



PCOS & Natural Therapies

Sandra Villella

BAppSci. (Naturopathy), MAppSci (Acupuncture)

Overview

- Prevalence of CAM use for PCOS in Australia
- Review of the evidence for nutritional and herbal treatments for PCOS
- Discussion of treatment based on insulin resistance as well as presenting concerns



CAM use in Australian women with PCOS

- 493 women
 - PCOS support group (POSAA), social media invitations & self-referrals
- Most participants aged 25-34 years, Australian born, tertiary qualifications, employed, held private health insurance
- 304/432 (70.4% \pm 4.30 95% CI) used CAM in previous 12 months



CAM use in Australian women with PCOS

- 56.9% (± 4.67) used dietary supplements including vitamins, minerals & food nutrients such as fish oils, herbal supplements
- 41.9% (± 4.65) used herbal medicines including herbal tea (for therapeutic reasons), tablets and liquids.
- 14.6% (± 3.33) used vitamins and/or minerals prescribed by a medical doctor
- 47.9% (± 4.71 95% CI) reported use of > 1 type CAM product.



CAM practitioner use

- 233/304 (76.6% ± 4.76 95% CI) CAM users consulted CAM practitioner in previous 12 months
- 136/304 (44.7% ± 5.59) used more than one type of CAM practitioner
- 118 (38.8% ± 5.48) consulted naturopath
- 103 (33.9% ± 5.32) consulted chiropractor
- 88 (28.9% ± 5.1) consulted acupuncturist
- 79 (25.1% ± 4.87) consulted massage therapist
- 41 (13.5% ± 3.84) consulted osteopath
- 36 (11.8% ± 3.63) consulted reflexologist, aromatherapist, iridologist
- 34 (11.2% ± 3.55) consulted homoeopath
- 27 (8.9% ± 3.2) consulted medical doctor for integrative medicine
- 20 (6.6% ± 2.79) consulted kinesiologist
- 14 (4.6% ± 2.35) consulted medical doctor for acupuncture





Naturopathic management of PCOS

As per clinical guidelines..

- Treatment aimed at addressing insulin resistance
- Modest 5-10% weight loss reduces insulin resistance dramatically and improves metabolic and reproductive features of PCOS.
- Diet more effective than exercise alone
 - Reduced carbohydrates, moderate protein & EFAs
- Exercise enhances weight loss, independently improves insulin sensitivity & menstrual regularity.
 - Regular exercise (1 hour/day) prevents weight regain following weight loss.



Treatment aims influenced by woman's presenting concerns

- Insulin resistance and metabolic features
 - Diet, exercise, Cinnamon, Chromium, omega-3 Fatty acids
 - Alpha lipoic acid, magnesium
- Hyperandrogenic features - hirsutism and acne
 - Hirsutism: anti-androgen herbs, zinc
 - Acne: zinc and Vitamin A, Chromium
- Anovulation and (in)fertility issues
 - Inositol, Peony & Licorice, Black Cohosh






Nutritional & herbal treatments to address insulin resistance


Cinnamon
cinnamomum cassia

- Insulin sensitizing effects – mechanism not completely understood
- Research on treating insulin resistance in Type 2 diabetes
 - Paucity of research specifically on PCOS
- Very small pilot study (n=15) showed significant reduction in fasting glucose, as well as in insulin resistance 1g/day (Wang 2007)
- Improved cycle regularity with 1.5g/day over 6 months (n=45)
 - No change in insulin resistance or androgens (Kort 2014)
- Dose: 2-4 g (1/2-1 teaspoon) – ensure species




Chromium - An Overview

- Forms part of glucose tolerance factor (GTF)- promotes efficient insulin function
- Improves insulin sensitivity at insulin receptor level
- Chromium picolinate most efficacious form of chromium
 - 200 -1000 ug
- Dietary chromium is poorly absorbed.



Chromium picolinate

- 1000 ug (n=100) improved insulin resistance, fasting insulin levels, body weight; induced ovulation & regular menstrual cycles in PCOS patients (Ashoush 2016)
- 200 ug decreased fasting blood sugar and insulin levels, and increased insulin sensitivity in clomiphene-citrate resistant PCOS patients (n= 92) over 3 months
 - Comparable effects to 1500mg daily of metformin but decreased hyperandrogenism with metformin (Amooee 2013)
- Higher pregnancy rate compared to placebo with 200ug over 8 weeks: 16.7 % (5/30) vs.3.3 % (1/30)
 - Also prevalence of acne decreased and reduced hirsutism (Jamilian 2015)



Omega-3 fatty acids

- Promising evidence emerging that may improve insulin sensitivity in PCOS patients.
 - no significant effects on weight, BMI, waist circumference
- Some limited evidence may be useful for hirsutism
- Suggested mechanisms:
 - On insulin sensitivity-modifying the levels of glucose transporters (GLUT1 and GLUT4) in muscle and adipose tissue and suppression of both the activity and the expression of glucose-6-phosphatase.
 - Anti-inflammatory action of omega 3FAs and theory of inflammation and increased pro-inflammatory cytokines in PCOS





Infertility & oligomenorrhoea


Treatment - infertility & amenorrhoea/oligomenorrhoea

Improve ovulation and fertility.


- 5-10% loss of body weight- diet & exercise
- *Paeonia lactiflora* Peony & *Glycyrrhiza glabra* Licorice
 - Reduces T and improves E2:T ratio after 4 weeks
 - Proposed mechanism: promotes aromatase activity in ovary → greater rate of E2 from T, improved pregnancy rates
- Licorice 1:1 30 ml, Peony 1:2 70 ml
 - Dose 5 ml BD



OCC1(O)C(O)C(O)C(O)C(O)O1




Myo-Inositol




Inositol

- A polyalcohol existing as 9 different stereoisomers, 2 shown to be insulin mediators: myo-inositol(MI) and D-chiro-inositol (DCI)
 - MI may be superior (Faccinetti 2015)
- Insulin sensitizing
- Second messengers of insulin.
 - (MI is converted to an inositolphosphoglycan (IPG) insulin second messenger (MI-IPG) involved in cellular glucose uptake, whereas DCI is converted to an IPG insulin second messenger (DCI-IPG) involved in glycogen synthesis)



Inositol Summary

- 70 studies- 6 RCT, 300 PCOS patients
- Dose 2-4 g
- Improves several of the hormonal disturbances of PCOS, (level I_a evidence)
- Improves insulin sensitivity of target tissues, resulting in a positive effect on the reproductive axis
 - (restores ovulation and improves oocyte quality) and hormonal functions
- Reduces clinical and biochemical hyperandrogenism and dyslipidaemia through the reduction of insulin plasma levels. (Dinicola 2014)



Inositol

- Combined Myo-inositol plus D-chiro-inositol improved oocyte & embryo quality, & pregnancy rates. (Colazingari 2013)
- 2 g myo-inositol BD improved oocyte and embryo quality in euglycaemic PCOS patients. (Unfer 2011)
- Restoration of spontaneous ovulation in amenorrhoeic PCOS patients. (Venturella 2012)
- Combined MYO & D-chiro-inositol improved lipid profiles and reduced CV risk. (Minozzi 2013)
- Both myo-inositol (MI-PG) and D-chiro inositol (DCI-PG) significantly improved regularity of the menstrual cycle, the acne Score, the endocrine and metabolic parameters and the insulin-resistant n 137 young, overweight, PCOS patients over 6 months (Formusco 2015)



Dosage and safety of Inositol

- Dose in research 2 g/day up to 2 g BD
- Often used Italian product Inofolic™ (2 g myo-inositol, folic acid 200 µg).
- Appears safe in humans.
- Only highest dose (12 g/day) induced mild gastrointestinal side effects - nausea, flatus and diarrhoea.



Vitamin D linked with infertility

- In PCOS patients, Vitamin D and Calcium with Metformin → higher rate of follicle formation compared with metformin alone.
- Lower success rate of IVF with Vitamin D deficiency.



Treatment - infertility & amenorrhoea/oligomenorrhoea

- *Vitex agnus-castus*- often used as part of herbal management of amenorrhoea and oligomenorrhoea- not indicated in PCOS as worsens cycle regularity



***Cimicifuga racemosa*
Ovulation induction in PCOS**

- Infertile women with PCOS <35 years, were randomized to either group I (clomiphene citrate; CC) (n= 98) or group II (CC plus *Cimicifuga racemosa*; CR) (n=96).
- CR plus CC group had significantly higher clinical pregnancies per cycle (33/192 (17.2%) versus 71/204 (34.8%), p<0.01), compared to the CC only group.
- Authors (inaccurately) attribute the action of *Cimicifuga racemosa* to phytoestrogens and suggest they may be useful as part of ovulation induction for(PCOS). (Shahin 2014)





Management of hyperandrogenic symptoms

Hirsutism - *Serenoa repens*

- 3/12 topical Serenoa extract in lotion & shampoo base in 34 men and 28 women (18-48 years) - 35% increase in hair density and 67% increase in sebum reduction assessed by sebometry, pH metry, hydration studies & phototrichogram. (study presented at the fourth intercontinental meeting of hair research societies, June 17-19, 2004)
- 2 yr trial vs finasteride suggests improvement in androgenic alopecia in men. (Rossi A et al 2012)



Spearmint tea *Mentha spicata*

- Cup of *M. Spicata* BD 5/7 during follicular phase significantly decreases free T & increases in LH, FSH & E2 in 21 females with hirsutism (12 PCOS, 9 idiopathic).
 - No significant decreases in total T or DHEAS levels.
- Significant decrease in free & total T & increased LH & FSH with spearmint tea (herbal tea bags with a standardized content of dried leaves BD drink two cups over 30 day RCT of 42 women with PCOS)
 - Significant reduction in subjective assessments of hirsutism but no significant reduction in objective Ferriman-Galwey scale (Grant P, 2010)



Acne

- Seems to respond better to traditional herbal "alteratives" and nutritional treatment rather than anti-androgen naturopathic.
- Low GI/GL diet.
 - Chromium picolinate
- Zinc 30 mg (picolinate or citrate).
 - Antibacterial, anti-inflammatory actions and may decrease sebum production (Brandt 2013)
- Vitamin A 10,000-20,000 IU (avoid if trying to conceive).
- Topical tea tree acne facial wash



Conclusions

- Primary focus on diet and exercise to improve metabolic and reproductive features
- Insulin sensitizing agents
 - Evidence increasing for chromium picolinate and Cinnamon
 - ½-1 teaspoon may be useful dietary intervention
- Licorice and Peony combination often employed by herbalists
- Greatest amount of research on Inositol
- Spearmint tea- harmless intervention for possible hirsutism management



References

- [No authors listed] 2004. A scientific review: the role of chromium in insulin resistance. *Diabetes Educ Suppl*:2-14.
- Amooee S, Parsanezhad ME, Ravanbod Shirazi M, Alborzi S, Samsami A. 2013. Metformin versus chromium picolinate in clomiphene citrate resistant patients with PCOS: A double-blind randomized clinical trial. *Iran J Reprod Med* 11(8):611-8
- Arentz S, Smith CA, Abbott JA, Bensoussan A. 2014. Herbal medicine for the management of polycystic ovary syndrome (PCOS) and associated oligo/amenorrhoea and hyperandrogenism: a review of the laboratory evidence for effects with corroborative clinical findings. *BMC Complement Alt Med* 4:511
- Arentz S, Smith CA, Abbott JA, Bensoussan A. 2014. A survey of the use of complementary medicine by a self-directed community group of Australian women with polycystic ovary syndrome. *BMC Complement Alt Med* 14:472
- Armanini D, Mattarello MJ, Fiore C, Bonanni G. 2004. Licorice reduces serum testosterone in healthy women. *Steroids* 59(11-12):763-6.
- Ashoush S, Abou-Gamrah A, Bayoumy H, Othman N. 2016. Chromium picolinate reduces insulin resistance in polycystic ovary syndrome: Randomized controlled trial. *J Obstet Gynaecol Res* 42(3):279-85.
- Brandt S. 2013. The clinical effects of zinc as a topical or oral agent on the clinical response and pathophysiologic mechanism of acne: a systemic review of the literature. *J Drugs Dermatol* 12(5):542-5.
- Cappelli V, Di Sabatino A, Musacchio MC, De Leo V. 2013. [Evaluation of a new association between insulin-sensitizers and alpha-lipoic acid in obese women affected by PCOS] [Article in Italian]. *Minerva Ginecol* 65(4):425-433.
- De Leo V, La Marca A, Cappelli, Stendardi A et al 2012. [Evaluation of the treatment with D-chiro-inositol on levels of oxidative stress in PCOS patients] [article in Italian]. *Minerva Ginecol* 64(6):531-8.
- Dinicola S, Chiu TT, Unfer V, Carlomagno G, Bizzarri M. 2014. The rationale of myo-inositol and D-chiro-inositol combined treatment for polycystic ovary syndrome. *J Clin Pharmacol* 54(10):1079-92.
- Facchinetti F, Bizzarri M, Barvenga S, D'Anna R et al. 2015. Results from the International Consensus Conference on Myo-inositol and d-chiro-inositol in Obstetrics and Gynaecology: the link between metabolic syndrome and PCOS. *European Journal of Obstetrics & Gynaecology and Reproductive Biology* 195:72-76
- Formuaco C, Straquadanio M, Ciotta L. 2015. Myo-inositol vs D-Chiro inositol in PCOS treatment. *Minerva Ginecol* 67(4):321-5
- Grant, P. 2010. 'Spearmint herbal tea has significant anti-androgen effects in polycystic ovarian syndrome. A randomized controlled trial.' *Phytother Res.* 24 (2): 186-8.



References

- Grant, P, Ramasamy, S 2012. 'An Update on Plant Derived Anti-Androgens'. *Int J Endocrinol Metab.* 10(2):497-502.
- Hruby A, Meigs JB, O'Donnell CJ, Jacques PF et al 2013. 'Higher magnesium intake reduces risk of impaired glucose and insulin metabolism, and progression from prediabetes to diabetes in middle-aged Americans'. *Diabetes Care* Oct 2[Epub ahead of print].
- Jamilian M, Bahmani F, Siavashani MA, Mazloomi M, Asemi Z, Esmailzadeh A. 2015. The effects of Chromium Supplementation on Endocrine Profiles, Biomarkers of Inflammation, and Oxidative Stress in women with Polycystic Ovary Syndrome: a Randomized Double-Blind, Placebo-Controlled Trial. *Biol Trace Elem Res* Nov 28. [Epub ahead of print]
- Jamilian M, Foroozanfar F, Bahani F, Taleae R, Monavari M, Asemi Z. 2016. Effects of Zinc Supplementation on Endocrine Outcomes in Women with Polycystic Ovary Syndrome: a randomized, Double-Blind, Placebo-Controlled Trial. *Biol Trace Elem Res* 170(2):271-8. Korf DH, Lobo RA. 2014. Preliminary evidence that cinnamon improves menstrual cyclicity in women with polycystic ovary syndrome: a randomized controlled trial. *Am J Obstet Gynecol* 211(5):487.e 1-6.
- Lydic ML, McNurran M, Bembo S, Mitchell L et al 2006. 'Chromium picolinate improves insulin sensitivity in obese subjects with polycystic ovary syndrome'. *Fertil Steril* 86(1):242-6.
- Lucidi RS, Thyer AC, Easton CA, Holden AE et al 2005. 'Effect of chromium supplementation on insulin resistance and ovarian and menstrual cyclicity in women with polycystic ovary syndrome'. *Fertil Steril* 84(6):1755-7.
- Masharani U, Gjerde C, Evans JL, Youngren JF et al 2010. 'Effects of Controlled-Release Alpha Lipoic Acid in Lean, Nondiabetic Patients with Polycystic Ovary Syndrome'. *J of Diabetes Science and Technology* 4 (2): 359-64.
- Murugusundram S. 2009. 'Serenoa Repens: Does It have any Role in the Management of Androgenetic Alopecia ?'. *J Cutan Aesthet Surg* 2(1):31-2.



References

- Oner G, Muderris II. 2013. Efficacy of omega-3 in the treatment of polycystic ovary syndrome. *J Obstet Gynaecol* 33(3):289-91.
- Raifraf M, Mohammadi E, Asghari-Jafarabadi M, Farzadi L. 2012. Omega- 3 fatty acids improve glucose metabolism without effects on obesity values and serum visfatin levels in women with polycystic ovary syndrome. *J Am Coll Nutr* 31(5):361-8.
- Rossi A, Mari E, Scamo M, Garelli V, et al 2012. 'Comparative effectiveness of finasteride vs Serenoa repens in male androgenic alopecia: a two-year study'. *Int J Immunopathol Pharmacol* 25(4):1167-73
- Shahin, AY, Mohammed, SA. 2014. 'Adding the phytoestrogen Cimicifugae Racemosae to clomiphene induction cycles with timed intercourse in polycystic ovary syndrome improves cycle outcomes and pregnancy rates- a randomized trial'. *Gynecol Endocrinol* 30(7):505-10
- Sharifi F, Mazloomi S, Hajhosseini R, Mazloomzadeh S. 2012 'Serum magnesium concentrates in polycystic ovary syndrome and its association with insulin resistance' *Gynecol Endocrinol* 28(1):7-11.
- Takahashi K, Kitao M. 1994. Effect of TJ-68 (Shakuyaku-Kanzo-To) on Polycystic Ovarian Disease. *Int J Fertil* 39(2):69-76
- Takeuchi T, Nishii O, Okamura T, Yaginuma T. 1991. 'Effect of paeoniflorin, glycyrrhizin and glycyrrhetic acid on ovarian androgen production'. *Am J Chin Med*. 19(1):73-8.
- Wang J, Pursuitte G, Olsendzi BC, Wedick NM et al 2013. 'Dietary Magnesium Intake Improves Resistance among Non-Diabetic Individuals with Metabolic Syndrome Participating in a Dietary Trial' *Nutrients* 5 (10):3910-3919.
- Wang JG, Anderson RA, Graham GM 3rd, Chu MC et al 2007. 'The effect of cinnamon extract on insulin resistance parameters in polycystic ovary syndrome: a pilot study'. *Fertil Steril* 88(1):240-3