**Review article**

The optimal diet for women with polycystic ovary syndrome?

Kate Marsh* and Jennie Brand-Miller

_Human Nutrition Unit, School of Molecular and Microbial Biosciences, University of Sydney, NSW Australia 2006_

(Received 31 May 2004 – Revised 17 February 2005 – Accepted 23 February 2005)

An optimal diet is one that not only prevents nutrient deficiencies by providing sufficient nutrients and energy for human growth and reproduction, but that also promotes health and longevity and reduces the risk of diet-related chronic diseases. The composition of the optimal diet for women with polycystic ovary syndrome (PCOS) is not yet known, but such a diet must not only assist short term with weight management, symptoms and fertility, but also specifically target the long-term risks of type 2 diabetes, CVD and certain cancers. With insulin resistance and compensatory hyperinsulinaemia now recognised as a key factor in the pathogenesis of PCOS, it has become clear that reducing insulin levels and improving insulin sensitivity are an essential part of management. Diet plays a significant role in the regulation of blood glucose and insulin levels, yet research into the dietary management of PCOS is lacking and most studies have focused on energy restriction rather than dietary composition _per se_. On the balance of evidence to date, a diet low in saturated fat and high in fibre from predominantly low-glycaemic-index-carbohydrate foods is recommended. Because PCOS carries significant metabolic risks, more research is clearly needed.

**Polycystic ovary syndrome: Insulin resistance: Glycaemic index**

Sabate (2003) defines an optimal diet as one that not only prevents nutrient deficiencies by providing sufficient nutrients and energy for human growth and reproduction, but that also promotes health and longevity and reduces the risk of diet-related chronic diseases. The composition of the optimal diet for women with polycystic ovary syndrome (PCOS) is not yet known. Research findings allow us, however, to speculate on the type of eating pattern that could best address the health concerns that women with this condition face.

In the short term, the dietary management of PCOS needs to focus on weight loss, the amelioration of symptoms such as acne and hirsutism, and improved fertility in those who wish to fall pregnant. In the long term, dietary management must address the increased risk of type 2 diabetes, CVD and certain cancers, which are associated with this condition.

**Polycystic ovary syndrome: pathophysiology and associated health risks**

PCOS is the most common endocrine disorder in women, affecting an estimated 5–10% of women of reproductive age (Franks, 1995; Knöchelhauer et al. 1998; Asuncion et al. 2000). Once thought of as a fertility problem, it is now known that PCOS is a metabolic disorder with serious health consequences. Classic features of the syndrome include oligomenorrhoea or amenorrhoea, anovulation, infertility, hirsutism, acne and accelerated scalp hair loss. Diagnosis requires the presence of two out of three of the following: (1) oligo- or anovulation; (2) clinical and/or biochemical signs of hyperandrogenism; (3) polycystic ovaries, with the exclusion of other aetiologies such as congenital adrenal hyperplasia, androgen-secreting tumours and Cushing’s syndrome (Rotterdam ESHRE/ ASRM-Sponsored PCOS Consensus Workshop Group, 2004).

Insulin resistance, with compensatory hyperinsulinaemia, has been identified as a key component in the pathophysiology of PCOS in both lean and obese women, putting them at risk of developing type 2 diabetes and CVD (Chang et al. 1983; Dunaif et al. 1989; Dunaif, 1997). It is estimated that 50–70% of women with PCOS have insulin resistance.

Studies have shown an increased prevalence of impaired glucose tolerance (IGT) and type 2 diabetes in both normal-weight and obese women with PCOS (Dunaif et al. 1987; Dahlgren et al. 1992b; Ehrmann et al. 1999; Legro et al. 1999; Wild et al. 2000; Elting et al. 2001; Norman et al. 2001; Weerakijet et al. 2001). The rate of conversion from normoglycaemia to IGT and type 2 diabetes is also increased (Ehrmann et al. 1999; Norman et al. 2001).

In addition, gestational diabetes appears to be more common in women with PCOS (Lanza et al. 1995; Lesser & Garcia, 1997; Holte et al. 1998; Paradisi et al. 1998; Radon et al. 1999; Bjercke et al. 2002) and there is an increased risk of miscarriage in these women (Glueck et al. 1999).

**Abbreviations:** DASH, Dietary Approaches to Stop Hypertension; GI, glycaemic index; GL, glycaemic load; IGT, impaired glucose tolerance; PCOS, polycystic ovary syndrome.

*Corresponding author:* Kate Marsh, fax +61 2 9415 1446, email K.Marsh@mmb.usyd.edu.au
A number of studies have also found a higher incidence of risk factors for CVD in women with PCOS. Risk factors include dyslipidaemia (predominantly high triacylglycerols and low HDL) and hypertension, with hyperinsulinaemia a strong predictor of CVD risk (Conway et al. 1992; Dahlgren et al. 1992a; Wild et al. 1992; Talbott et al. 1995; Wild, 1995; Robinson et al. 1996; Talbott et al. 1998; Mather et al. 2000; Elting et al. 2001; Legro et al. 2001; Pirwany et al. 2001; Strowitzki et al. 2002; Fenkci et al. 2003). Smaller LDL particle size (Sampson et al. 1996; Dejager et al. 2001; Pirwany et al. 2001), elevated plasminogen activator inhibitor-1 levels (Dahlgren et al. 1994; Talbott et al. 2000), elevated serum C-reactive protein (Fenkci et al. 2003) and raised plasma homocysteine levels (Wijeyarante et al. 2003) have also been demonstrated in women with PCOS. Finally, studies have demonstrated increased oxidative stress and decreased antioxidant levels in these women (Sabuncu et al. 2001; Fenkci et al. 2003). Despite these risk factors, however, evidence of an increased mortality from CVD in PCOS is lacking and further studies are needed (Pierpoint et al. 1998; Wild et al. 2000; Legro, 2003).

Evidence of an increased incidence of endometrial cancer in women with PCOS is limited despite concerns of a higher risk due to chronic anovulation with consequent unopposed oestrogen secretion (Hardiman et al. 2003). There is some evidence that the risk is higher in those who are overweight or obese (Coulam et al. 1983; Furberg & Thune, 2003). One study has shown a positive association between PCOS and family history of breast cancer (Atimo et al. 2003), while PCOS does carry some risks for breast cancer including hyperinsulinaemia and obesity, no links have yet been established.

**Dietary management of polycystic ovary syndrome**

Research into the dietary management of PCOS is lacking, despite the fact that lifestyle modifications including diet, exercise and weight loss have been shown to be beneficial. A reduction in weight of as little as 5% of total body weight has been shown to reduce insulin levels, improve menstrual function, reduce testosterone levels and improve symptoms of hirsutism and acne (Pasquali et al. 1989; Kiddy et al. 1992; Guzick et al. 1994; Andersen et al. 1995; Clark et al. 1995; Crave et al. 1995; Holte et al. 1995; Jakubowicz & Nestler, 1997; Clark et al. 1998; Huber-Buchholz et al. 1999; Wahrenberg et al. 1999; Pasquali et al. 2000) van Dam et al. 2002; Crosignani et al. 2003; Moran et al. 2003; Gambineri et al. 2004; Moran et al. 2004; Stamets et al. 2004). These findings are summarised in Table 1.

Approximately 50% of women with PCOS are obese and this obesity is associated with a greater degree of insulin resistance, hyperinsulinaemia, lipid abnormalities, hyperandrogenism, hirsutism and menstrual irregularities (Pasquali & Casimirri, 1993; Pasquali et al. 1993, 1994; Andersen et al. 1995; Ciaraldi et al. 1997; Gambineri et al. 2002). Furthermore, there is a higher prevalence of abdominal fat distribution in women with PCOS, even those of a normal body weight, and this increase in visceral fat has been shown to be associated with glucose intolerance and dyslipidaemia (Kirchengaust & Huber, 2001; Yildirim et al. 2003).

Women with PCOS often report difficulties losing weight, although some studies have not shown this to be the case (Jakubowitz & Nestler, 1997; Pasquali et al. 2000). Clark et al. (1995), however, found that obese, infertile women presenting to a weight-loss programme aimed at improving fertility outcomes had experienced an average weight gain ten times that of the normal population before starting the programme. In addition, Holte et al. (1995) found that while insulin resistance in obese women with PCOS was reduced by weight loss to similar levels as BMI-matched controls, there was a persistent increased early insulin response to glucose, which could provide a stimulus to weight gain.

Most of the studies of dietary intervention in women with PCOS have focused on energy restriction rather than dietary composition per se, yet the weight loss seen in most of these studies has been small in comparison with the outcomes achieved. And while the incidence of insulin resistance is higher in women with PCOS who are obese, and weight loss clearly improves outcomes for these women, not all women with PCOS who have insulin resistance are overweight or obese. Studies have demonstrated a higher incidence of insulin resistance, IGT and type 2 diabetes in women with PCOS of normal weight (Chang et al. 1983; Jialal et al. 1987; Dunail et al. 1989; Fenkci et al. 2003), suggesting that dietary management of this condition must go beyond weight loss.

In most of the dietary studies in women with PCOS, improvements in metabolic and reproductive outcomes have been closely related to improvements in insulin sensitivity, suggesting that dietary modification designed to improve insulin resistance may produce benefits greater than those achieved by energy restriction alone.

With the high incidence of insulin resistance and IGT and the increased risk of type 2 diabetes in women with PCOS, research into the effects of diet and exercise on diabetes prevention is highly relevant to this group. The Diabetes Prevention Program achieved a 58% reduction in risk of progression from IGT to type 2 diabetes with lifestyle modification, with the average weight loss a modest 5·6 kg (Diabetes Prevention Program Research Group, 2002). These results were similar to the Finnish Diabetes Prevention Study, which also achieved a 58% reduction in risk of diabetes with lifestyle changes including diet and exercise (Tuomilehto et al. 2001). In this study average weight loss in the intervention group was 4·2 kg. While the Diabetes Prevention Program and Diabetes Prevention Study included only overweight and obese subjects, the Da Qing Study in China achieved a reduction in the incidence of diabetes with diet and exercise that was equally successful in normal-weight and obese subjects, suggesting that the benefits of diet and exercise were not related only to weight loss (Pan et al. 1997).

With insulin resistance and compensatory hyperinsulinaemia now recognised as key factors in the pathogenesis of PCOS, it has become clear that reducing insulin levels and improving insulin sensitivity are an essential part of the management of this condition. While much of the recent research has focused on the insulin-sensitising agent, metformin, diet also plays a significant role in the regulation of blood glucose and insulin levels. In fact the Diabetes Prevention Program showed that lifestyle modification (diet and exercise) in individuals with IGT produced a greater reduction in risk of developing type 2 diabetes than metformin (Diabetes Prevention Program Group, 2002). In addition, a recent meta-analysis of the effects of metformin use in PCOS found that while metformin does improve ovulation rate, both alone and in combination with clomiphene, equal or better ovulation rates have been achieved using lifestyle modification (Lord et al. 2003).
Table 1. Summary of studies of dietary intervention in polycystic ovary syndrome

<table>
<thead>
<tr>
<th>Reference</th>
<th>Subjects (n)</th>
<th>Duration</th>
<th>Dietary intervention</th>
<th>Mean baseline BMI (kg/m²)</th>
<th>Weight loss achieved</th>
<th>WC and WHR</th>
<th>FBG</th>
<th>Fasting insulin</th>
<th>Blood fats</th>
<th>MC</th>
<th>Hirsutism</th>
<th>Free testosterone</th>
<th>MC</th>
<th>Hirsutism</th>
<th>Free testosterone</th>
<th>SHBG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kiddy et al. (1992)</td>
<td>24</td>
<td>6–7 months</td>
<td>4200 kJ/d</td>
<td>34</td>
<td>7·5 %</td>
<td>N/A</td>
<td>N/A</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Crave et al. (1995)</td>
<td>24</td>
<td>4 months</td>
<td>Lowfat (20 g/d) 6300 kJ/d</td>
<td>33</td>
<td>5·8 %</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Holte et al. (1995)</td>
<td>13</td>
<td>14·9 months</td>
<td>Low fat (30 %) 5040 kJ/d</td>
<td>32</td>
<td>14 %</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Jakubowicz &amp; Nestler (1997)</td>
<td>12</td>
<td>8 weeks</td>
<td>4200–5040 kJ/d</td>
<td>32</td>
<td>7·5 %</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Huber-Buchholz et al. (1999)</td>
<td>18</td>
<td>6 months</td>
<td>Diet and exercise programme</td>
<td>35 RO</td>
<td>2–5 %</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Wahrenberg et al. (1999)</td>
<td>9</td>
<td>3 months</td>
<td>VLCD</td>
<td>38</td>
<td>14·8 %</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Parquail et al. (2000)</td>
<td>20</td>
<td>7 months</td>
<td>5040–5880 kJ/d (50 % carbohydrate, 30 % fat, 20 % protein)</td>
<td>40</td>
<td>4·9 %</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>van Dam et al. (2002)</td>
<td>15</td>
<td>7 d</td>
<td>VLCD (4200 kJ/d)</td>
<td>39</td>
<td>2·6 %</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Crosignani et al. (2003)</td>
<td>33</td>
<td>10–39 weeks</td>
<td>liquid diet</td>
<td>5040 kJ/d</td>
<td>76 % lost &gt;5%</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Moran et al. (2003)‡</td>
<td>28</td>
<td>16 weeks</td>
<td>6000 kJ/d</td>
<td>38</td>
<td>33 % lost &gt;10 %</td>
<td>7·5 %</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Gamberini et al. (2004)</td>
<td>40</td>
<td>7 months</td>
<td>5040–5880 kJ/d (50 % carbohydrate, 30 % fat, 20 % protein)</td>
<td>38</td>
<td>5·9 %</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>
### Table 1. Continued

<table>
<thead>
<tr>
<th>Reference</th>
<th>Subjects</th>
<th>Duration</th>
<th>Dietary intervention</th>
<th>Mean baseline</th>
<th>Weight loss achieved</th>
<th>Weight loss</th>
<th>WHR</th>
<th>BMI (kg/m²)</th>
<th>WC</th>
<th>WHR</th>
<th>Fasting insulin</th>
<th>Free fats</th>
<th>Fasting insulin</th>
<th>SHBG</th>
<th>Total cholesterol</th>
<th>TC</th>
<th>LDL</th>
<th>HDL</th>
<th>Total cholesterol</th>
<th>HDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moran et al. (2004)†</td>
<td>26</td>
<td>16 weeks</td>
<td>6000 kJ/d deficit, 4200 kJ/d deficit</td>
<td>3.5±4 g HP</td>
<td>3.9±3.4 cm</td>
<td>38</td>
<td>7.5±5</td>
<td>6000 kJ/d deficit</td>
<td>37 HC</td>
<td>HC (55% carbohydrate, 30% fat, 15% protein)</td>
<td>38</td>
<td>7.5±5</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang et al. (2004)</td>
<td>20</td>
<td>16 weeks</td>
<td>6000 kJ/d deficit, 4200 kJ/d deficit</td>
<td>3.5±4 g HP</td>
<td>3.9±3.4 cm</td>
<td>38</td>
<td>7.5±5</td>
<td>6000 kJ/d deficit</td>
<td>37 HC</td>
<td>HC (55% carbohydrate, 30% fat, 15% protein)</td>
<td>38</td>
<td>7.5±5</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DiGirolamo, 1992</td>
<td>26</td>
<td>4 weeks</td>
<td>4200 kJ/d deficit</td>
<td>4.2±4 g HP</td>
<td>4.2±4 cm</td>
<td>38</td>
<td>7.5±5</td>
<td>4200 kJ/d deficit</td>
<td>38</td>
<td>HP (40% fat, 30% protein)</td>
<td>38</td>
<td>7.5±5</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Only a few studies have compared the use of metformin with diet and exercise in women with PCOS and the findings have been conflicting. A recent study found that while the addition of metformin to a hypoenergetic diet improved menstrual function, there was no improvement in insulin sensitivity and hyperinsulinaemia (Gambineri et al. 2004). Similarly, Hoeger et al. (2004) found no benefits on insulin sensitivity or glucose metabolism with the addition of metformin to lifestyle changes, although the combination did result in a greater weight loss and reduction in androgen levels compared with lifestyle changes or metformin alone.

### Dietary management of insulin resistance

Weight loss and exercise are known to improve insulin sensitivity and reduce the risk of conversion from IGT to diabetes. Altering the composition of the diet, however, independent of weight loss, may also influence insulin sensitivity. Reducing glycaemic load (GL) can reduce postprandial glucose levels and the resulting hyperinsulinaemia that characterises this condition. What is not clear is the best way to achieve a reduction in GL – reducing glycaemic index (GI) or reducing carbohydrate intake. While both types of dietary change will reduce insulin levels, resulting in short-term benefits, the long-term impact of these changes is likely to be quite different. If carbohydrate intake is reduced, it must be replaced by either fat or protein – both of these strategies have potential problems for women with PCOS (see Table 2). Furthermore, while low-carbohydrate diets result in an immediate lowering of blood glucose levels, long-term ingestion of such diets results in an increase in hepatic glucose production and a reduction in peripheral glucose utilisation, a state of insulin resistance (Colagiaru & Brand Miller, 2002).

#### Dietary fat

While animal studies demonstrate that a diet high in fat, particularly saturated fat, may lead to insulin resistance, human intervention studies investigating changes in dietary fat intake have been inconclusive, possibly due to their short duration and inadequate sample size (Riccadi & Rivellese, 2000). A review by Vessby (2000) found no significant changes in insulin sensitivity with any of the randomised controlled trials conducted in patients with type 2 diabetes or non-diabetic subjects.

Epidemiological studies, however, do suggest an association between a high fat, particularly saturated fat, intake and reduced insulin sensitivity (Feskens & Kromhout, 1990; Lovejoy & DiGirolamo, 1992; Mayer et al. 1993; Parker et al. 1993; Marshall et al. 1997; Mayer-Davis et al. 1997). An increased risk of developing type 2 diabetes has also been associated with the consumption of higher-fat diets (Marshall et al. 1991; Tsunehara et al. 1991; Colditz et al. 1992; Marshall et al. 1994). Furthermore, subjects with insulin resistance and type 2 diabetes have been found to have changes in the fatty acid pattern in serum cholesterol esters (a marker of dietary fat intake) with a higher proportion of saturated fatty acids and lower proportions of linoleic acid (Salomaa et al. 1990; Vessby et al. 1994a,b; Öhrvall et al. 1996; Wang et al. 2003).

Some studies also indicate that a high-fat diet is more deleterious in those who are inactive, supporting the importance of the role of exercise in managing insulin resistance (Marshall et al. 1991; Mayer et al. 1993; Mayer-Davis et al. 1997).
While studies comparing high-monounsaturated fat with high-carbohydrate diets have found a high-monounsaturated-fat diet results in reduced triacylglycerols and increased HDL-cholesterol, there is little evidence of the benefits of such diets for improving insulin resistance (Garg, 1998). However, one study of 162 healthy individuals, randomised to a high-saturated-fat or high-MUFA diet for 3 months, found that a high-MUFA diet significantly improved insulin sensitivity (Vessby, for the Kanwu Study Group, 1999). Interestingly, the beneficial effect disappeared when total fat intake exceeded 38%, possibly explaining why other studies have not found the same benefits of a high-MUFA diet. A recent study in which carbohydrates were exchanged for monounsaturated fats in an energy-restricted diet in thirty-two overweight subjects found a significant reduction in fasting insulin levels along with weight loss that was independent of dietary composition (Collette et al. 2003). Total fat contributed 39% and monounsaturated fat 23% of energy in this study.

Despite the possible benefits of a higher-fat diet for those with insulin resistance, a major concern with these diets is the possibility of weight gain resulting from the higher energy density (kJ/g food). High-fat diets have been shown to contribute to obesity while ad libitum low-fat diets have been shown to prevent weight gain in normal-weight subjects and cause weight loss in overweight subjects (Bray & Popkin, 1998; Astrup et al. 2000; Hays et al. 2004). Nevertheless, most of the studies to date have been isoenergetic and short-term; thus ad libitum long-term studies are needed to clarify the issue. In one such study, the ad libitum low-fat high-carbohydrate diet induced weight loss in individuals over a 6-week period while the high-monounsaturated-fat diet did not (Gerhard et al. 2004). There was no significant difference in blood fats or blood glucose control between the two diets.

Another concern for those with insulin resistance is the effects of a high-fat diet on thrombogenesis. The optimal anti-thrombogenic diet is one that is low in fat and high in complex carbohydrate and dietary fibre, with fatty acid composition being of minor importance (Marckmann, 2000). Other studies, however, have found a low-fat diet to be associated with potentially adverse effects on haemostatic factors, while replacing saturated fats with MUFA resulted in positive changes (Kris-Etherton et al. 2002). PUFA-rich diets may not be as helpful as MUFA-rich diets. One study in women with PCOS found that an increased intake of PUFA resulted in a significant increase in fasting glucose levels and a reduction in plasma NEFA but no change in insulin levels, blood lipids, testosterone or sex hormone-binding globulin levels (Kasis-Karakas et al. 2004).

### High-protein diets

Recent times have seen a renewed interest in high-protein diets for weight loss, diabetes management and for women with PCOS. To date, however, there is little evidence to suggest benefits of high-protein diets on insulin resistance and some evidence that this type of diet may worsen insulin resistance and impair glucose metabolism (Rossetti et al. 1989; Lariviere et al. 1994; Linn et al. 1996, 2000; Krebs et al. 2002).

A number of studies in women with PCOS, overweight and obese subjects, as well as those with hyperinsulinaemia and type 2 diabetes have failed to show significant long-term benefits of a high-protein diet on weight loss or insulin sensitivity (Parker et al. 2002; Farnsworth et al. 2003; Foster et al. 2003; Moran et al. 2003; Stamets et al. 2004; Stern et al. 2004).

Two studies in women with PCOS have shown that while a hypoenergetic diet results in significant weight loss and
consequent improvement in metabolic and reproductive abnormalities, a high-protein diet is no more effective than a high-carbohydrate diet (Moran et al. 2004; Stamets et al. 2004).

Only one study, of seventy-nine obese subjects with a high prevalence of type 2 diabetes or the metabolic syndrome, found a greater weight loss and a relative improvement in insulin sensitivity and triacylglycerol levels independent of weight loss following 6 months on a low-carbohydrate, higher-protein diet (37 % carbohydrate, 22 % protein) (Samaha et al. 2003). At 12 months follow-up, however, differences in weight loss and insulin levels were not significant (Stern et al. 2004). Previously, Baba et al. (1999) failed to show a significant difference in fasting insulin levels between a high-protein and high-carbohydrate diet in thirteen obese hyperinsulinemic males despite a greater weight loss on the high-protein diet. Fat loss was not significantly different between the two diets.

Skov et al. (1999) studied the effect of replacement of carbohydrate by protein in ad libitum fat-reduced diets in sixty-five overweight and obese subjects and found that those following the high-protein diet achieved a greater loss of weight and body fat over the 6-month study period. No differences between total cholesterol and HDL-cholesterol were seen between the groups and while a greater reduction in plasma triacylglycerols was seen after 3 months in the high protein group, there were no significant differences at 6 months. Insulin levels were not measured.

Farnsworth et al. (2003) also found a greater reduction in fasting triacylglycerols with a higher-protein diet in a study of fifty-seven overweight men and women over 16 weeks, although weight loss was similar to the standard-protein diet. Whether these differences would be sustained over a longer time period is questionable, considering the results from longer-term studies (Skov et al. 1999; Foster et al. 2003).

Finally, a short 6 d study, comparing a low-GI, low-fat, high-protein diet with the conventional American Heart Association phase 1 diet (high carbohydrate, moderate protein) in abdominally obese men found the low-GI, high-protein diet resulted in favourable changes in the metabolic risk profile, which were significantly different from changes with the American Heart Association diet (Dumesnil et al. 2001). The low-GI, high-protein diet, consumed ad libitum, resulted in a 25 % reduction in energy intake with no increase in hunger, and a significant decrease in triacylglycerols (35 %) and plasma insulin levels and a significant increase in LDL peak particle size. Whether the benefits achieved with this diet were a result of the lower carbohydrate and higher protein intake, the low GI of the carbohydrate foods consumed, or the combination of these, however, was unclear.

While not increasing blood glucose levels to the same extent as carbohydrate foods, protein foods do elicit an insulin response and the impact of this in those with insulin resistance is not clear. There are also concerns about the safety of high-protein, low-carbohydrate diets including the effects on kidney function, bone mineral density and the reduction in intake of protective foods such as fruit, vegetables and whole grains. Three recent studies have also shown a positive association between dietary haem-Fe intake in women (Lee et al. 2004; Song et al. 2004) and haem-Fe from red meat in men (Jiang et al. 2004) and the risk of type 2 diabetes, while a positive association between intake of red meat, processed meats and animal protein and incidence of type 2 diabetes in women has also been found (Schulze et al. 2003; Song et al. 2004). While the findings of these studies need to be confirmed, they provide further evidence that diets high in animal protein may be detrimental to those with insulin resistance.

Finally, with a high intake of fruits, vegetables and whole grains shown to protect against CVD, diabetes and cancer, and some studies showing a high intake of animal protein may increase cancer risk (World Cancer Research Fund, 1997), the role of dietary protein needs further investigation for management of this condition. Risk of endometrial cancer, in particular, has been shown to be inversely associated with a higher intake of plant foods, whole grains and soy products and positively associated with a higher intake of energy, fat and animal foods (Zheng et al. 1995; Goodman et al. 1997; McCann et al. 2000; Littman et al. 2001; Petridou et al. 2002).

Carbohydrates, dietary fibre and glycaemic index

Unlike diets high in fat or protein, there is now a significant body of evidence demonstrating the benefits of low-GI diets. While many of the features of insulin resistance, including postprandial glycaemia and insulinaemia, hypertriglycerolaemia, low HDL levels and fibrinolysis may be worsened by a high-carbohydrate diet, there is increasing evidence that the type of carbohydrate in the diet is important. In particular, many studies show that low- and high-GI foods have significantly different effects on metabolism (Jenkins et al. 2002).

The concept of GI was first introduced in the early 1980s as a method for classifying carbohydrate foods according to their effect on postprandial glycaemia (Jenkins et al. 1981). Early research was concentrated on diabetes and a recent meta-analysis confirmed the benefits of a low-GI diet for individuals with diabetes (Brand-Miller et al. 2003).

Since this time, there have been a number of studies showing that a low-GI diet can improve insulin resistance as well as many of its metabolic consequences including increasing HDL and plasminogen activator inhibitor-1 levels (Jenkins et al. 1985, 1987; Woler, 1992; Wolever et al. 1992; Frost et al. 1999; Jarvi et al. 1999). A high-GI diet, in contrast, has been shown to worsen postprandial insulin resistance (Brynes et al. 2003).

Several epidemiological studies have also associated a low-GI diet with reduced risk of CVD and type 2 diabetes (Salmeron et al. 1997a,b; Liu et al. 2000). Of interest, Salmeron et al. (1997a,b) found that in both men and women, the association between high dietary GI and an increased risk of type 2 diabetes was related to GI and not the amount of dietary carbohydrate, challenging the idea that a high carbohydrate intake is detrimental to those with insulin resistance. Similarly, McKeown et al. (2004) found a positive association between GI and both insulin resistance and prevalence of the metabolic syndrome but no association with total carbohydrate intake.

Both the San Luis Valley study and the Iowa Women’s Health Study failed to show a relationship between the amount of carbohydrate and either hyperinsulinemia or the onset of diabetes (Marshall et al. 1994; Meyer et al. 2000). A more recent prospective study found that a low-fat high-carbohydrate diet (54 % carbohydrate) was associated with improved glucose tolerance and a reduced progression to diabetes in subjects with IGT (Swinburn et al. 2001).

Saldana et al. (2004) examined the relationship between macronutrient intake in early pregnancy and the development of glucose intolerance in nearly 1700 women. They found that both the
substitution of carbohydrate for fat and the addition of carbohydrate, without controlling for total energy, significantly reduced the risk of IGT and gestational diabetes mellitus. Predicted probabilities of IGT and gestational diabetes mellitus were reduced by one half with a 10% decrease in dietary fat and a 10% increase in dietary carbohydrate.

Wolever & Mehling (2002) found that reducing the GI of the diet without altering total carbohydrate intake reduced postprandial glucose by the same amount as lowering total carbohydrate intake, but only the low-GI diet resulted in significant reduction of NEFA. Lowering NEFA is desirable because high levels are linked with dyslipidaemia (Byrne et al. 1994), hypertension (Fagot-Campagna et al. 1998) and an increased risk of type 2 diabetes (Paolisso et al. 1995) and CVD (Carlsson et al. 2000).

The Dietary Approaches to Stop Hypertension (DASH) study also highlighted the benefits of a high-carbohydrate diet (Appel et al. 1997). The DASH study showed a significant improvement in lipids and blood pressure with dietary modification, despite a relatively high (57%) carbohydrate diet. While not specifically looking at insulin resistance or dietary GI, the intervention diet was high in fruit, vegetables, whole grains and low-fat dairy products and was therefore likely to have been a relatively low-GI diet. The effects of this dietary pattern on insulin sensitivity have since been tested in the PREMIER Interventions on Insulin Sensitivity study, in which a comprehensive behavioural intervention for hypertension (weight loss, reduced Na intake, increased physical activity and moderate alcohol intake) was trialled with and without the DASH dietary pattern. A greater improvement in insulin sensitivity was found with the DASH diet than the comprehensive behavioural intervention alone, supporting the benefits of a high-carbohydrate, high-fibre dietary pattern (Ard et al. 2004).

The third National Health and Nutrition Examination Survey found that carbohydrate intakes were not associated with HbA1c, plasma glucose, or serum insulin concentrations but were inversely associated with the risk of elevated serum C-peptide, again supporting the benefits of a higher carbohydrate intake (Yang et al. 2003).

Several studies have shown fibre consumption to be associated with a reduced risk of type 2 diabetes (Marshall et al. 1997; Boeing et al. 2000; Meyer et al. 2000). In the Health Professionals Follow-up Study and the Nurses’ Health Study there was an independent inverse association between both cereal fibre intake and a low-GI diet and the risk of type 2 diabetes (Salmeron et al. 1997a,b).

A higher intake of whole grains has also been shown to be associated with a reduced risk of type 2 diabetes (Liu et al. 2000; Meyer et al. 2000; Montonen et al. 2003). Supporting this, Pereira et al. (2002) demonstrated improved insulin sensitivity in overweight subjects, independent of body weight, when refined grains were replaced with whole grains over a 6-week period and Liese et al. (2003) found a higher intake of whole grains to be associated with increased insulin sensitivity in a study of 978 subjects with normal glucose tolerance or IGT. Intake of high-fibre whole-grain foods has also been shown to be inversely associated with weight gain in middle-aged women (Liu et al. 2003).

Considering their increased risk of IGT and type 2 diabetes, these studies are of particular relevance to women with PCOS.

While more research is still needed, studies to date suggest that a moderately high-carbohydrate, lower-GI diet may assist in weight management by influencing appetite and fuel partitioning. Short-term feeding studies have generally found low-GI foods to increase satiety, reduce hunger or lower subsequent voluntary food intake while high-GI foods are associated with increased appetite and higher energy intake (Ludwig et al. 1994a,b; Ludwig, 2000; Roberts, 2000). High-GI foods have also been shown to be associated with a greater oxidation of carbohydrate and a lower oxidation of fat (Febbraio et al. 2000; Pawlak et al. 2000). A recent study looking at the effects of high-carbohydrate meals with different GI on substrate utilisation during subsequent exercise found that the low-GI meal resulted in a higher rate of fat oxidation during exercise compared with the higher-GI meal (Wu et al. 2003). While some of these studies are underpowered, differences consistently favour a low-GI diet.

In human subjects, a hypenergetic high-GI diet has been shown to reduce resting energy expenditure to a greater extent than a hypenergetic low-GI diet, despite similar weight loss over 1 week (Agus et al. 2000). A low-GI diet in overweight men resulted in greater fat loss compared with a high-GI diet of similar nutrient content (Bouche et al. 2002). A limited number of studies in both adults and children have also shown that weight loss and body-fat loss may be superior on a diet modified to lower GI (Slabber et al. 1994; Spieth et al. 2000; Dumesnil et al. 2001; Brynes et al. 2003; Ebbeling et al. 2003). In pregnant women, low-GI diets have been shown to reduce weight gain compared with high-GI diets despite similar energy and macronutrient contents (Clapp, 1997). Animal studies provide further evidence of long-term effects on body weight. A recent study in rats found that the high-GI diet resulted in significantly more body fat and less lean body mass than the macronutrient-matched low-GI diet over 18 weeks (Pawlak et al. 2004). Despite similar body weights, the high GI group showed impairments in glucose tolerance and fat metabolism and evidence of β-cell destruction.

Low-GI diets have also been associated with a reduced risk of endometrial cancer (Augustin et al. 2003), breast cancer (Augustin et al. 2001), colon cancer (Franceschi et al. 2001) and ovarian cancer (Jenkins et al. 2003), all of which may be linked with high insulin levels.

Finally, with little research into dietary composition in PCOS, two studies investigating the effects of diet on modifying hormonal profiles in women are of interest. The first study, in postmenopausal women with high testosterone levels, found that a comprehensive dietary change designed to reduce insulin resistance resulted in a significant increase in sex hormone-binding globulin and a significant decrease in testosterone, body weight, waist:hip ratio, total cholesterol, fasting blood glucose and insulin (Berrino et al. 2001). The diet focused on lowering intake of animal fats and increasing intake of fibre, low-GI carbohydrates, monounsaturated and n-3 polyunsaturated fats and phyto-oestrogens. The second study found that a diet designed to evoke a low insulin response (with a focus on low-GI carbohydrates) reduced insulin concentrations and weight in obese hyperinsulinaemic females significantly more than a conventional diet with the same energy and macronutrient content (Slabber et al. 1994). These studies support the hypothesis that a low-GI diet may provide the greatest benefits for women with PCOS and insulin resistance. Carbohydrate intake in these studies was relatively high (51 and 50% of energy, respectively).
Diet, weight loss and fertility

Studies using lifestyle modification have demonstrated improvements in ovulation and fertility with modest weight losses of 5–10% of initial body weight (Kiddy et al. 1992; Holte et al. 1995; Huber-Buchholz et al. 1999; Pasquali et al. 2000; Crosignani et al. 2003; Moran et al. 2003). Energy restriction alone, independent of weight loss, has also been shown to improve reproductive parameters (Moran et al. 2003). To date, studies of the effect of dietary composition per se on fertility in women with PCOS are limited. One study found no difference in menstrual cyclicity between a high-protein and low-protein diet (Moran et al. 2003). Another found that a PUFA-rich diet significantly increased urinary pregnanediol 3-glucuronide in women with PCOS, although only two of the seventeen subjects showed signs of ovulation. Luteinising hormone, follicle-stimulating hormone, sex hormone-binding globulin, dehydroepiandrostosterone sulfate and testosterone levels did not change (Kasim-Karakas et al. 2004).

Conclusion

The recognition of the link between PCOS and insulin resistance offers an excellent opportunity for the early intervention to prevent or delay the onset of type 2 diabetes and CVD in women with PCOS. While the dietary management of PCOS should focus on weight reduction for those who are overweight, consideration also needs to be given to the role of varying dietary composition in increasing insulin sensitivity. On the balance of evidence, a diet low in saturated fat and high in fibre with predominantly low-GI-carbohydrate foods would appear to be the most logical choice. Such a diet may help short term in improving the symptoms of this condition, as well as long term, in reducing the risk of diseases linked with insulin resistance.

References


Optimal diet for polycystic ovary syndrome


activity in lean women with and without the polycystic ovary syn-
Stamets K, Taylor DS, Demers LM, Pielman CL & Legro RS (2004) A randomized trial of the effects of two types of short-term hypocaloric diets on weight loss in women with polycystic ovary syn-
Talbott E, Clerici A, Berga SL, Kuller L, Guizick D, Detre K, Daniels T & Engberg RA (1998) Adverse lipid and coronary heart disease risk pro-
Talbott EO, Zborowski JV, Guizick DS, et al. (2000) Increased PAI-1 levels in women with polycystic ovary syndrome: Evidence for a specific ‘PCOS’ effect independent of age and BMI. In Programs and Abstracts of the 40th Annual Conference on Cardiovascular Dis-
Vessby B, for the Kanwu Study Group (1999) Effect of dietary fat on insulin sensitivity and insulin secretion. The Kanwu Study. Diabetolo-
gia 42, Suppl., 1, A46.
Weerakiet S, Srisomboon C, Bunnag P, Sangtong S, Chuangoongnoen N & Rojansakul A (2001) Prevalence of type 2 diabetes mellitus and impaired glucose tolerance in Asian women with polycystic ovary syn-
Wijeyaratne CN, Niranharakumar K, Balen AH, Barth JH, Sheriffl R & Belchetz PE (2004) Plasma homocysteine in polycystic ovary syn-
Wild RA, Alpauvic P & Parker LJ (1992) Lipid and apolipoprotein abnormalities in hirsute women I. The association with insulin resist-
Wild S, Pierpoint T, McKeigpe P & Jacobs HS (2000) Cardiovascular dis-
ease in women with polycystic ovary syndrome at long-term follow-up: a retrospective cohort study. Clin Endocrinol 52, 595–600.
Wolever TMS & Mehling C (2002) Long-term effect of varying the source or amount of dietary carbohydrate on postprandial plasma glu-
cose, insulin, triacylglycerol, and free fatty acid concentrations in sub-
jects with impaired glucose tolerance. Am J Clin Nutr 77, 612–621.
Wu CL, Nicholas C, Williams C, Took A & Hardy L (2003) The influence of high-carbohydrate meals with different glycaemic indices on sub-
Yildirim B, Sabir N & Kaleli B (2003) Relation of intra-abdominal fat dis-