35 Woman with Hirsutism, Acne and Weight Gain

Sikarin Upala, MD, MS
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Learning Objectives

• Understand the relationship between epilepsy, valproic acid and PCOS
• Review metformin treatment in PCOS
• Recognized GLP-1 receptor agonist as a potential treatment of PCOS
HPI

• 35 y Caucasian woman referred for PCOS/weight management
• Diagnosis at age 26 by OB-GYN when she presented with infertility
  – Had features of hyperandrogenism (facial hair, acne)
  – Irregular menstruation
  – Confirmed polycystic ovaries by ultrasound
HPI

• At diagnosis: metformin and clomiphene initiated
• Has two children after clomiphene treatment
• Now metformin 500 mg bid
• Never been on OCP (history of migraine)
HPI

• Weight gain from 180 to 266 lbs over 4 years
• Tries diet control (carb counting 1200 Kcal/day) and exercise (treadmills 1.30 hrs/day) with 10 lbs weight loss in 6 months duration
• PCP prescribe phentermine/topiramate (qsymia) in 2016
• Now her weight is 226 lbs
HPI

• Ob/gyn history
  – Menarche: 11 years old
  – Menstrual cycles were initially regular
  – Subsequently at age 16, menses became irregular with a frequency of approximately 6 times per year
  – LMP: 1 month prior to her visit in clinic, her previous period was 4 months before
  – G10 P2 AB8
  – History of HELLP, pre-eclampsia
  – No gestational diabetes
Past Medical History

- Depression
- Anxiety
- HTN
- PCOS
- Migraine
- Dyslipidemia

Past Surgical History

- Back surgery (Fractures L 5-S1)
Social History

- Live with her husband
- Work as a pediatric nurse
- Former smoker, stopped in 2009
- No EtOH
- No Illicit drugs
- No problem with sexual function
Family History

- Caucasian
- Denies family history of endocrinopathies, DM or thyroid disease
- PCOS: sister, aunt
- Father had CAD s/p stent at age 54

Allergy

- Penicillin
- Sulfamethoxazole-Trimethoprim
Medication Prior Visit

- Cholecalciferol (Vitamin D3) 1,000 unit 1 tab qd
- Fenofibrate 145 mg 1 tab qd
- Lorazepam 2 mg/mL 1 mg prn
- Metformin 500 mg 1 tab bid
- Metoprolol 50 mg 1 tab bid
- Naproxen 1 tab prn
- Phentermine/Topiramate (QSYMIA) 7.5-46 mg 1 tab od
- Valsartan-Hydrochlorothiazide 80-12.5 mg 1 tab od
- Venlafaxine 150 mg 1 tab od
ROS

• + Acne, anxiety and depression
• Prior treatment with anti-epileptics for seizure disorder, taken valproic acid from age 13-18 (last seizure was at age 16)
• Denies galactorrhea, headaches, vision changes
• No neck mass or goiter, symptoms of hypothyroidism
• No evidence to suggest lipodystrophy
• Never been on steroids
• No eating disorders
• Other systems are negative
Physical Exam

- Vitals: BP 95/63 | Pulse 87 | Ht 160 cm (5' 3") | Wt 102.7 kg (226 lb 6.4 oz) | BMI 40.1 kg/m²
- General: No apparent distress. Appears stated age. Obese female
- HEENT: No pharyngeal erythema. PERRL, EOMI
- Neck: No neck pain. No thyromegaly or thyroid nodules appreciated. No thyroid bruit
- Cardiovascular: regular rate and rhythm. Peripheral pulses 2+ symmetric, no edema
- Pulmonary/Chest: clear to auscultation bilaterally
- Gastrointestinal: soft, non-tender, non-distended abdomen. No rebound or guarding
- Musculoskeletal: normal strength, range of motion of joints, normal tone
- Neurological: AOx3, no focal deficits. No proximal muscle weakness, normal DTRs
- Lymph: No cervical, supraclavicular, axillary or inguinal lymphadenopathy
- Derm: No rash. No thinning of the hair or hairline recession. + acne at left eyebrow. No buffalo hump, no moon faces, no violaceous striae, + facial hair
Ferriman-Gallwey Score

- Upper Lip: 2
- Chin: 2
- Chest: 0
- Upper Abdomen: 0
- Lower Abdomen: 0
- Upper Back: 0
- Lower Back: 0
- Upper Arm: 0
- Inner Thigh: 0
- Total: 4

Legro et al. (2013). JCEM; 12:4565-92
### Labs

- A1C 5.6(2015) -> 5.3%(2017)
- Urine pregnancy test: negative

<table>
<thead>
<tr>
<th>Lipid panel</th>
<th>11/30/13</th>
<th>4/5/16</th>
<th>8/19/17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>197</td>
<td></td>
<td>70</td>
</tr>
<tr>
<td>HDL</td>
<td>27</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>LDL</td>
<td>97</td>
<td></td>
<td>29</td>
</tr>
<tr>
<td>TG</td>
<td>302</td>
<td>476</td>
<td>70</td>
</tr>
</tbody>
</table>
Clinical Questions

• Epilepsy and abnormalities in the HPO axis?
• Any relationship between valproic acid and PCOS? What mechanisms?
Pathogenesis of PCOS

Epilepsy and PCOS

Epilepsy and PCOS

• Observational study
• Objective: To determine the incidence and risk factors of PCOS in Chinese women with epilepsy
• N=102 women with epilepsy
• Results: PCOS was found in 12.7% of women with epilepsy comparing to 6.8% of women in general population
• Their average age at the start of seizure was 13.8±6.5 years

### Epilepsy and PCOS

**Table 2**  
Incidence and risk factor analysis of PCOS and its isolated components in Chinese WWE (n = 102).

<table>
<thead>
<tr>
<th>AEDs</th>
<th>Polycystic ovaries</th>
<th>A/oligomenorrhoea</th>
<th>Hyperandrogenism</th>
<th>PCOS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=29</td>
<td>N=20</td>
<td>N=7</td>
<td>N=13</td>
</tr>
<tr>
<td>Number of cases (%)</td>
<td>73 (71.6)</td>
<td>29 (28.4)</td>
<td>82 (80.4)</td>
<td>20 (19.6)</td>
</tr>
<tr>
<td>Age of seizure start (mean ± SD years)</td>
<td>17.2 ± 8.6</td>
<td>14.0 ± 4.9</td>
<td>16.7 ± 8.5</td>
<td>14.6 ± 7.1</td>
</tr>
<tr>
<td>Duration of seizure (mean ± SD years)</td>
<td>6.3 ± 5.9</td>
<td>5.7 ± 4.6</td>
<td>6.1 ± 5.8</td>
<td>6.3 ± 4.5</td>
</tr>
<tr>
<td>Type of seizure [n (%)]</td>
<td>SPS/CPS (n = 17)</td>
<td>11 (64.7)</td>
<td>6 (35.2)</td>
<td>15 (88.2)</td>
</tr>
<tr>
<td></td>
<td>PG/PSG (n = 60)</td>
<td>46 (76.7)</td>
<td>14 (23.3)</td>
<td>48 (80.0)</td>
</tr>
<tr>
<td></td>
<td>Unclassified (n = 25)</td>
<td>16 (64.0)</td>
<td>9 (36.0)</td>
<td>19 (76.0)</td>
</tr>
<tr>
<td>Frequency of seizure</td>
<td>Free in 3 months (n = 52)</td>
<td>36 (69.2)</td>
<td>16 (30.8)</td>
<td>40 (76.9)</td>
</tr>
<tr>
<td></td>
<td>Experience in 3 months (n = 50)</td>
<td>37 (74.0)</td>
<td>13 (26.0)</td>
<td>42 (84.0)</td>
</tr>
<tr>
<td>AEDs therapy [n (%)]</td>
<td>No therapy (n = 30)</td>
<td>25 (83.3)</td>
<td>5 (16.7)</td>
<td>27 (90.0)</td>
</tr>
<tr>
<td></td>
<td>AEDs therapy (n = 72)</td>
<td>48 (66.7)</td>
<td>24 (33.3)</td>
<td>55 (76.4)</td>
</tr>
<tr>
<td>Duration of AEDs therapy (mean ± SD years)</td>
<td>2.5 ± 3.1</td>
<td>3.7 ± 3.7</td>
<td>2.6 ± 3.2</td>
<td>3.6 ± 3.6</td>
</tr>
</tbody>
</table>

* p < 0.05, vs. negative (−) patients, in an unpaired t-test.  
* p < 0.05, vs. no AEDs therapy, in a Chi-square test.  
** p < 0.01, vs. no AEDs therapy, in a Chi-square test.

Valproic Acid and PCOS

<table>
<thead>
<tr>
<th>AEDs</th>
<th>Polycystic ovaries</th>
<th>A/Oligomenorrhea</th>
<th>Hyperandrogenism</th>
<th>PCOS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>−</td>
<td>+</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>VPA (n=21)</td>
<td>11 (52.4)</td>
<td>10 (47.6)*</td>
<td>13 (61.9)</td>
<td>17 (80.9)</td>
</tr>
<tr>
<td>Another AED (n=28)</td>
<td>22 (78.6)</td>
<td>6 (21.4)</td>
<td>26 (92.9)</td>
<td>26 (92.9)</td>
</tr>
<tr>
<td>≥2 AEDs [n (%)]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-VPA AEDs (n=12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VPA+other AEDs (n=11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AEDs therapy [n (%)]</td>
<td>10 (83.3)</td>
<td>2 (16.7)</td>
<td>10 (83.3)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>VPA (n=32)</td>
<td>16 (50.0)</td>
<td>10 (31.3)*</td>
<td>19 (59.4)</td>
<td>21 (65.5)</td>
</tr>
</tbody>
</table>

a Among them 13 patients used CBZ, 6 LTG, 5 TPM, and 4 OXC.
* p < 0.05, vs. non-VPA AEDs therapy, in a Chi-square test.
# p < 0.01, vs. non-VPA AEDs therapy, in a Chi-square test.

No VPA / VPA: 2 vs 11

Valproic Acid and PCOS

- Cross-sectional study
- Objective: To study an association of long-term effects of valproic acid on reproductive endocrine functions in women with epilepsy in Turkey
- N=71 (VPA: 40 and other AED: 31)

Valproic Acid and PCOS

Table 1. Main results of the study

<table>
<thead>
<tr>
<th></th>
<th>WWE on VA monotherapy</th>
<th>WWE on non-VA therapy</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number</strong></td>
<td>40 (56.3%)</td>
<td>31 (43.7%)</td>
<td></td>
</tr>
<tr>
<td><strong>Menstrual disorders</strong></td>
<td>29 (72.5%)</td>
<td>13 (41.9%)</td>
<td>0.009</td>
</tr>
<tr>
<td>PCO</td>
<td>22 (55%)</td>
<td>14 (45.2%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hyperandrogenism</td>
<td>15 (37.5%)</td>
<td>7 (22.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>PCOS</td>
<td>25 (62.5%)</td>
<td>10 (32.3%)</td>
<td>0.011</td>
</tr>
</tbody>
</table>

NS = Not significant.

Table 2. Demonstration of dose- and duration-related PCOS and menstrual disturbance

<table>
<thead>
<tr>
<th>Duration of therapy</th>
<th>PCOS (+) (n = 25)</th>
<th>PCOS (-) (n = 15)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;34 months</td>
<td>926 ± 412</td>
<td>953 ± 190</td>
<td>NS</td>
</tr>
<tr>
<td>≥34 months</td>
<td>976 ± 376</td>
<td>832 ± 213</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = Not significant.

Valproic Acid and PCOS

Fig. 1   PCOS of VPA vs other AEDs, accepting different definitions of PCOS.

Hu et al. (2011). Epilepsy Res;97:73-82
Mechanisms of Proposed Hyperandrogenism by Valproic Acid

Valproic Acid and PCOS

- Polycystic ovarian morphology or an elevated testosterone level found in 80% of women who started taking valproate before age 20.
- Reproductive endocrine effects of VPA may be reversible after the medication discontinuation.
- In a follow-up study of 5 years, 60% of the patients who were on VPA during the follow-up study had PCOS as compared to 5.5% of women whose medication had been discontinued.

Hu et al. (2011). Epilepsy Res;97:73-82
Clinical Questions

• Recommendation on metformin use in non-diabetic PCOS?
• Any evidence on weight loss treatment in PCOS with Qsymia?
• Role of GLP-1 receptor agonist in PCOS
Metformin Use in PCOS

• **Strong recommendation:**
  – Recommend metformin in women with PCOS who have T2DM or IGT who fail lifestyle modification

• **Weak recommendation:**
  – The use of metformin as a first-line treatment of cutaneous manifestations, for prevention of pregnancy complications, or for the treatment of obesity.
  – For women with PCOS with menstrual irregularity who cannot take or do not tolerate HCs, suggest metformin as second-line therapy

Legro et al. (2013). JCEM; 12:4565-92
Metformin Use in PCOS

- Guidelines support use
  - Glucose intolerance

- No clear benefit of use
  - Treatment of hirsutism, acne, androgenic alopecia
  - Regulation of menses
  - Restoration of fertility
  - Live birth rate

- Benefit to be established
  - Weight loss
  - Improved body composition

Sam & Ehrmann. (2017). Diabetologia
Qsymia (Phentermine/Topiramate)

- PHEN/TPM combined with lifestyle modification may be an effective and well-tolerated treatment for obesity and weight-related metabolic complications
- Long-term efficacy and safety have yet to be defined
- Frequent side-effects: paresthesia, dry mouth, constipation and insomnia

Kiortsis et al. (2013). Hormones; 12: 507-16
Qsymia (Phentermine/Topiramate)

- Phentermine: sympathomimetic amine which acts as an appetite suppressant
- Topiramate: anticonvulsant that has weight loss side effects
- FDA approved in 2012
- Endocrine society: do not use in patient with Hx of heart disease, uncontrolled HTN
- No study in PCOS subgroup

Kiortsis et al. (2013). Hormones; 12: 507-16
# Qsymia (Phentermine/Topiramate)

## PHENTERMINE/TOPIRAMATE for weight loss in adults who are overweight (with weight-related health problems) or obese

<table>
<thead>
<tr>
<th>Patient population</th>
<th>3,754 adults age 18-65 (mean age 48) who were either:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>overweight</strong> (Body Mass Index [BMI] of 27 to 29.9) with weight-related problems—high blood pressure, high cholesterol, heart disease, type 2 diabetes or sleep apnea</td>
</tr>
<tr>
<td></td>
<td><strong>obese</strong> (BMI of 30 or higher)</td>
</tr>
<tr>
<td></td>
<td>74% women, mean weight 236 pounds, mean BMI 39</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Design</th>
<th>Double blind, superiority (40% drop out)</th>
</tr>
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<tbody>
<tr>
<td>Duration</td>
<td>1 year</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight loss counseling for all groups</th>
<th>Reduced-calorie diet (500 calories less) Nutritional and lifestyle counseling offered</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Results</th>
<th>PHENTERMINE/TOPIRAMATE</th>
<th>PHENTERMINE/TOPIRAMATE</th>
<th>PLACEBO</th>
<th>Absolute Difference [95% CI] (7.5mg/46mg minus placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHENTERMINE/TOPIRAMATE 15mg/92mg qd</td>
<td>Lost 11% of weight</td>
<td>Lost 9% of weight</td>
<td>Lost 2% of weight</td>
<td>7% [6%-8%] more weight lost</td>
</tr>
<tr>
<td>PHENTERMINE/TOPIRAMATE 7.5mg/46mg qd</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>How did the drug help?</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean % of body weight lost at 1 year</strong></td>
<td>Lost 11% of weight</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Percent of people who lost various amounts of weight</th>
<th>Lost 5%-9% of their weight</th>
<th>Lost 10%-14% of their weight</th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>21%</td>
<td>18%</td>
<td>25%</td>
<td>18%</td>
<td>12%</td>
</tr>
<tr>
<td></td>
<td>13% [8%-17%] more people</td>
<td>14% [10%-17%] more</td>
<td>---</td>
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<td>---</td>
</tr>
</tbody>
</table>

Qsymia on Cardiometabolic Variables

- SEQUEL trial
- Two-year sustained weight loss and metabolic benefits with qsymia in obese and overweight adults: a randomized, placebo-controlled extension study
- N=676
- Placebo vs qsymia (7.5/46) vs qsymia (15/92)

Qsymia on Cardiometabolic Variables

Liraglutide and PCOS

• 12-week open-label, prospective study
• N=40 (nondiabetes, pretreated with metformin for at least 6 months)
• Metformin 1000 mg BID : liraglutide (LIRA) 1.2 mg QD : combined MET 1000 mg BID and LIRA (COMBI) 1.2 mg QD
• Primary outcome: change in body weight

Liraglutide and PCOS

Subjects treated with COMBI lost on average 6.5±2.8 kg compared with a 3.8±3.7 kg loss in the LIRA group and 1.2±1.4 kg loss in the MET group (P<0.001 for the differences between the COMBI and MET therapy arms)

Liraglutide and PCOS

• 26-week double blind, randomized trial
• N=72
• Liraglutide 1.8 mg QD : placebo
• Outcome: bleeding pattern, sex hormones and gonadotrophins

# Liraglutide and PCOS


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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding ratio</td>
<td>0.67 [0.33 to 0.83]</td>
<td>0.28 [0.20 to 0.36]</td>
<td>&lt;0.001</td>
<td>0.58 [0.33 to 0.83]</td>
<td>0.14 [0.02 to 0.26]</td>
<td>&lt;0.05</td>
<td>0.14 [0.03 to 0.24]</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Ovarian volume (ml)</td>
<td>12.8 [3.5]*</td>
<td>-2.0 [-3.1 to -0.9]*</td>
<td>&lt;0.001</td>
<td>12.1 [4.9]*</td>
<td>-0.2 [-1.7 to 1.4]*</td>
<td>NS</td>
<td>-1.6 [-3.3 to 0.1]</td>
<td>NS</td>
</tr>
<tr>
<td>Antral follicle count</td>
<td>29.0 [22.5 to 44.0]*</td>
<td>-2.0 [-6.0 to 2.0]*</td>
<td>NS</td>
<td>28.0 [16.0 to 43.0]*</td>
<td>2.5 [-2.0 to 7.0]</td>
<td>NS</td>
<td>0.88 [0.74 to 1.06]*</td>
<td>NS</td>
</tr>
<tr>
<td>Stroma volume (ml)</td>
<td>11.4 [2.9]*</td>
<td>-1.9 [-3.1 to -0.8]*</td>
<td>&lt;0.01</td>
<td>10.7 [4.5]*</td>
<td>-0.2 [-1.7 to 1.2]*</td>
<td>NS</td>
<td>0.86 [0.71 to 1.03]*</td>
<td>NS</td>
</tr>
<tr>
<td>AMH (pmol/L)</td>
<td>70.5 [39.7 to 113.4]</td>
<td>-8.4 [-17.4 to 0.6]</td>
<td>NS</td>
<td>72.3 [27.5 to 104.7]*</td>
<td>3.5 [-13.9 to 21.0]*</td>
<td>NS</td>
<td>0.87 [0.72 to 1.04]*</td>
<td>NS</td>
</tr>
<tr>
<td>LH (IU/L)</td>
<td>8.0 [5.1 to 12.9]</td>
<td>-1.7 [-5.9 to 2.6]</td>
<td>NS</td>
<td>8.7 [4.5 to 14.2]</td>
<td>1.0 [-2.7 to 4.6]</td>
<td>NS</td>
<td>1.08 [0.73 to 1.59]*</td>
<td>NS</td>
</tr>
<tr>
<td>FSH (IU/L)</td>
<td>6.1 [3.8 to 7.9]</td>
<td>-0.3 [-1.3 to 0.8]</td>
<td>NS</td>
<td>5.8 [4.6 to 6.6]</td>
<td>0.2 [-1.3 to 1.7]</td>
<td>NS</td>
<td>0.95 [0.74 to 1.21]*</td>
<td>NS</td>
</tr>
<tr>
<td>Oestradiol (nmol/L)</td>
<td>0.25 [0.17 to 0.58]</td>
<td>-0.06 [-0.07 to 0.14]</td>
<td>NS</td>
<td>0.24 [0.19 to 0.39]</td>
<td>0.02 [-0.14 to 0.11]</td>
<td>NS</td>
<td>1.01 [0.74 to 1.39]*</td>
<td>NS</td>
</tr>
<tr>
<td>Total testosterone (nmol/L)</td>
<td>1.23 [0.91 to 1.63]</td>
<td>-0.07 [-0.25 to 0.10]</td>
<td>NS</td>
<td>1.35 [0.95 to 1.93]</td>
<td>0.15 [-0.10 to 0.39]</td>
<td>NS</td>
<td>0.88 [0.71 to 1.09]*</td>
<td>NS</td>
</tr>
<tr>
<td>Free testosterone (nmol/L)</td>
<td>0.026 [0.021 to 0.038]</td>
<td>-0.005 [-0.009 to -0.001]</td>
<td>&lt;0.01</td>
<td>0.033 [0.023 to 0.040]</td>
<td>0.004 [-0.003 to 0.011]</td>
<td>NS</td>
<td>0.81 [0.65 to 1.00]</td>
<td>0.05</td>
</tr>
<tr>
<td>Free androgen index</td>
<td>3.84 [2.78 to 6.54]</td>
<td>-1.34 [-2.19 to -0.48]</td>
<td>&lt;0.01</td>
<td>4.95 [3.08 to 6.32]</td>
<td>0.80 [-0.42 to 2.01]</td>
<td>NS</td>
<td>0.74 [0.58 to 0.95]*</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>AMH (ng/mL)</td>
<td>6.31 [4.39 to 7.93]*</td>
<td>-0.69 [-1.44 to 0.06]</td>
<td>NS</td>
<td>6.29 [4.63 to 8.84]</td>
<td>0.76 [-0.39 to 1.92]</td>
<td>NS</td>
<td>0.85 [0.70 to 1.04]*</td>
<td>NS</td>
</tr>
<tr>
<td>SHBG (nmol/L)</td>
<td>31.0 [22.0 to 44.5]*</td>
<td>-7.4 [4.10 to 17.7]</td>
<td>&lt;0.001</td>
<td>20.5 [30.5 to 37.5]</td>
<td>2.0 [-2.9 to 7.0]</td>
<td>NS</td>
<td>1.19 [1.02 to 1.39]*</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Data presented as mean (SD), median (p25–p75) and differences as mean (95% CI). No missing cases. One woman with regular menstruation at baseline did not significantly alter the results. Exclusion of the 16 women with regular menstruation at baseline did not alter the results.
Exenatide and PCOS

• 24-week double blind, randomized trial
• N=176
• Exenatide 10 μg BID : metformin (MET) 1000 mg BID first 12 weeks then MET alone during the second 12 weeks
• Outcome: body weight, rate of pregnancy

Liu et al. (2017). Clin Endocrinol
Exenatide and PCOS

**TABLE 3** Natural pregnancy rate in two groups during the second 12 weeks

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Natural pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXE</td>
<td>78</td>
<td>34 (43.6%)</td>
</tr>
<tr>
<td>MET</td>
<td>80</td>
<td>15 (18.7%)</td>
</tr>
</tbody>
</table>

χ² = 11.39*  

*P < .05.

Liu et al. (2017). Clin Endocrinol
This Patient

• Metformin increased to metformin XR 1000 mg bid
• Started on progesterone (provera) 12 days to regulate her cycle
• Monitor HTN, lipid abnormalities
• Referred to dermatology for laser hair removal
• Encouraged therapeutic lifestyle modifications of diet and exercise to promote weight loss
• Stop qsymia
• Consider GLP-1 receptor agonist
References

• Sam S, Ehrmann DA. Metformin therapy for the reproductive and metabolic consequences of polycystic ovary syndrome. Diabetologia. 2017 Aug 3.