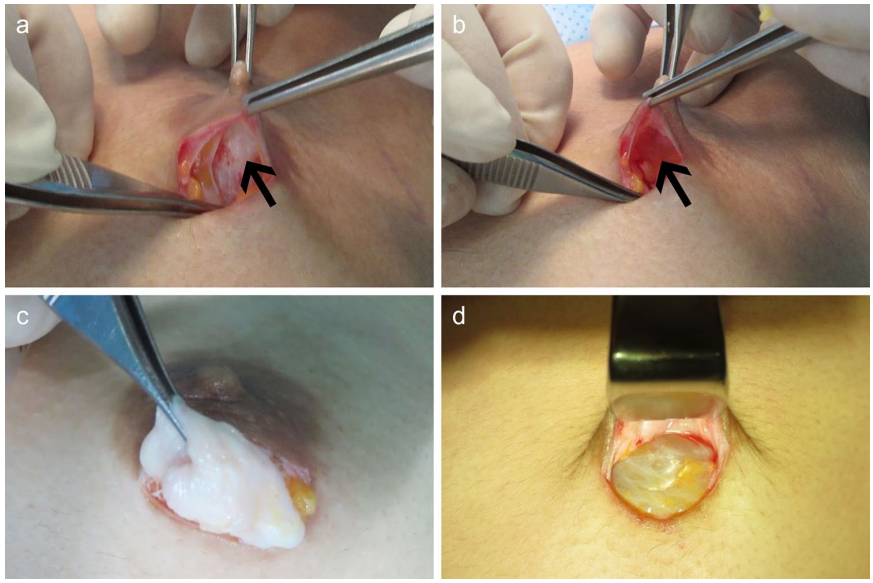

Figure 1. Surgical technique. (a) Mammary tissue attached to the nipple. (b) Complete separation of mammary tissue from nipple. (c) Complete excision of mammary tissue. (d) The submammary fat layer is visible, and no remnant mammary tissue is present.

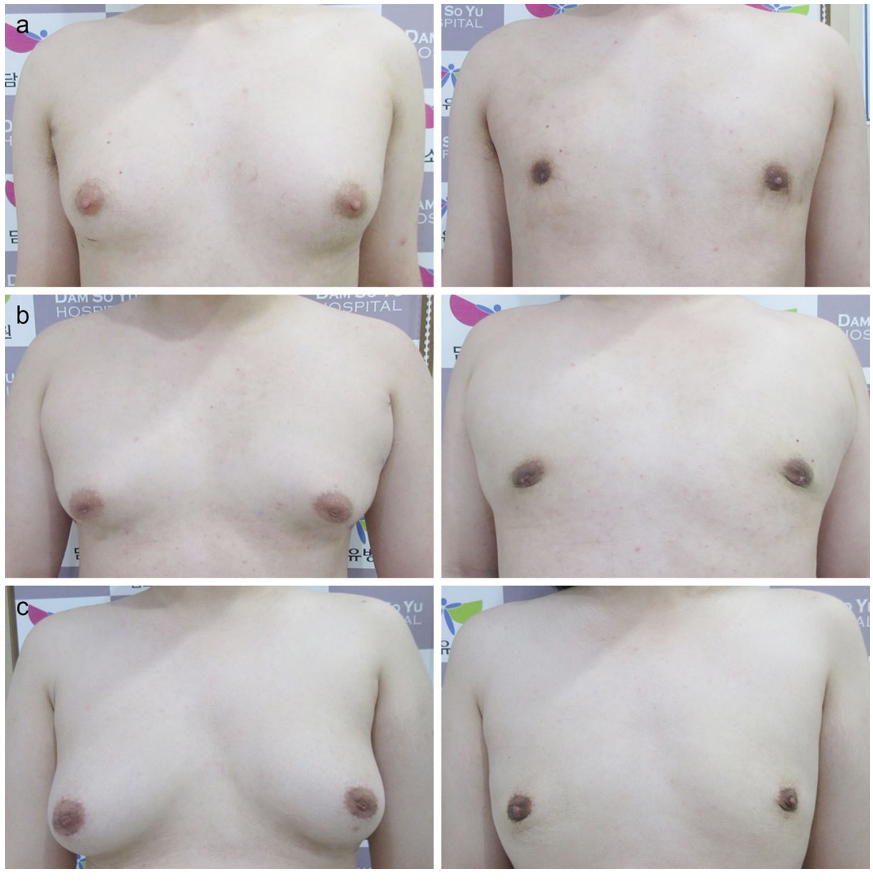

Figure 2. Preoperative and postoperative appearance of gynecomastia in a patient. (a) Simon's class I in a 30-year-old man. (b) Simon's class IIA in a 32-year-old man. (c) Simon's class IIB in a 22-year-old man.

Table 1. Patient Characteristics.

	Patients taking finasteride ($N = 52$)	Patients not taking finasteride ($N = 1{,}621$)	p value
Age, years	26.5 (24.75–30)	25 (22–30)	.017
Body mass index, kg/m^2	24.55 (22.95–26.45)	25 (23.2–27.4)	.253
Simon's classification			.133
I	4 (7.7)	38 (2.3)	
IIA	37 (71.2)	1117 (68.9)	
IIB	11 (21.2)	454 (28.0)	
III	0 (0.0)	12 (0.7)	
Follow-up period, months	48 (38.5–56)	47 (39–56)	.563
Duration of finasteride use before surgery, months	12 (5–25.75)		
Duration of finasteride use after surgery, months	33 (27.5–40.5)		

Note. Data are presented as median (interquartile range) or *n* (%). Categorical variables were tested by chi-square test or Fisher's exact test. Continuous variables were tested by independent sample *t* test or Wilcoxon rank sum test.
p value is rounded to the fourth decimal place and the remaining values are rounded to the third decimal place.

3: *neither*; 4: *little pain, satisfactory appearance*; and 5: *no pain, very satisfactory appearance;* Ridha, Colville, & Vesely, 2009).

Statistical Analysis

All statistical analyses were performed using R software version 3.4.3 (R Development Core Team, Vienna, Austria; http://www.R-project.org). Continuous variables are presented as mean ± standard deviation for normally distributed data and as median and interquartile range for nonnormally distributed data. The Shapiro–Wilk test was used to check for normality of the continuous variables. Categorical variables are presented as frequency and percentage.

Results

The patients' characteristics are presented in Table 1. In total, 52 patients were taking finasteride for treatment of alopecia before mastectomy. The median duration of finasteride therapy before and after surgery was 12 (5–25.75) and 33 (27.5–40.5) months, respectively. There were no statistically significant differences between the groups with and without the use of finasteride with respect to the median age, body mass index and the weight of the mammary tissue removed, and the mean volume of fat obtained from liposuction. Postoperative complications and recurrence rates were not significantly different between the two groups. No recurrence was noted during the follow-up period in the group of patients taking finasteride. Most of the patients were satisfied with the operation results with a median satisfaction score of 5 (4–5) and no statistical differences were identified between the two groups ($p = .530$). The surgical outcomes are presented in Table 2. Eight of the patients who did not take finasteride received reoperation, which was mainly performed to correct the skin contour. In detail, five patients were treated with liposuction and adhesiolysis, and the remaining three received scar revision, nipple reduction, and redundant skin excision, respectively.

Discussion

Gynecomastia generally occurs due to an imbalance between androgen and estrogen hormones. Estrogen promotes breast growth while androgen inhibits it (Braunstein, 1999; Dimitrakakis et al., 2002). An imbalance in the androgen-to-estrogen ratio can be caused by increased levels of estrogen in the blood and decreased levels of androgen or impaired androgen receptors (Braunstein, 1999; Hedlund & Henriksson, 2000; Kanhai, Hage, van Diest, Bloemena, & Mulder, 2000; Klein et al., 1999; Staiman & Lowe, 1997).

Finasteride is a 5-alphareductase inhibitor that mainly acts on type 2 5-alphareductase, inhibiting the conversion of testosterone to DHT and reducing serum DHT by about 70% (Bartsch, Rittmaster, & Klocker, 2002; Traish et al., 2011). When the synthesis of DHT is reduced, the metabolism of testosterone can move toward estradiol, resulting in a change in the ratio of estrogen to androgen, which increases the risk of gynecomastia (Ganzer et al., 2015; Traish et al., 2011).

Finasteride has been used at a dosage of 5 mg/day for benign prostate hyperplasia and prostate cancer prevention, and gynecomastia may be a common complication in such patients (Green, Wysowski, & Fourcroy, 1996; Hagberg, Divan, Fang, Nickel, & Jick, 2017; Miller

Table 2. Surgical Outcomes.

	Patients taking finasteride ($N = 52$)	Patients not taking finasteride ($N = 1{,}621$)	p value
Weight of the specimen, g	74.5 (40.25–114)	81.5 (54–121)	.337
Liposuction volume, ml	392.4 ± 186.8 (106–842)	404.5 ± 284.7 (100–2445)	.563
Operation time, min	51.0 ± 9.7 (40–65)	51.6 ± 6.0 (40–70)	.126
Hospital stay time, hr	8 (7–9.25)	8 (7–10)	.661
Complications			.280
Hematoma	2 (3.8)	41 (2.5)	
Seroma	3 (5.8)	35 (2.2)	
Satisfaction score	5 (4–5)	5 (4–5)	.530
Reoperation			
Recurrence	0 (0.0)	0 (0.0)	
Correction of skin contour	0 (0.0)	8 (0.5)	1.000

Note. Data are presented as median (interquartile range), mean ± standard deviation (range), or *n* (%). Categorical variables were tested by chi-square test or Fisher's exact test. Continuous variables were tested by independent sample *t* test or Wilcoxon rank sum test. *p* value is rounded to the fourth decimal place and the remaining values are rounded to the third decimal place.

Pramanik, & Gilhooly, 1999). In the Prostate Cancer Prevention Trial, gynecomastia was a common complication of finasteride (Thompson, Tangen, Goodman, Lucia, & Klein, 2009). Notably, gynecomastia did not occur in double-blind, placebo-controlled, randomized, multicenter studies or in large studies on the treatment of alopecia with finasteride at a dose of 1 mg/day (Kaufman et al., 1998). However, 0.4% of breast-related adverse events were observed in the same study, and many cases of finasteride-induced gynecomastia have been reported at a dose of 1 mg (Ferrando, Grimalt, Alsina, Bulla, & Manasievska, 2002; Mansouri, Farshi, & Safar, 2009; Ramot et al., 2009; Wade & Sinclair, 2000). Therefore, a low dose of finasteride cannot be expected to have no effect on gynecomastia.

In the present study, 52 patients who underwent mastectomy were taking finasteride for the treatment of alopecia. Finasteride is relatively well known to induce gynecomastia, but the effect of finasteride on the recurrence of gynecomastia after mastectomy is unknown. No case reports have described patients taking finasteride for alopecia after mastectomy for finasteride-induced gynecomastia (Ferrando et al., 2002; Mansouri et al., 2009; Ramot et al., 2009; Wade & Sinclair, 2000). In principle, even if a hormonal imbalance occurs due to finasteride, complete resection of the mammary gland should not be associated with recurrence because no mammary gland is present to undergo stimulation and growth. No study has evaluated the effect of taking finasteride after surgery on the prognosis; this prevents surgeons from providing an adequate explanation of the possibility of drug-induced recurrence in patients who want to take finasteride after mastectomy. Recurrence mainly presents as regrowth of adipose tissue and mammary tissue due to incomplete resection of mammary tissue during the initial surgery (Fricke, Lehner, Stark, & Penna, 2017; Innocenti, Melita, Mori, Ciancio, & Innocenti, 2017). In this study, surgeons performed complete excision of the glandular tissue for treatment of gynecomastia. No patients taking finasteride after mastectomy developed recurrence. This suggests that finasteride for alopecia treatment has no effect on recurrence after complete resection of the mammary gland.

This study had some limitations. It was a retrospective study with a limited number of patients. Although 52 patients may seem to be a small sample, the number of patients taking finasteride for treatment of alopecia and undergoing mastectomy for gynecomastia seems to be significant. The patients included in the present study were already taking finasteride preoperatively, but it was difficult to determine the effect of drug administration on the incidence and severity of gynecomastia. For these reasons, the researchers' ability to evaluate the effect on the prognosis was also limited. Therefore, future studies of finasteride-induced gynecomastia will need to evaluate the effects of finasteride on the prognosis in patients who are more susceptible to drugs. Most patients did not have a hormonal study. As Malhotra et al. and Boccara et al. have pointed out, routine hormonal studies in all gynecomastia patients are not cost-effective and do not significantly alter treatment outcomes (Boccara et al., 2019; Malhotra, Amed, Bucevska, Bush, & Arneja, 2018). So evaluation of the effect of finasteride on the hormonal status of patients before and after the surgery was unobtainable. Hence, there is a limit to theoretically explaining the effect of finasteride on postoperative recurrence. However, continuous postoperative treatment with finasteride does not affect recurrence in patients who had been taking finasteride even before the surgery, which seems to be very important information for the surgeons performing the operation. Therefore, further studies including the hormonal status of the patients will be needed in the future.

Conclusion

The present study has indicated that after complete excision of the mammary gland, finasteride treatment might not affect the recurrence of gynecomastia; however, additional prospective studies are needed. Surgeons may recommend continuation of finasteride in patients who wish to take it after mastectomy for gynecomastia.

Authors' Note

This study was presented as a Poster Presentation in the Global Breast Cancer Conference 2018 (November 3, 2018, Incheon, Republic of Korea).

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Declaration of Conflicting Interests

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Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards and was approved by the Institutional Review Board of Damsoyu Hospital: DSY-2017-017.

Informed Consent

Written informed consent was obtained from all individual patients or their parents/guardians.

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