

Letter to the Editor Regarding “Effect of Propolis on Precocious Puberty in Female Rats” - Does Propolis Induce Thelarche and Gynecomastia in Prepubertal Children?

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Dear Editor,

Propolis is a product obtained from plants by honeybees and has been reported to have various biological effects such as anti-inflammatory, anti-microbial, anti-viral, and anti-oxidative. It consists of a mixture of various chemicals such as flavonoids, coumaric acid, and caffeic acid, some of which have phytoestrogenic effects (1). Phytoestrogens are substances that are structurally and functionally like estrogens. In vivo experiments on rats have shown that phytoestrogens bind to estrogen receptors and cause ductal cell proliferation in the uterus and mammary glands without an increase in endogenous estrogen production (1,2,3). Okamoto et al. (1) reported that propolis induced the expression of estrogen-responsive genes in their study on ovariectomized rats.

In this context, we read the article “Effect of Propolis on Precocious Puberty in Female Rats” recently published in your journal, with interest (3). We aimed to contribute to this article by reporting 4 girls and 4 boys who presented to our outpatient clinic with premature thelarche and prepubertal gynecomastia and had a history of propolis use.

Four girls aged between 4.9 and 8.2 years presented with breast development that had been present for an average of two months. They did not describe a growth spurt or a family history of precocious puberty. Their height and body mass index (BMI) standard deviation score (SDS) ranged

between -0.17 – 0.67 SDS and -0.16 – 1.2 SDS respectively. Three girls had breast budding which is consistent with Tanner stage 2, and one girl had breast development consistent with Tanner stage 3. None of them did have pubic hair. All of them had luteinizing hormone (LH) levels <0.1 IU/L and E2 levels <5 pg/mL, and their FSH levels were between 0.3-2.8 IU/L. Uterus, ovary, and endometrial thickness in ultrasonography were compatible with the prepubertal period. Bone ages were compatible with their own ages. Prepubertal LH response was obtained in the LHRH stimulation test.

The ages of boys presenting with prepubertal gynecomastia ranged from 2.4 to 10 years. They did not describe a growth spurt. Their family history was unremarkable for gynecomastia. Only one had bilateral gynecomastia, while the others had unilateral gynecomastia. All had bilateral prepubertal testicular sizes (below 4 cc) and they had no pubic hair. Their height and BMI SDS ranged between -0.97 – 1.21 and -1.3 – 0.17 2 SDS respectively. Serum FSH, LH, total testosterone levels were prepubertal. All had normal serum estradiol and prolactin levels. All were reported to take oral propolis drop for a mean of 3.9 months (2-12 months). After the cessation of propolis intake, breast development resolved in all cases at the mean follow-up visit 3 months later.

Premature thelarche is characterized by isolated breast development in girls without other pubertal signs and



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prepubertal gynecomastia is a rare condition characterized by the presence of unilateral or bilateral breast tissue in boys without other pubertal signs. The use of drugs and herbal products containing phytoestrogens can cause premature thelarche and prepubertal gynecomastia. Ramsey et al. (4) reported three cases of premature thelarche and one case of prepubertal gynecomastia with the use of fragrances containing lavender, a phytoestrogen-containing product. In the article published in your journal (3), it was shown that propolis, probably triggers precocious puberty in female rats by interacting with estrogen receptors, and the regression of breast development in our patient group with the discontinuation of propolis intake suggested that propolis may trigger mammary duct proliferation with its phytoestrogenic effects in prepubertal children.

Ethics

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: Elif Eviz, Gül Yeşiltepe Mutlu, Şükrü Hatun,
Design: Elif Eviz, Gül Yeşiltepe Mutlu, Şükrü Hatun, Data

Collection or Processing: Elif Eviz, Gül Yeşiltepe Mutlu, Sebahat Yılmaz Ağladioğlu, Şükrü Hatun, Literature Search: Elif Eviz, Gül Yeşiltepe Mutlu, Şükrü Hatun, Writing: Elif Eviz, Gül Yeşiltepe Mutlu, Şükrü Hatun.

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