A retrospective audit of patients with polycystic ovary syndrome: the effects of a reduced glycaemic load diet

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Abstract

Background

Polycystic Ovary Syndrome (PCOS) is characterized by hyperandrogenism and chronic anovulation. The aim of this retrospective audit was to determine the patient profile, including anthropometrics, biochemistry and symptoms and evaluate the influence of a dietary intervention in women with PCOS.

Methods

Data was collected retrospectively from dietetic and medical records from all PCOS patients (n=88) who attended a dietetic consultation from July 2004 to July 2006. As standard clinic practice a reduced glycaemic load diet had been prescribed, with energy reduction in overweight patients. Follow up data was available for 59 patients.

Results

Fifty eight patients had a body mass index (BMI) $\leq$24.9 kgm^{-2} and 30 had a BMI $\geq$25 kgm^{-2}. Thirty six patients, with a BMI $\leq$24.9 kgm^{-2}, self-reported central weight gain at their initial appointment. Over two thirds of patients self reported one or more of the following symptoms; carbohydrate cravings, hypoglycaemia, tiredness and hunger. At the follow up appointment BMI and waist circumference significantly decreased in

overweight patients ($p<0.05$). Seventy one percent of women self reported hypoglycaemia initially, this reduced to 13% at follow up appointment ($p<0.01$).

Conclusion

The audit indicated a low glycaemic load diet in combination with medication may contribute to an improvement in symptom relief in patients with PCOS.

Introduction

Polycystic Ovary Syndrome (PCOS) is a heterogeneous condition affecting 5-10% of women of reproductive age and is characterized by hyperandrogenism and chronic anovulation (Dunaif, 1997). Patients with the condition are at increased risk of a number of health problems, including coronary heart disease, type 2 diabetes, hypertension, (AACE, 2005), gestational diabetes, spontaneous abortion (Schroder *et al*. 2004), breast and endometrial cancer (Balen, 2001). It is also the commonest cause for anovulatory infertility (Adams *et al*. 1986). A multitude of other symptoms have been reported in the literature and within the clinical setting, resulting in the development of quality of life questionnaires for both clinical and research purposes (Jones *et al*. 2004). Anecdotal reports of carbohydrate craving (Hirschberg 2004) have been postulated to be due to hyperinsulinaemia out of proportion to insulin sensitivity leading to low post-prandial glucose levels and subsequent craving of carbohydrate foods (Hirschberg 2004; Heller and Heller 1994). Of interest, reactive hypoglycaemia and has been reported in 50% of lean young women with PCOS Altuntas (2005). It is useful to understand symptom profile in detail when considering treatment for the syndrome.

Environmental factors have an important influence on the expression of PCOS (Franks *et al.* 2005), with insulin resistance and resultant hyperinsulinaemia implied in PCOS

pathogenesis (Dunaif, 1997). Hyperinsulinaemia stimulates thecal androgen production and decreases hepatic sex hormone-binding globulin, resulting in hyperandrogenism and the associated clinical features of PCOS (Poretsky 1999). Insulin resistance is exacerbated by weight gain, particularly in the abdominal region, which is common in patients with PCOS with a reported 10-50% of patients overweight or obese (Moran & Norman, 2004). Even though obese PCOS patients are generally thought to be more symptomatic and at greater health risk, normal weight PCOS patients are also at increased risk (AACE, 2005, Chang *et al*. 1983; Dunaif *et al.* 1989) and suffer debilitating symptoms (Sheehan, 2004). Therefore, it is important to investigate all patients with PCOS not just the overweight.

Diet and lifestyle modification is advocated as one of the primary treatments to manage the symptoms of PCOS (Moran & Norman, 2004). There has been limited research into dietary modification and to date, this has focused on the benefits of weight loss in obese and overweight patients with PCOS (Moran & Norman, 2004; Norman *et al*. 2004; Stamets *et al*. 2004). Reduced glycaemic load diets have been associated with reduced post-prandial glucose and subsequent hyperinsulinaemia (Wolever, 1996; McMillan-Price *et al.* 2006). There remains debate over what the optimal dietary components for PCOS should be and, in a survey of dietitians practicing in the UK, there was a lack of consistency in the dietary advice given to women with PCOS, with 27% of dietitians focused on advising lower glycaemic index foods (Jeanes *et al.* 2007). In addition to lifestyle modification, common medications, including insulin sensitizing agents and hormone replacement, are used.

The aim of this audit was to determine patient profiles of patients with PCOS and document self-reported symptoms potentially related to insulin resistance. It is also important for the advancement of PCOS treatment in both lean and overweight patients to monitor the effectiveness of health care interventions in the clinical setting. Therefore, we also assessed the influence of a reduced glycaemic load diet and lifestyle advice in combination with commonly prescribed medications on anthropometry, glycaemic indices and commonly reported symptoms.

Materials and methods

Subjects

All PCOS patients aged ≥15 years referred to a private registered dietitian over a 2-year period between July 2004 and July 2006 were included (n=88). Patients were under the management of a consultant gynaecologist or endocrinologist at a private health and hormone clinic, and referred to the specialist dietitian affiliated to the clinic at varying stages post-diagnosis (newly diagnosed to several years) for an initial 90-minute dietetic consultation.The consultants at the clinic diagnosed the patients with insulin resistance, although method of diagnosis was not available for this audit.

An individualized diet aimed to improve glycaemia and insulinaemia was advised; this included healthy eating, low glycaemic load diet (low glycaemic index foods, reduced carbohydrate approximately 40-45% energy, higher protein approximately 30% energy, reduced saturated fat approximately 10%energy and no snacking). The dietary advice is standard practice at the clinic and is based on the specialist dietitians surmise of the published literature in the absence of published guidelines for dietary advice for women

with PCOS. Overweight and obese patients were advised to reduce energy density by increasing the vegetable proportion of their diet. Recommendations for physical activity consisted of approximately 30min of moderate activity/day. A subsequent 30-min review consultation was advised, but not attended by all patients. Follow-up data obtained from dietetic and medical records was available for 59 patients, ranging between 2 weeks and 12 months after initial consultation; categorized to < 3months (n=29), 3-6 months (n= 13) and > 6 months (n=17).

Ethical approval to conduct the audit was given by the Clinical Director at The Surrey Park Clinic and Roehampton University ethics board. No funding was sought for the audit.

Data collection

The data were collected retrospectively by review of dietetic and medical records. Dietary intake data were not included in the audit as initial dietary intake was not consistently recorded in sufficient detail for meaningful analysis. Pre- and post-dietetic intervention data were compared to assess the impact of dietary and lifestyle advice on anthropometrics, biochemistry and symptom relief (the audit did not control medication prescribed).

1. Anthropometric measurements were obtained from the patients' dietetic records or, if unavailable, from time corresponding medical records and included weight (indoor clothing, no shoes), body mass index (BMI) using self-reported height. Waist circumference, in many cases (especially lean patients), was not routinely measured.

2. Self-reported physical activity levels were categorized using values based on American Diabetes Association recommendations (Sigal *et al*., 2006): low, <90 min moderate activity per week; moderate, 90mins-150min moderate or 90min vigorous activity per week; high, >150mins moderate or >90mins vigorous activity per week.
3. Biochemical results, if available, pre- and post-initial dietetic and medical intervention were obtained from medical records and included: fasting glucose and insulin, glucose and insulin measured 2 hour post-oral glucose tolerance test (OGTT). Oestradiol was only recorded predietetic intervention. Androgen values were not available as they were not routinely measured. Blood sampling was conducted using standard procedures within the clinic and sent to a hospital laboratory for analysis (insulin and oestradiol were measured using an Immulite 2000 (Siemens Healthcare Diagnostics, New York, USA) and glucose was measured using an automated analyzer (Dimension Expand; Siemens Healthcare Diagnostics).
4. Commonly reported symptoms were recorded from the medical or dietetic notes at the time of the initial dietetic consultation and at the time of the follow-up appointment. The self reported symptoms included carbohydrate cravings (i.e. craving for sugary or starchy foods or both), central weight gain, hypoglycaemia (described variously as ‘shaky’, dizzy’, ‘light headed’), tiredness/lethargy and hunger; the dietitian or consultant asked if the patient was experiencing the symptoms. The incidence of gastrointestinal type symptoms defined by patients as

irritable bowel syndrome symptoms or food intolerances/allergies were frequently mentioned and therefore also reported.

The audit did not control medication prescribed. Medications relating directly to PCOS treatment at the time of the initial dietetic consultation were recorded. These included oestrogen, progesterone, contraceptive pill (hormone replacement therapy) and metformin (insulin sensitizing agent). During the period of this audit, weight loss medication was not commonly prescribed and therefore not recorded.

Statistical analysis

Data analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Normality was assessed using the Kolmogorov-Smirnov test. The chi-square test was used to determine if there is a difference in symptoms between overweight and normal weight. A paired *t*-test was used to compare weight, BMI, waist circumference, glucose and insulin values pre- and post-dietetic intervention. Symptoms pre- and post-intervention were assigned an index to enable a Wilcoxon signed rank test to test the null hypothesis of no difference. For all analyses, a $P < 0.05$ was considered statistically significant. Data were split into two groups for analysis: BMI ≥ 25 kgm^{-2} (overweight and obese) and BMI 18-24.9kgm^{-2} (under/normal weight).

Results

Patients

Eighty–eight patients with PCOS were seen by the specialist dietitian over the 2-year period (July 2004 to July 2006). In total, 67 patients were prescribed hormone replacement therapy. Serum oestradiol levels were measured in 45 patients; the mean

level was at the lower end of the normal range (200-1000pmL^{-1}) and 78% (n=35) of these patients were prescribed oestrogen replacement. The incidence of previous or current eating disorders was self-reported as 17% (n=15).

Baseline characteristics

Anthropometrics and biochemistry

The majority of patients (66%) had a BMI ≤24.9 kgm^{-2}; three patients had a BMI< 18 kgm^{-2}. The average age was 32.4 (SD 9.1 years). There was no significant difference in the age of lean patients (BMI ≤24.9 kgm^{-2}) compared to overweight and obese patients (BMI ≥25 kgm^{-2}). Waist circumference was measured in 46 patients, 18 (39%) had a waist circumference ≥88cm denoting a substantially increased risk to health, and an additional seven patients (15%) had a waist circumference ≥80cm (increased risk to health) (WHO, 2000). Mean values for lean, overweight and obese patients are shown in Table 1.

Table 1. Mean anthropometric values categorised by BMI at initial dietetic consultation

	BMI (kgm^{-2})*		Weight (kg)*		WC (cm)*	
	N (n=55)	O (n=30)	N (n=55)	O (n=30)	N (n=21)	O (n=25)
Mean (SD)	21.4 (1.9)	32.8 (6.0)	59.1 (6.1)	89.2 (16.0)	71 (4.3)	95.0 (11.5)
Range	18.2-24.4	25.3-50.3	59.1-72.0	66.8-127.3	64-83	76-119

N: under/normal weight (BMI=18-24.9 kgm^{-2}), O: overweight/ obese (BMI≥25 kgm^{-2})
WC: waist circumference. * Significant difference between normal weight and overweight ($p<0.05$) for BMI, weight and WC

Mean fasting glucose (n=71) and insulin levels (n=70) were within the normal reference ranges (3.5-5.8 mmolL^{-1} and 0-88pmolL^{-1}, respectively) (Table 2). Overweight/ obese patients had significantly higher insulin levels ($P<0.01$) (Table 2).

Table 2. Biochemical measures prior to initial dietetic consultation

	Fasting glucose mmol/L		2-hour glucose mmol/L		Fasting insulin pmol/L*		2-hour insulin pmol/L*	
	N (n=45)	O (n=24)	N (n=42)	O (n=23)	N (n=44)	O (n=24)	N (n=43)	O (n=23)
Mean (SD)	4.7 (0.48)	5.0 (1.4)	4.6 (1.1)	5.0 (1.4)	37 (30)	85 (65)	225 (121)	330 (199)
Range	3.6-5.7	4.3-6.7	2.3-6.8	2.5-7.4	14-164	16-257	31-571	69-815

N: under/normal weight (BMI=18-24.9 kgm^{-2}), O: overweight/ obese (BMI≥25 kgm^{-2})
* Significant difference between normal weight and overweight ($p<0.05$) for fasting and 2 hr post glucose load insulin

The majority of patients (87%) were prescribed metformin after their initial glucose tolerance test, although 18% (n=16) reported that they were not actively taking it. At the time of the initial dietetic consultation three patients had a fasting glucose above 5.8 $mmolL^{-1}$ and 11 had a raised fasting insulin level; all patients with abnormal fasting levels were prescribed metformin. Two-hour insulin levels were above the normal reference range (<189 $pmolL^{-1}$) in the majority of normal weight (28 out of 42 measured; 67%), overweight (five out of eight measured; 63%) and obese patients (12 out of 15 measured; 80%).

Self reported symptoms

Seventy percent (n=59) of patients self-reported symptoms of carbohydrate cravings, the proportion of patients reporting carbohydrate craving was similar in lean and overweight patients (Table 3). Lean patients more frequently self-reported symptoms of hypoglycaemia compared with overweight patients (73% and 43% respectively; $P<0.05$) (Table 3). Self-reported central weight gain and hunger was more frequently reported in overweight/ obese patients (93% and 86%, respectively), this was significantly greater than the number of lean patients who also reported these symptoms (47% and 59%,

respectively; P<0.05). However, it should be highlighted that approximately half of lean patients reported central weight gain and hunger. Tiredness/ lethargy was reported by the majority of patients (82%).

Gastrointestinal symptoms were reported by 68% of all patients. Symptoms were described either as irritable bowel syndrome type symptoms (bloating, constipation etc) or food intolerance/allergies. A higher proportion, (n=14; 16%), were reported to be semi/vegetarian, compared to the published population prevalence of 5.4% (Realeat, 1997).

Table 3. Number of patients reporting symptoms possibly related to insulin resistance at initial dietetic consultation

	Symptom present		Symptom absent		Not reported
	N	O	N	O	N and O
Central weight gain*	25 (36%)	25 (83%)	22 (40%)	2 (7%)	11
CHO cravings	39 (70%)	21 (70%)	2 (4%)	2 (7%)	4
Self reported Hypoglycaemia*	40 (73%)	13 (43%)	13 (24%)	14 (47%)	5
Hunger*	34 (61%)	24 (80%)	17 (31%)	4 (13%)	6
Tiredness/lethargy	44 (80%)	26 (86%)	11 (20%)	3 (10%)	1

N: under/ normal weight (BMI=18-24.9 kgm^{-2}), O: overweight/ obese (BMI≥25 kgm^{-2})
CHO: Carbohydrate. * Significant difference ($p<0.05$) in number of normal weight compared with overweight patients analysed by Chi-square.

Physical activity

Forty percent of patients had a low level of physical activity (<90 min moderate activity/ week) with only 34% of patients achieving American Diabetes Association recommendations (2006) of at least 150 min of moderate activity/ week or more than 90 min vigorous activity/ week.

Post dietetic intervention results

Follow-up data was available for 59 patients. Post-dietetic intervention, there were only data for seven patients regarding their physical activity, and three of these patients had increased their physical activity.

Anthropometrics and biochemistry

There was a significant decrease in weight, BMI and waist circumference in overweight/obese patients after the dietetic intervention but no difference was reported in normal weight patients (Table 4); this remained the case when patients were split into categories for the time of follow up: < 3 months, 3-6 months and >6 months.

Table 4. Anthropometric measurements pre and post dietetic intervention

	Weight (kg)		BMI (kgm^{-2})		WC (cm)	
	Pre	Post	Pre	Post	Pre	Post
N	(n=32)	(n=32)	(n=32)	(n=32)	(n=5)	(n=5)
Mean (SD)	59.5 (6.8)	59.6 (7.2)	21.5 (2.0)	21.7 (2.2)	72.4 (6.3)	70.6 (8.2)
O	(n=17)	(n=17)	(n=17)	(n=17)	(n=11)	(n=11)
Mean (SD)	90.9* (17.1)	87.5* (14.5)	33.1* (5.4)	32.0* (4.8)	96.0* (10.3)	91.8* (11.3)

N: under/normal weight (BMI=18-24.9 kgm^{-2}), O: overweight/ obese (BMI≥25 kgm^{-2})
WC: waist circumference. * Significant difference ($p<0.05$) in pre and post dietetic intervention weight, BMI and WC in overweight/ obese patients using paired t test.

Thirteen patients had values for fasting glucose and insulin pre- and post-dietetic consultation, fasting glucose values were significantly reduced [5.1 (SD0.6) and 4.7 (SD 0.5), respectively; P=0.02]; there were no significant differences in fasting insulin values [80.1 (SD 77.1) and 65.3 (SD38.5), respectively; P=0.25]. All these patients were prescribed metformin before the initial dietetic consultation; change in prescription was not recorded.

Self reported symptoms

There were 50 patients with pre and post data on carbohydrate craving, 52% (n=26) reported a reduction in their carbohydrate craving (P<0.001) (Table 5). There was a similar reduction in reported carbohydrate cravings in lean and overweight patients. The incidence of self-reported hypoglycaemia also reduced, most markedly in those of normal weight from 73% (n=25) to only 11% (n=4) (P<0.001). The number of patients reporting symptoms of hunger and tiredness/ lethargy also substantially reduced from 54% to 29% and 83% to 40%, respectively (P=0.007 and P=0.016, respectively).

Table 5. Number (and percentage) of patients reporting symptoms related to insulin resistance pre and post dietetic intervention

	Pre		Post		
	Symptom present	Symptom absent	Symptom present	Symptom reduced	Symptom absent
Carbohydrate cravings * (n=50)	**38 (76)**	**12 (24)**	**8 (16)**	**26 (52)**	**16 (32)**
N (n=35)	25 (71)	10 (29)	6 (17)	17 (49)	12 (34)
O (n=15)	13 (87)	2 (13)	2 (13)	9 (60)	4 (27)
Self reported Hypoglycaemia* (n=48)	**34 (71)**	**14 (29)**	**6 (13)**	**18 (37)**	**24 (50)**
N (n=34)	25 (73)	9 (27)	4 (11)	12 (35)	18 (53)
O (n=14)	9 (64)	5 (36)	2 (14)	6 (43)	6 (43)
Hunger * (n=48)	**26 (54)**	**22 (46)**	**14 (29)**	**15 (31)**	**19 (40)**
N (n=33)	20 (61)	13 (39)	8 (24)	12 (36)	13 (40)
O (n=15)	13 (87)	2 (13)	6 (40)	3 (20)	6 (40)
Tiredness/lethargy * (n= 48)	**40 (83)**	**8 (17)**	**19 (40)**	**20 (42)**	**9 (18)**
N (n=35)	27 (77)	8 (23)	15 (43)	13 (37)	7 (20)
O (n=13)	13 (100)	0 (0)	4 (31)	7 (54)	2 (15)

N: under/normal weight (BMI=18-24.9 kgm^{-2}), O: overweight/ obese (BMI≥25 kgm^{-2}). * Significant difference (p<0.01) in pre and post dietetic intervention. Symptoms pre and post intervention were assigned an index analysis by Wilcoxon Signed Rank.

Discussion

Less than 50% of the patients were overweight. This is contrary to published literature (Hart *et al*., 2004) and the general perception that women with PCOS are either overweight or obese. The setting for the audit was in a private clinic which may offer an explanation for the differing population. A survey by Jeanes *et al.* (2007) reported that only 24% of UK dietitians surveyed reported seeing lean women with PCOS for dietary advice. The high proportion of lean patients provides valuable information on commonly reported symptoms that are not solely attributable to being overweight. The audit also indicated that 17% of patients had a previous or current eating disorder, which is higher than in the general population (Hoek & van Hocken, 2003), in concurrence with McCluskey *et al*. (1991) and Jananfar *et al*. (1995) who observed a significant association between bulimia and PCOS.

Waist circumference was not routinely measured (particularly in lean women); however, 36% reported central weight gain when questioned, and this is of interest because central weight gain is associated with insulin resistance (Smith *et al.,* 2001). All PCOS patients in this audit had also been diagnosed with insulin resistance by the consultants and the majority had been prescribed insulin-sensitizing medication. The symptoms reported in this audit, although mentioned in published literature, have not been studied in detail, and this is the first time the prevalence of some of these symptoms have been reported in women with PCOS. Subjective carbohydrate cravings were reported by the majority of patients. Carbohydrate craving is difficult to measure and there is an ongoing debate regarding what the best tool to use is (Christensen, 2007). It has been proposed that carbohydrate craving and hunger may result from hyperinsulinaemia leading to a

reduction in blood glucose levels and a physiological drive for carbohydrate replacement (Heller and Heller, 1994; Hirschberg *et al*, 2004), this in turn may lead to an increased risk of weight gain, as well as having a possible association with enhanced insulin resistance (Bjoervell *et al.*, 1985; Holte, 1996). Moran & Norman (2004) reported that hunger and satiety may be impaired in PCOS; adding to the literature in this area, our audit found that over half of patients (and a greater proportion of overweight patients) reporting hunger, for which the possible mechanism has been described above.

Hypoglycaemia, reported to be experienced by almost two-thirds of lean patients prior to their dietetic consultation, was similar to the incidence observed by Altuntas *et al*. (2005) who reported 50% prevalence of reactive hypoglycaemia in 64 lean women with PCOS. They also linked reactive hypoglycaemia with insulin resistance and postulated that this together with DHEA-S level could predict development of type 2 diabetes in lean women with PCOS.

Weight loss has been shown to be effective in improving insulin resistance and reproductive function (Crosignani *et al*., 2003; Stamets *et al*., 2004; Tolino *et al*.,2005). However, there are no studies investigating the efficacy of dietary or lifestyle interventions in lean women with PCOS. Lean patients in this audit were given a eucaloric version of the same reduced glycaemic load, hypocaloric diet prescribed for patients requiring weight loss. The results from this audit demonstrate the possibility of providing dietary advice aimed at improving glycaemia and insulinaemia that also produces a significant reduction in weight in the overweight and obese, but maintains weight in those who are lean if energy intake is adjusted accordingly. A small number of patients had pre- and post-glucose and insulin measurements, whereby an improvement

in fasting glucose was observed. This is likely to be attributable to a combination of insulin sensitizing medication and lifestyle modifications; however, without a control group, the impact of the interaction with healthcare professionals alone can not be ruled out. The findings of the audit are in agreement with the study by Goldenberg *et al.* (2005) who demonstrated that metformin with a low carbohydrate, high protein diet resulted in benefits in metabolic and menstrual parameters in PCOS patients. Importantly, the number of patients in the audit reporting symptoms of carbohydrate craving and hunger were substantially reduced at the follow-up appointment, which is a promising finding in trying to promote weight loss. Furthermore, the reported reduction in self-reported hypoglycaemia may be partly attributable to the reduced post-prandial hyperinsulinaemia and stable glycaemia observed with low glycaemic load diets (Brand-Miller *et al*., 2002) which may also impact on tiredness/lethargy by maintaining more sustained energy levels.

The limited availability of post-intervention glucose and insulin results and wide variation in follow-up data make it difficult to draw any firm conclusions with regards to medical and lifestyle interventions; however, the results available indicate a positive role for the dietary advice provided. Furthermore, it is difficult to elucidate which intervention (medication, diet or exercise) had the greatest impact on the results. Certain medications can influence body weight and hormones but this was not taken into consideration in the current audit and may have influenced the results and, thus, should be a consideration in a prospective dietary intervention. This retrospective audit highlights the need for well controlled intervention studies with a control group; likewise any future studies should also include androgen values. Despite some methodological limitations, the audit offers

valuable information to healthcare professionals regarding the PCOS population, particularly in view of the lack of published information on lean women with PCOS. The results from this audit support the use of low glycaemic load diets in clinical practice in association with medication and lifestyle advice in both overweight/obese and lean patients with PCOS. The audit also emphasizes the need for research into altered macronutrient profiles for the dietary management of lean PCOS patients, in order to enable optimal dietary treatment to be elucidated without the confounding effects of weight loss.

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