

Role of Pro-Anthocyanidin in Gynecomastia and Related Oligospermia and Asthenospermia

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Abstract

A case of 15 years old boy, with gynecomastia, absence of secondary sexual characters, low sperm count and low sperm motility on semen analysis is presented. His hormonal profile was normal for age. The patient was prescribed proanthocyanidin 75 mg dosage twice a day and followed up regularly. In the following 5 years, his gynecomastia improved, secondary sexual characters appeared and sperm count normalized. The case is described for the novel indication of proanthocyanidin in treating gynecomastia, oligo- and asthenospermia in the presence of a normal hormonal profile. Its plausible mode of action is debatable.

Keywords: Asthenospermia; Gynecomastia; Oligospermia

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Introduction

Gynecomastia [1] /ˌɡaɪnɪkəˈmæstɪə/ is a common endocrine disorder in which there is a benign enlargement of breast tissue in males [2,3]. Most adolescent boys, up to 70%, [4,5] have some breast development during puberty [2]. Newborn and adolescent males frequently experience temporary gynecomastia due to the influence of maternal hormones and hormonal changes during puberty, respectively. The treatment options [5] are too few and far between, proanthocyanidin seems a plausible alternative.

Patient and methods

A 15 year-old-student had reported on March 28, 2009 with asymptomatic, insidiously enlarging swelling in and around both the nipples for the past couple of years so much so it acquired the size of the breast or gynecomastia (**Figure 1**). There were neither nocturnal emissions of seminal fluid while asleep nor was there semblance of any hair growth. Weak orgasm was not pleasurable. There was absence of hair above the upper lip and chin, the secondary sexual characters. Pubic hairs were scanty. The penis was small. Testes too were small and soft. His height was 170.18 centimeter while weight was 65 Kg.

Ultrasonography of the scrotum: Right testes measured 50 × 24.8 mm, while left testes measured 48 × 20.7 mm. Both the testes had uniformly reduced echogenecity. Neither calcification nor para-testicular fluid was seen in either of the testes, suggesting bilateral testicular atrophy.

The semen analysis [5] and hormonal profile [6] was done on

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regular interval starting from the day of reporting to evaluate its status, the synopsis of which are portrayed in the adjoining **Tables 1 and 2**. He was administered proanthocyanidin (GRAVINOI) orally in the doses of 150 mg a day in two equal divided doses of 75 mg each for a period of three months. Follow up was done every month for first 3 months, every three months for 6 months, every



Figure 1 Displaying bi-lateral enlargement of the breast, the gynecomastia.

Table 1 Semen Analysis.

Period of Abstinence <3 days	Results 2009	Results 2012	Results 2014	Range	Units	Biological Reference Interval
Time of collection	2:52 PM	13:55 PM	3:50 PM	-	-	-
Volume	4.5	4.0	3.5	-	ml	1.5-6.8
PH	Alkaline	Alkaline	8.0	7.0-8.0		> or =7.2
Color	Whitish	Whitish	Gray-white	-	-	-
Liquifaction	30	-	70		Minutes	High 15-60
Viability	Low 40	-	72	50-100	%	> or =58
Motility	50	50	42	50-100		> or = 40
Motility-Grade 0	50	50	28		%	Low 32-72
Motility-Grade 1&2	40	20	14	-	%	1-18
Motility-Grade 3&4	10	30	58	-	%	22-59
Sperm Count	Low 02	45	38	20.0-150.0	Mill/ml	15-213
Abnormal Forms	10	-	13	0-20	%	-
Head	05	-	8	-	%	-
Pin Heads	02	-	2	-	%	-
Giant Heads	02	-	1	-	%	-
Double Heads	01	-	0	-	%	-
Neck	02	02	-	-		-
Bent	01	01	-	-	%	-
CYT(Cytoplasm)	01	01	-	-	%	-
Tail	03	03	5	-	%	-
Short Tail	01	01	1	-	%	-
Curled Tail	02	02	-	-	%	-
Red Cells	0-1	-	Not Detected	Not detected	/hpf	Not Detected
Pus Cells	2-3	3-5	0-1	0-5	/hpf	0-5
Epithelial cells	0-1	1-2	Not Detected	0-5	/hpf	0-5
Crystal	-	-	Not Detected	-	-	Not Detected
Amorphous Deposit	-	-	Not Detected	-	-	Not Detected
Bacteria	-	-	Not Detected	-	-	Not Detected

Table 2 Hormonal Profile.

Hormones Method: Chemiluminescence	March.28, 2009	Aug. 4, 2010	Dec.30, 2014	Biological Reference Interval
Follicle Stimulating Hormone(F.S.H)	3.58 mIU/ml	2.36 mIU/ml	2.76 mIU/ml	1.40-18.10
Luteinising Hormone(L.H)	3.16 mIU/ml	8.06 mIU/ml	6.01 mIU/ml	1.50-9.30
Prolactin	14.09 ng/ml	12.40 ng/ml	6.30 ng/ml	2.10-17.70
Testosterone	12.76 ng/ml	207.78 ng/ml	467.40 ng/ml	241.00-827.00

six months for a year, every year for 2, 3 and 4 years respectively. During the period in addition to physical checkup semen analysis and hormonal profile was also undertaken at regular intervals (**Tables 1 and 2**) at the end of 4 years treatment, a substantial change in his physique was apparent. The growth of hair on the upper lip, chin, beard and pubic area were striking so also was his current height (190.5 centimeter) and weight (95 kg). There was marked improvement in gynecomastia, low sperm count (oligospermia) and low motility (asthenospermia) on semen analysis (**Table 1**).

Discussion

Pharmacokinetics

Proanthocyanidins (pycnogenol), are a class of polyphenols,

discovered, developed and patented for the extraction of oligomeric proanthocyanidins from pine bark and grape seeds for the first time in the year 1947 by Jacques Masquelier [7]. They are oligomeric flavonoids [8], many of which are catechin and epicatechin, and their gallic acid esters. Colorless proanthocyanidins are a strictly defined group of 3 flavanols naturally occurring as a mix of monomers, di-mers, and tri-mers of the catechin building block, which is a 4 × -hydroxylation of the flavan-3-olcore.

Mode of action

Proanthocyanidin (Pycnogenol), a type of flavonoid and antioxidant is found in the skin of fruits and vegetables. It plays an important role in blood vessels, and helps in stabilizing collagen [9,10] and maintenance of elastin [11] within the body. Collagen

and elastin are the two principle proteins, which are used in the formation of connective tissue in the body. In addition, it inhibits platelet aggregation and vascular constriction; thus preventing stroke [12-15]. Furthermore, it increases intracellular vitamin c levels, scavenges oxidants and free radicals. Hence it inhibits destruction of collagen. Besides, sleepiness, loss of appetite, skin rashes, nausea and itching are its adverse reactions. It is contraindicated in those with known hypersensitivity to grape seed. Its safety and efficacy in pregnancy and lactation is lacking. Concomitant administration of Proanthocyanidin, and vitamin C should be avoided in hypertensive, for it may result in increase in blood pressure.

However, the precise mode of action of proanthocyanidin is speculative in gynaecomastia and related changes in the semen and hormonal undertones. It seems to be a vital growth factor in which interplay of some or all modes of action (*vide supra*) may participate. Further research on its probable mode of action at the molecular level, may provide a promising treatment option for gynecomastia and delayed puberty in males. Besides, it might prove useful in hair growth in male [16] and female [17] pattern androgenetic alopecia and erectile dysfunction (ED) [18]. The combine therapy of pro-anthrocynidin and L-arginine [19], in erectile dysfunction, in particular, is currently a topic of intriguing dialogue, warranting perspective studies.

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