PKOS da Hirsutizm

Yılmaz Şahin

Erciyes Üni Tıp Fakültesi

Kadın Hast. ve Doğum AB Dalı

İVF Ünitesi, Kayseri

Ankara PKOS Sempozyumu 22 mayıs 2016

Hirsutizm nedenleri

Polikistik over sendromu	% 80
İdyopatik hirsutizm	% 18
Kongenital adrenal hiperplazi	< % 1
Androjen sekrete eden over tümörü	< % 1
Cushing sendromu	< % 1
Androjen sekrete eden adrenal tümör	< % 1
Eksojen androjenik etkili ilaç alımı	< % 1

Exp Clin Endocrinol Diabetes 112: 504-509, 2004

K. Unluhizarci
C. Gokce
H. Atmaca
F. Bayram
F. Kelestimur

A Detailed Investigation of Hirsutism in a Turkish Population: Idiopathic Hyperandrogenemia as a Perplexing Issue

	n	%
PCOS	96	57.1
Idiopathic hirsutism	27	16
NCAH	12	7.1
Adrenal Ca	3	1.8
Cushing syndrome	1	0.6
Idiopathic hyperandrogenemia	29	17.4

İdyoptik HA: PKOS'un hafif formu olabilir

veya

İdyoptik hiperandrojenemi → PKOS

83 PKOS hastanın

- %65 oligomenore
- %5 amenore
- %30 ömenore
- %100 hiperandrojenemi (fT>11.1 pmol/l)
- %92 hirsutizm
- %40 LH/FSH>2

Şahin Y, Keleştimur F. Eur J Endocrinol 1997

Hirsutizm, akne

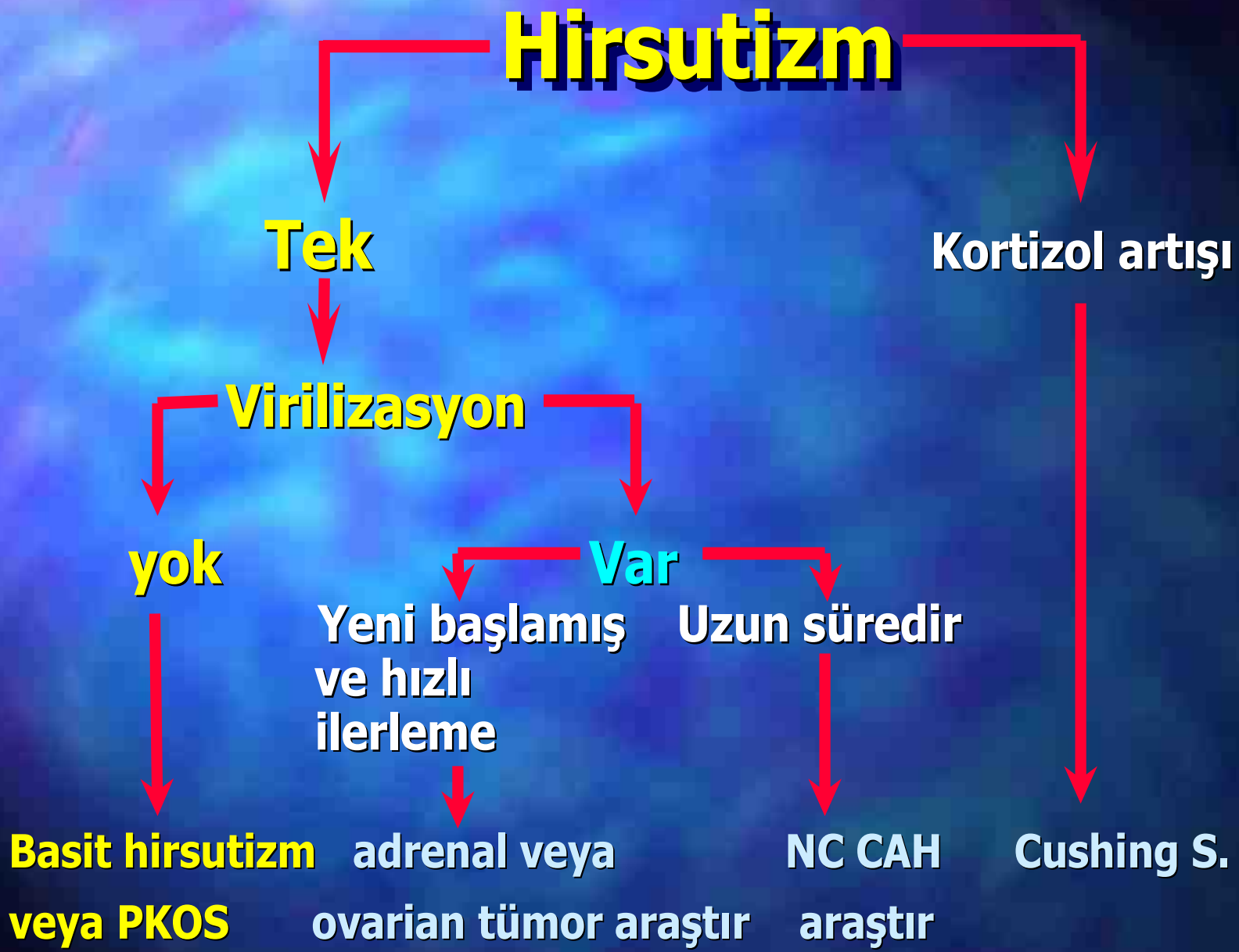
Aynı hasta

Hypertrikozis + Hirsutizm

Hipertrikozis + Hirsutizm

Ön kol ve alt bacakta aşırı kıl gelişmesi hirsutizm değildir, bu bölgelerde terminal ve vellus kıllar karışık olur.

Ön kol
Hipertrikozis, Genetik varyasyon


Hirsutizm
Tek
Kortizol artışı
Virilizasyon
yok
Var
Yeni başlamış ve hızlı ilerleme
Uzun süredir
Basit hirsutizm veya PKOS
adrenal veya ovarian tümor araştır
NC CAH araştır
Cushing S.

Hirsutizm - Tedavi

1- Obezite tedavisi

2- İlaç tedavisi

3- Kozmetik tedavi

4- Eğitim ve psikoterapi

5- Kombine yaklaşım

Kıllar siklik büyür

Klinik cevap için

en az 6 - 9 ay tedavi gerekir

Zayıflama

Egzersiz ve diyet

* Açlık insülin seviyesini azaltır
* SHBG yi artırıp androgenleri düşürerek HA iyileştirir.

Giallauria, 2009

Hirsutizm tedavisi - Dual yaklaşım

- **Hiperandrojeneminin farmakolojik tedavisi**

  Androjen sekresyonu ve/veya etkisini azaltmak

- **Mevcut terminal kılların yok edilmesi**

İlaç tedavisi

Table 1. Anti-androgen drugs, their new combinations, and insulin sensitizers used in the treatment of hirsutism.

Anti-androgen drugs and the new combinations

Anti-androgen drugs
- Spironolactone
- Cyproterone acetate
- Finasteride
- Flutamide

Anti-androgen combinations
- Cyproterone acetate and ethinyloestradiol plus spironolactone
- Cyproterone acetate and ethinyloestradiol plus finasteride
- Cyproterone acetate and ethinyloestradiol plus flutamide
- Spironolactone plus finasteride

Insulin sensitizers

Metformin
Thiazolidinediones

Şahin Y and Keleştimur F. Medical treatment regimens of hirsutism. RBM Online. 2004

Anti-androgen tedavi

1. Gonadotropin supresyonu
2. SHBG sentezi stimülasyonu
3. 5-α redüktaz enzimi inhibisyonu
4. Androgen reseptörlerine bağlanma
5. Steroid biyosentezine etkiler

Anti-androgenler

- Siproteron asetat (Etinil Estradiol + 2 mg SA)
- Spironolakton (100-200 mg/gün
- Finasterid (2.5-5 mg/gün)
- Flutamid (62.5-250 mg/gün)

Kombine tedaviler

Human Reproduction Update Advance Access published November 6, 2011
Human Reproduction Update, Vol.0, No.0 pp. 1–25, 2011
doi:10.1093/humupd/dmr042

human reproduction update

Epidemiology, diagnosis and management of hirsutism: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome Society

H.F. Escobar-Morreale[1,*], E. Carmina[2], D. Dewailly[3], A. Gambineri[4], F. Kelestimur[5], P. Moghetti[6], M. Pugeat[7], J. Qiao[8], C.N. Wijeyaratne[9], S.F. Witchel[10], and R.I. Norman[11]

Table IV Summary of RCTs comparing the efficacy of different antiandrogen drugs on hirsutism.

Author, year	Blinding	Months	Sample size	Disorders	Regimens compared[a]	Outcome	Efficacy on hirsutism
Belisle and Love (1986)	Double	12	158	Hirsutism (mFG > 14)	(1) Diane (2) Diane + CPA 100	mFG	Diane + CPA > Diane
McLellan et al. (1989)	Double	9	22	Hirsutism	(1) Spironolactone 100 (2) Placebo	Diameter Self-evaluation	No difference
Barth et al. (1991)	Double	12	38	Hirsutism	(1) Diane (2) Diane + CPA 20 (3) Diane + CPA 100	mFG Hair diameter Linear growth	No difference
Cusan et al. (1994)	Single	9	53	Hirsutism (mFG > 13)	(1) Flutamide 500 mg + OCP (2) Spironolactone 100 + OCP	mFG	Flutamide + OCP > Spironolactone + OCP
Ciotta et al. (1995)	Single	9	18	PCOS Idiopathic hirsutism	(1) Finasteride 7.5 (2) Placebo	mFG	Finasteride > Placebo
Wong et al. (1995)	None	6	14	Hirsutism (mFG > 11)	(1) Spironolactone 100 (2) Finasteride 5	mFG Hair diameter Self-evaluation	No difference
Grigoriou et al. (1996)	None	9	22	Idiopathic hirsutism	(1) CPA 100 (2) Flutamide 500	mFG	No difference
Erenus et al. (1997)	Single	9	40	Idiopathic hirsutism (mFG > 10)	(1) Spironolactone 100 (2) Finasteride 5	mFG	Spironolactone > Finasteride
Falsetti et al. (1997)	None	6	44	PCOS (mFG 11–24)	(1) Finasteride 5 (2) Flutamide 500	mFG Hair diameter	No difference
Muderris et al. (1997)	Single	12	65	Hirsutism	(1) Flutamide 250 (2) Flutamide 500	mFG	No difference
Kelestimur and Sahin (1998)	Single	12	50	Hirsutism (mFG > 8)	(1) Diane (2) Diane + Spironolactone 100	mFG	Diane + Spironolactone > Diane
Sahin et al. (1998)	Single	9	42	PCOS Idiopathic hirsutism	(1) Diane (2) Finasteride 5	mFG	Diane > Finasteride
Falsetti et al. (1999)	None	12	110	PCOS Idiopathic hirsutism (mFG 11–23)	(1) Finasteride 5 (2) Flutamide 500	mFG Hair diameter	Flutamide > Finasteride

Author, year	Blinding	Months	Sample size	Disorders	Regimens compared[a]	Outcome	Efficacy on hirsutism
Fruzzetti et al. (1999)	Single	12	45	Hirsutism	(1) Finasteride 5 (2) CPA 25+ EE 0.020 (3) Flutamide 500	mFG	No difference
Pazos et al. (1999)	None	9	33	Functional ovarian hyperandrogenism Idiopathic hirsutism	(1) GnRHa + OCP (2) CPA 100 + OCP (3) Flutamide 500 + OCP	mFG	Flutamide > (CPA = GnRHa)
Venturoli et al. (1999)	None	12	66	PCOS Idiopathic hirsutism NCCAH	(1) Flutamide 250 (2) Finasteride 5 (3) Ketoconazole 300 (4) 3) CPA 12.5 + EE 0.010–0.020	mFG Hair diameter Linear growth	(CPA = Flutamide) > Finasteride Ketoconazole 50% drop out rate
De Leo et al. (2000)	None	6	35	PCOS	(1) GnRHa (2) GnRHa + Diane (3) GnRHa + Flutamide 250	mFG	No difference
Moghetti et al. (2000a)	Double	6	40	Hirsutism	(1) Spironolactone 100 (2) Finasteride 5 (3) Flutamide 250 (4) Placebo	mFG Hair diameter Self-evaluation	(Spironolactone = Finasteride = Flutamide) > Placebo
Mudemis et al. (2000)	Single	12	70	Hirsutism (mFG > 8)	(1) Flutamide 250 (2) Finasteride 5	mFG	Flutamide > Finasteride
Spritzer et al. (2000)	None	12	44	PCOS Idiopathic hirsutism (mFG 11–35)	(1) Spironolactone 200 (2) CPA 50 + EE 0.035	mFG	No difference
Tartagni et al. (2000)	Single	6	50	PCOS Idiopathic hirsutism	(1) Diane (2) Diane + Finasteride 5	mFG Self-evaluation	Diane + Finasteride > Diane
Sahin et al. (2001)	Single	12	40	Hirsutism	(1) Diane (2) Diane + Finasteride 5	mFG	Diane + Finasteride > Diane
Bayram et al. (2002)	None	12	46	PCOS Idiopathic hirsutism (mFG > 12)	(1) Finasteride 2.5 (2) Finasteride 5	mFG	No difference
Taner et al. (2002)	None	6	84	Hirsutism	(1) Flutamide 250 (2) Flutamide 250 + Diane	mFG	No difference

Unluhizarci et al. (2002)	Single	6	34	PCOS Idiopathic hirsutism	(1) Spironolactone 100 (2) Spironolactone 100 + Finasteride 5	mFG	Spironolactone + Finasteride > Spironolactone
Lakryc et al. (2003)	Double	6	24	PCOS Idiopathic hirsutism	(1) Finasteride 5 (2) Placebo	mFG Self-evaluation	Finasteride > Placebo
Beigi et al. (2004)	None	9	40	PCOS Idiopathic hirsutism	(1) Finasteride 5 (2) CPA 25 + EE 0.020	mFG	No difference
Ganie et al. (2004)	None	6	69	PCOS	(1) Spironolactone 50 (2) Metformin 1000	mFG	Spironolactone > Metformin
Kelestimur et al. (2004)	Single	12	65	PCOS Idiopathic hirsutism	(1) Spironolactone 100 (2) Spironolactone 100 + Finasteride 5	mFG	Spironolactone + Finasteride > Spironolactone
Tartagni et al. (2004)	Single	10	38	PCOS Idiopathic hirsutism (mFG > 10)	(1) Finasteride 2.5 once daily (2) Finasteride 2.5 every 3 days	mFG	No difference
Gambineri et al. (2006)	Single	12	76	PCOS	(1) Diet (2) Diet + Metformin 1700 (3) Flutamide 500 (4) Diet + Metformin 1700 + Flutamide 500	mFG	(Flutamide = Flutamide + Metformin) > (metformin + diet = diet)
Calaf et al. (2007)	Double	12	119	PCOS Idiopathic hirsutism (mFG > 15)	(1) OCP (2) Flutamide 125 + OCP (3) Flutamide 250 + OCP (4) Flutamide 375 + OCP	mFG	Flutamide (125 = 250 = 375) + OCP > OCP

CPA, cyproterone acetate; Diane, cyproterone acetate 2 mg plus ethinylestradiol 35 μg; EE, ethinylestradiol; mFG, modified Ferriman–Gallwey score; GnRHa, GnRH analog; OCP, oral contraceptive pill.
[a]Doses are mg per day unless stated otherwise.

İnsülin hassaslaştırıcılar-Metformin

Table V Summary of RCTs of interventions with insulin sensitizers for hirsutism.

Author, year	Blinding	Months	Sample size	Disorders	Regimens compared*	Outcome	Efficacy on hirsutism
Insulin sensitizers versus placebo							
Moghetti et al. (2000b)	Double	6	23	PCOS	(1) Metformin 1500 (2) Placebo	mFG	No difference
Pasquali et al. (2000)	Double	6	20	PCOS	(1) Diet + Metformin 1700 (2) Diet + Placebo	FG	Metformin > placebo
Azziz et al. (2001)	Double	11	410	PCOS	(1) Troglitazone 150, 300 and 600 (2) Placebo	mFG	Troglitazone 600 > placebo
Kelly and Gordon (2002)	Double	6	16	PCOS	(1) Metformin 1500 (2) Placebo	FG Hair growth Self-assessment	Metformin > placebo Metformin > placebo Metformin > placebo
Gambineri et al. (2004)	Single	6	20	PCOS	(1) Diet + Metformin 1700 (2) Diet + Placebo	FG	No difference
Hoeger et al. (2004)	Double	11	18	PCOS	(1) Metformin 1700 (2) Placebo	mFG	No difference
Maciel et al. (2004)	Double	6	34	PCOS	(1) Metformin 1500 (2) Placebo	FG	No difference
Onalan et al. (2005)	Double	6	139	PCOS	(1) Metformin 1700 (2) Placebo	FG	No difference
Gambineri et al. (2006)	Single	12	40	PCOS	(1) Diet + Metformin 1700 (2) Diet + Placebo	FG	No difference
Aroda et al. (2009)	Unclear	6	28	PCOS	(1) Pioglitazone 45 (2) Placebo	FG	Pioglitazone > placebo
Romualdi et al. (2010)	Double	6	28	PCOS	(1) Metformin 1000 (2) Placebo	FG	Metformin > placebo
Insulin sensitizers versus OCPs							
Morin-Papunen et al. (2000)	None	6	18	PCOS	(1) Metformin 1000 → 2000 (2) Diane	FG	Diane > Metformin
Harborne et al. (2003)	Unclear	12	52	PCOS	(1) Metformin 1500 (2) Diane	FG Hair diameter Self-assessment	Metformin > Diane No difference Metformin > Diane
Morin-Papunen et al. (2003)	None	6	20	PCOS	(1) Metformin 1000 → 2000 (2) Diane	FG	Diane > Metformin

Allen et al. (2005)	None	6	35	PCOS	(1) Metformin 1000 (2) Norgestimate 0.25 + EE 0.035	mFG	No difference
Lemay et al. (2006)	None	6	28	PCOS	(1) Rosiglitazone 4 (2) Diane	FG	Diane > Rosiglitazone
Luque-Ramirez et al. (2007)	None	6	34	PCOS	(1) Metformin 1700 (2) Diane	mFG	Diane > Metformin
Meyer et al. (2007)	None	6	110	PCOS	(1) Metformin 2000 (2) Diane (3) Levonorgestrel 0.100 + EE 0.020 + Spironolactone 100	FG	No difference
Hoeger et al. (2008)	Double	6	43	PCOS	(1) Metformin 1700 (2) Desogestrel 0.15 + EE 0.030 (3) Life-style modification (4) Placebo	FG	No difference
Metformin and thiazolidinediones							
Yilmaz et al. (2005)	Single	6	96	PCOS	(1) Metformin 1700 (2) Rosiglitazone 4	FG	Rosiglitazone > Metformin
Ortega-Gonzalez et al. (2005)	None	6	52	PCOS	(1) Metformin 2550 (2) Pioglitazone 30	FG	No difference
Dereli et al. (2005)	None	8	40	PCOS	(1) Rosiglitazone 2 (2) Rosiglitazone 4	mFG	Rosiglitazone 4 > Rosiglitazone 2
Metformin versus antiandrogens							
Ganie et al. (2004)	None	6	69	PCOS	(1) Spironolactone 50 (2) Metformin 1000	mFG	Spironolactone > Metformin
Gambineri et al. (2004)	Single	6	20	PCOS	(1) Metformin 1700 (2) Flutamide 500	FG	Flutamide > Metformin
Gambineri et al. (2006)	Single	12	76	PCOS	(1) Diet (2) Diet + Metformin 1700 (3) Diet + Flutamide 500 (4) Diet + Metformin 1700 + Flutamide 500	mFG	(Flutamide = Flutamide + Metformin) > (metformin + diet = diet)

*Doses are mg per day unless stated otherwise.

İnsülin hassaslaştırıcılar hirsutizm tedavisinde önerilmez

A consensus statement by AE-PCOS Society, 2011

Myo-inositol - Hirsutizm

Efficacy of myo-inositol in the treatment of cutaneous disorders in young women with polycystic ovary syndrome

Zacche, 2009

Table II. Number of cases and severity of hirsutism at baseline, after 3 months and 6 months of treatment with myo-inositol (T1 = 3 months; T2 = 6 months).

	Baseline	T1	T2
Mild	20 (40%)	17 (34%)	16 (32%)
Moderate	21 (42%)	18 (36%)	15 (30%)
Severe	9 (18%)	7 (14%)	4 (8%)
Disappearance	–	8 (16%)	15 (30%)
Mean mFG score	11.4 ± 3.2	9.9 ± 2.8	8.1 ± 2.6*

Treatment of hirsutism with myo-inositol: a prospective clinical study

Minozzi, RBM Online, 2008

Flutamid

Fatal liver complications with flutamide

Osculati A, Castiglioni C.Lancet, 2006

- 18 yaş, hafif akne, hirsutizm, KcFT bakmadan
- 375 mg/gün 1 ay + OK
- 250 mg/gün 3 ay
- Toksik hepatit, kc yetmezliği
- 3 kere Kc transplantasyonu: başarısız
- 2 ay sonra ex

Annals of Hepatology

CASE REPORT

January-March, Vol. 10 No.1, 2011: 93-98

Acute and fulminant hepatitis induced by flutamide: Case series report and review of the literature

Javier Brahm,[*,†,||] Magdalena Brahm,[**] Roberto Segovia,[†,||] Ricardo Latorre,[*,†] Rodrigo Zapata,[‡,§] Jaime Poniachik,[*] Erwin Buckel,[||] Luis Contreras[¶]

[*] Department of Gastroenterology, Hospital Clínico Universidad de Chile, North Campus. [†] Department of Gastroenterology, Clínica Las Condes. [‡] Department of Gastroenterology, Hospital Salvador, University of Chile, Eastern Campus. [§] Department of Gastroenterology, Clínica Alemana. [||] Liver Transplant Unit, Clínica Las Condes. [¶] Department of Pathology, Clínica Las Condes. [**] Medical Student, Universidad de Chile.

ABSTRACT

Flutamide is a non-steroidal anti-androgenic drug, commonly used in the treatment of advanced prostate cancer, acne and hirsutism. This drug may induce various degrees of liver injury, including acute liver failure (ALF), with further need for liver transplantation. Here, we present a report of 10 consecutive patients seen in a period of 14 years, with acute liver toxicity induced by flutamide (in most cases severe hepatotoxicity): 3 men and 7 women, with a mean age of 75 and 29 years old, respectively. All men received flutamide as treatment of advanced prostate carcinoma and they developed hepatotoxicity without ALF, and three months after withdrawal of the drug, they recovered completely. In contrast, in 7 young female with liver toxicity caused by flutamide as treatment of various hyperandrogenic conditions (acne and hirsutism), ALF was observed in 5 patients, all of them requiring urgent liver transplantation, with excellent outcome and survival in 4 of them. Based on the above, we believe that flutamide treatment should be preferentially avoided in young female patients with benign pathologies, or if it is used, patients should be warned of its potential severe complications. Also, serial liver tests should be closely monitored and, in case of elevations, the drug should be immediately withdrawn.

Table 2. Hepatotoxicity induced by flutamide in women (n = 7).

Indications for treatment	Age	Days of ingeston	Hepatic alterations (maximum) Bil	AST	ALT	PT	Hepatitis	Outcome after withdrawal of flutamide
1. Hirsutism	44	90	4.2	390	605	90%	Acute	Good (1)
2. Hirsutism	27	60	27	1064	1803	10%	Fulminant	Good (2)
3. Hirsutism	32	60	25	1189	925	38%	Acute	Good (3)
4. Hirsutism	20	180	20	850	590	15%	Fulminant	Good (4)
5. Acne	22	180	25	1,576	1,116	14%	Fulminant	Good (5)
6. Acne	21	65	29	2,778	3,360	10%	Fulminant	Good (6)
7. Alopecia	38	90	44	2,130	1,430	24%	Fulminant	Died (7)

PT: Prothrombin time (%). Bil: Bilirubin (mg/dL). **AST:** Aspartate aminotransferase (IU/m). **ALT:** Alanine aminotransferase (IU/ml). **(1)** 1 month. **(2)** 4 months post transplant. **(3)** 3 months. **(4)** 7 months post transplant. **(5)** 53 months post transplant. **(6)** 53 months post transplant. **(7)** Post operative period.

(1996 – 2010) Hirsutizm, akne, alopesi: flutamid 125-250 mg/gün

7 hastada hepatotoksisite (60 – 80 gün)

Hepatik değişiklikler: 5 gün – 10 ay

5 hastada akut karaciğer yetmezliği ile acil Kc transplantasyonu

4 hasta yaşıyor

1'i postop exitus

İdiosenkratik , allerjik, genetik faktörler ?

Kombine tedaviler

Diane 35 + spironolactone F Keleştimur, Y Şahin. Fertil Steril, 1998

Diane 35 + finasteride Şahin Y, Dilber S, Keleştimur F. Fertil Steril, 2001

Spironolactone + finasteride Keleştimur F, Everest H, Unlühizarci K, Bayram F, Sahin Y. Eur J Endocrinol. 2004

Spironolactone 100 mg/gün + OC Erenus M, Yücelten D, Gürbüz O, Durmuşoğlu F, Pekin S. Fertil Steril, 1996

Sonuçlar-hirsutizm

İnsülin hassaslaştırıcılar ve Drospirenon içeren OK ler sınırlı etkiye sahip veya yararsız.

Bazı OK lerdeki dozda Drospirenon antiandrojenik değildir.

Bart, Fertil Steril, 2012. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ ASRM-Sponsored 3rd PCOS Consensus Workshop Group

Sonuçlar-hirsutizm

Antiandrogenler teratojenik potansiyele sahiptir

(Erkek fötusda ambiguous genitalia?)

Antiandrogenler yeterli kontrasepsiyonla kullanılmalı.

OK

Sonuçlar-hirsutizm

- Henüz hayat boyu kalıcı kıl eradikasyonu yapan hiçbir metod mevcut değildir.
- Tedavi öncesi hastaya bu gerçek söylenmeli hasta beklentisi: gerçekçi olmalı.

Sonuçlar-hirsutizm

Flutamid **Yan etki: Hepatotoksisite**

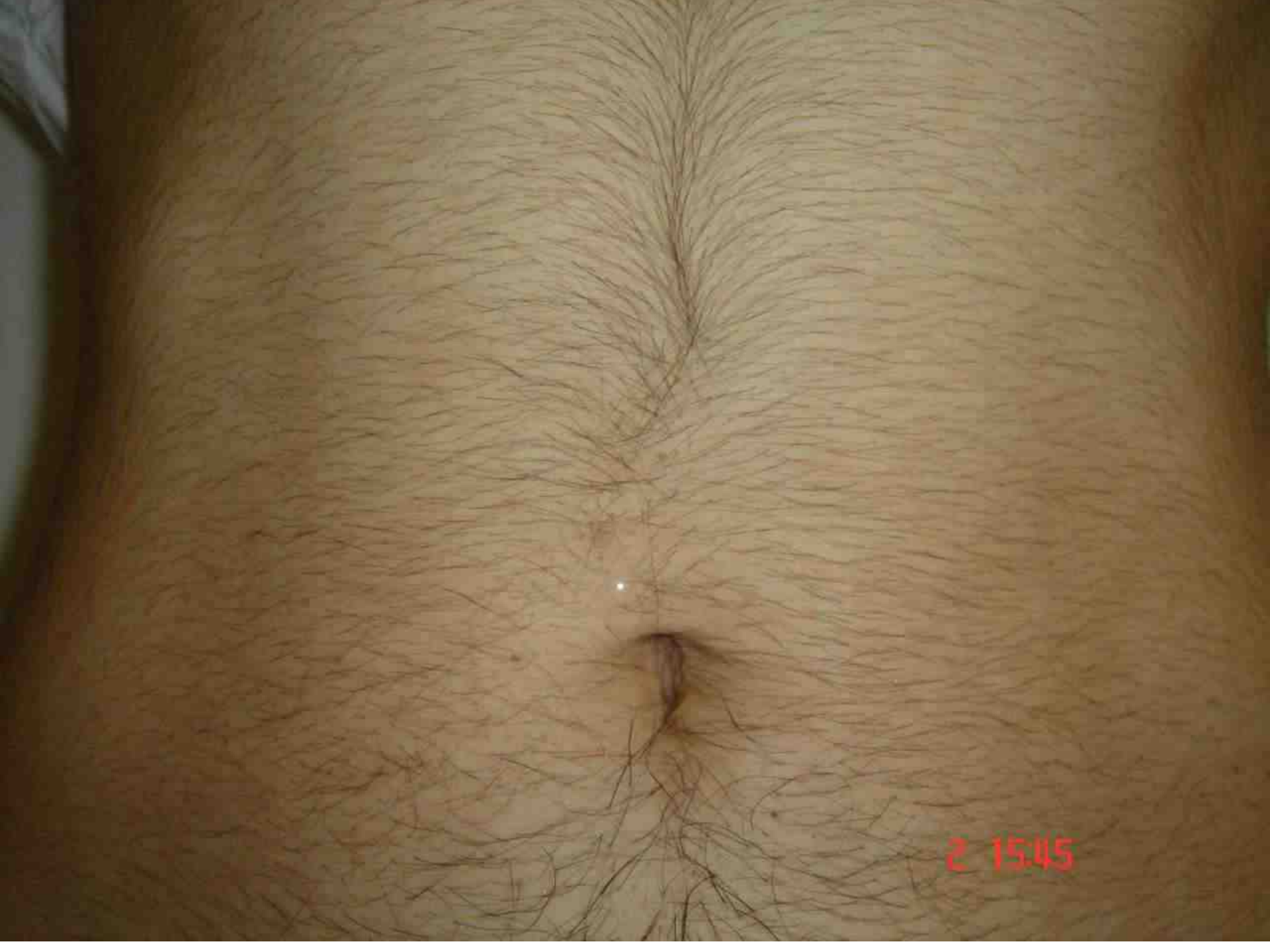
Düşük dozla da olabilir Osculati, 2006, Garcıa, 2001, Thole, 2004

Androgen Excess-PCOS Society hirsutizm tedavisinde flutamidi önermemektedir.

A consensus statement by AE-PCOS Society, 2011

KOZMETİK TEDAVİ

- İlaçların terminal kıllara etkisi çok azdır,
  - Elektrolizis
  - Lazer fototermolizis
- Bu metodların etkisi de daima kalıcı değildir.


2 15:45

Antiandrogenler teratojenik potansiyele sahiptir

(Erkek fötusda ambiguous genitalia?)

Antiandrogenler yeterli kontrasepsiyonla kullanılmalı.

Flutamid

Fatal liver complications with flutamide

Osculati A, Castiglioni C.Lancet, 2006

- **18 yaş, hafif akne, hirsutizm, KcFT bakmadan**
- **375 mg/gün 1 ay + OK**
- **250 mg/gün 3 ay**
- **Toksik hepatit, kc yetmezliği**
- **3 kere Kc transplantasyonu: başarısız**
- **2 ay sonra ex**

İlaç tedavisi

Table 1. Anti-androgen drugs, their new combinations, and insulin sensitizers used in the treatment of hirsutism.

Anti-androgen drugs and the new combinations

Anti-androgen drugs
- Spironolactone
- Cyproterone acetate
- Finasteride
- Flutamide

Anti-androgen combinations
- Cyproterone acetate and ethinyloestradiol plus spironolactone
- Cyproterone acetate and ethinyloestradiol plus finasteride
- Cyproterone acetate and ethinyloestradiol plus flutamide
- Spironolactone plus finasteride

Insulin sensitizers

Metformin
Thiazolidinediones

Şahin Y and Keleştimur F. Medical treatment regimens of hirsutism. RBM Online. 2004

Spironolakton

* Sentetik steroid
* DHT reseptörlerini tutar
* Androgen sentezi inhibisyonu

Spironolakton

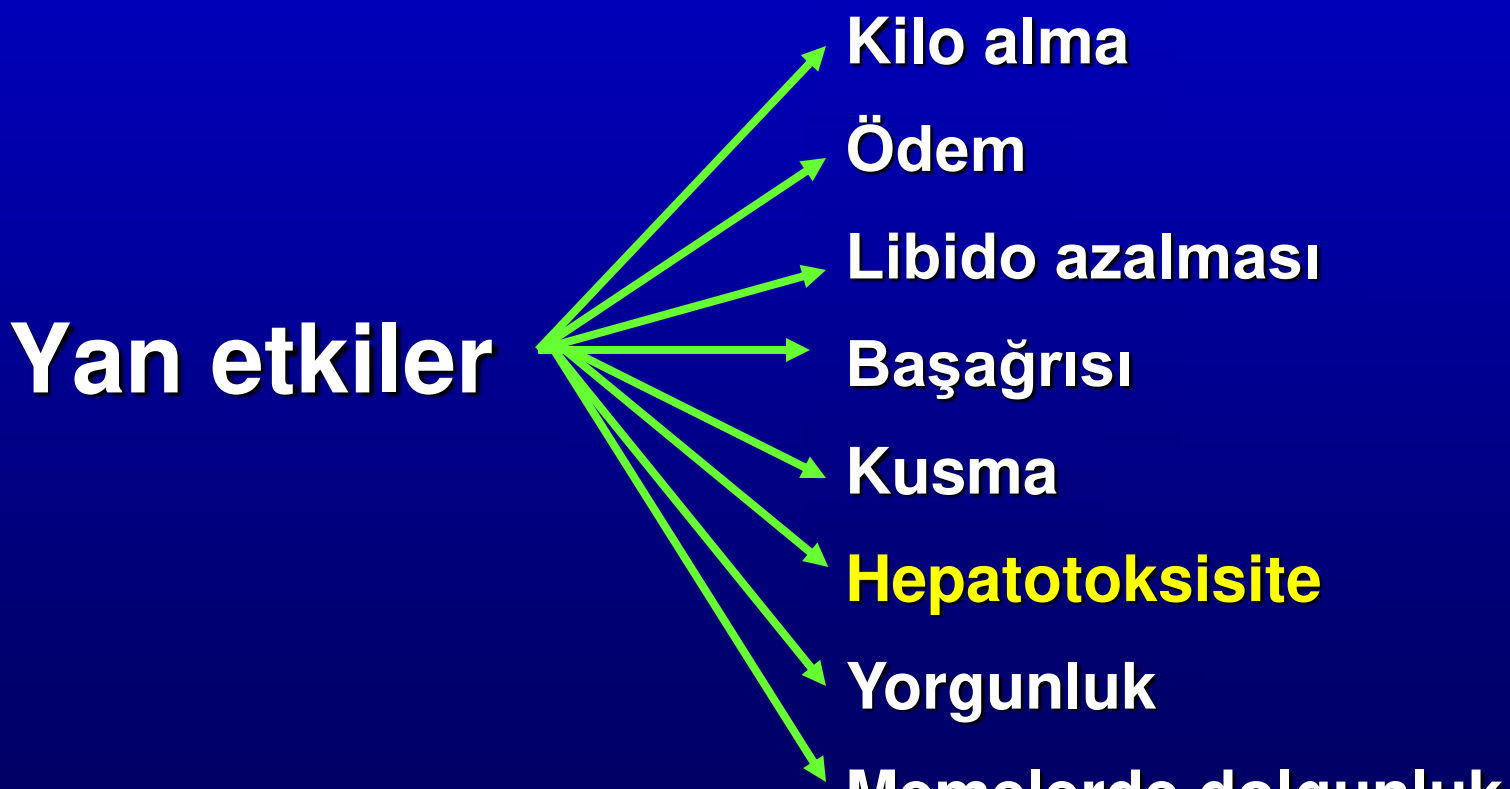
Yan etkiler

İrregüler menses (polimenore: %70)

Siproteron asetat

* 17-OHP derivesi steroidik anti-androgen
* T ve DHT reseptörlerine bağlanır
* LH inhibisyonu ile ovaryan T üretimini azaltır

Siproteron asetat yan etki



Finasterid

* 5 α-redüktaz inhibitörü
* T'un DHT'a konversiyonunu inhibe eder

Flutamid

Non-steroid, periferik androgen antagonisti

Hepatotoksisite

Düşük dozla da olabilir

Osculati, 2006, Garcıa, 2001, Thole, 2004

Hypertrikozis + Hirsutizm

Hipertrikozis genellikle herediterdir.


HA hipertrikozisi
artırabilir
2 15:45

Tedavi

1-Genel prensipler

- Varsa altta yatan hastalığın tanı ve tedavisi
- Obezite tedavisi

2-İlaç tedavisi

- Adrenal supresyon
- Ovarian supresyon
- Anti-androgen tedavi
- insulin rezistansı tedavisi

3-Kozmetik tedavi

4-Eğitim ve psikoterapi

5-Kombine tedaviler

Siproteron asetat

* 17-OHP derivesi steroidik anti-androgen
* T ve DHT reseptörlerine bağlanır
* LH inhibisyonu ile ovaryan T üretimini azaltır

Siproteron asetat

yan etki

Hepatotoksisite

Spironolakton

* Sentetik steroid
* DHT reseptörlerini tutar
* Androgen sentezi inhibisyonu

Spironolakton

Yan etkiler

İrregüler menses

(polimenore: %70)

Kelestimur F, Everest H, Unluhizarci K, Bayram F, Sahin Y. Eur J Endocrinol , 2004

Spironolakton

1- Emniyetlidir

2- Önemli yan etkisi yoktur

3- Etkilidir

Finasterid

* 5 α-redüktaz inhibitörü
* T'un DHT'a konversiyonunu inhibe eder

Flutamid

Non-steroid, periferik androgen antagonisti

Hepatotoksisite

Düşük dozla da olabilir

Osculati, 2006, Garcıa, 2001, Thole, 2004

Analysis 27.1. Comparison 27 Metformin 500 mg to 1500 mg per day versus placebo for 12 to 48 weeks, Outcome 1 Mean change from baseline in Ferriman-Gallwey score.

Review: Interventions for hirsutism (excluding laser and photoepilation therapy alone)

Comparison: 27 Metformin 500 mg to 1500 mg per day versus placebo for 12 to 48 weeks

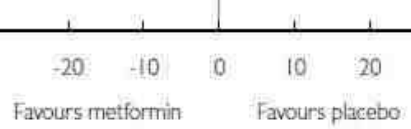
Outcome: 1 Mean change from baseline in Ferriman-Gallwey score

Study or subgroup	Metformin N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Gambineri 2006	20	-2.6 (5.37)	19	-1.3 (2.89)		19.4 %	-1.30 [-3.99, 1.39]
Hoeger 2004	5	-1.9 (9.49)	7	0.6 (2.58)		1.9 %	-2.50 [-11.03, 6.03]
Hoeger 2008	6	0.4 (2.04)	10	-0.9 (3.25)		20.9 %	1.30 [-1.29, 3.89]
Maciel 2004	15	-0.1 (3.6)	14	0.5 (3.6)		20.4 %	-0.60 [-3.22, 2.02]
Moghetti 2000B	12	0.7 (3.37)	11	1.8 (3.9)		15.7 %	-1.10 [-4.09, 1.89]
Onalan 2005	55	6.2 (50.06)	61	9.6 (20.2)		0.7 %	-3.40 [-17.57, 10.77]
Otta 2010	14	-0.13 (3.35)	15	-0.5 (3.77)		20.9 %	0.37 [-2.22, 2.96]
Total (95% CI)	**127**		**137**			**100.0 %**	**-0.27 [-1.46, 0.91]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.01$, $df = 6$ ($P = 0.81$); $I^2 = 0.0\%$

Test for overall effect: $Z = 0.45$ ($P = 0.65$)

Test for subgroup differences: Not applicable



Interventions for hirsutism(excluding laser and photoepilation therapy alone) (Review)

van Zuuren EJ, 2015, Cochrane Database of Systematic Reviews

Progestins with an antiandrogenic effect include drospirenone, chlormadinone, dienogest, and cyproterone acetate

(Blume-Peytavi 2011; Escobar-Morreale 2012;Martin 2008; Paparodis 2011; Shah 2009).

Aynı hasta