

# **Inositol and PCOS Research:**

Journal Abstracts



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# **Myo-inositol and D-chiro-inositol in Combination (ratio of 40:1)**

## **The combined therapy with myo-inositol and D-chiro-inositol reduces the risk of metabolic disease in PCOS overweight patients compared to myo-inositol supplementation alone.**

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### **Abstract**

**BACKGROUND:** PCOS is the main cause of infertility due to metabolic, hormonal and ovarian dysfunctions. Women affected by PCOS often suffer of insulin resistance and of a compensatory hyperinsulinemia. These conditions put the patients at risk of developing several metabolic disorders. Both myo-inositol (MI) and D-chiro inositol (DCI) glycans administration has been reported to exert beneficial effects at metabolic, hormonal and ovarian level. Beside these common features, MI and DCI are indeed different molecules: they belong to two different signal cascades and regulate different biological processes.

**AIM:** In this study, we aim to verify whether the two molecules have a synergistic action by acting on their specific cellular pathways. The effectiveness in reducing the risk of metabolic syndrome as well as in enhancing the ovarian functions of a combined therapy with MI and DCI was compared to a mono therapy in a randomized controlled trial.

**METHODS:** Fifty overweight women with PCOS were enrolled and divided in two groups to receive MI and DCL (MI+DCI group) or MI alone (MI group) for a period of six months. Baseline measurements were repeated at three months (T1) and at the end of the treatment (T2).

**RESULTS:** At the end of the treatment, both MI and MI+DCI groups showed an improvement of the metabolic parameters and no significant differences were found. As expected, the combined supplementation with MI and DCI resulted to be more effective, compared to the MI group, after three months of treatment.

**CONCLUSIONS:** The combined administration of MI and DCI in physiological plasma ratio (40:1) should be considered as the first line approach in PCOS overweight patients, being able to reduce the metabolic and clinical alteration of PCOS and, therefore, reduce the risk of metabolic syndrome.

PMID: 22774396 [PubMed - indexed for MEDLINE]

## **The Combined therapy myo-inositol plus D-Chiro-inositol, in a physiological ratio, reduces the cardiovascular risk by improving the lipid profile in PCOS patients.**

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### **Abstract**

**BACKGROUND:** Women with Polycystic Ovarian Syndrome (PCOS) present several factors that increase the cardiovascular risk, such as insulin resistance and dyslipidemia. Myo-inositol and D-chiro-inositol have been shown to improve insulin resistance, hyperandrogenism and to induce ovulation in PCOS women. However, their effects on dyslipidemia are less clear. The aim of the present study was to evaluate whether the combined therapy myo-inositol plus D-chiro-inositol (in a in a physiological ratio of 40:1) improve the metabolic profile, therefore, reducing cardiovascular risk in PCOS patients.

**PATIENTS AND METHODS:** Twenty obese PCOS patients [BMI  $33.7 \pm 6$  kg/m<sup>2</sup> (mean  $\pm$  SD)] were recruited. The lipid profile was assessed by measuring total cholesterol, LDL, HDL and triglycerides before and after 6 months treatment with the combined therapy. Secondary end points included changes in BMI, waist-hip ratio, percentage of body fat, HOMA-IR and blood pressure.

**RESULTS:** The combined therapy myo-inositol and D-chiro-inositol improved LDL levels ( $3.50 \pm 0.8$  mmol/L versus,  $3 \pm 1.2$  mmol/L  $p < 0.05$ ), HDL ( $1.1$  mmol/L  $\pm 0.3$  versus  $1.6$  mmol/L  $\pm 0.4$   $p < 0.05$ ) and triglycerides ( $2.3 \pm 1.5$  mmol/L versus  $1.75 \pm 1.9$  mmol/L  $p < 0.05$ ). Furthermore, significant improvements in HOMA-IR were also observed.

**CONCLUSIONS:** The combined therapy myo-inositol plus D-chiro-inositol is able to improve the metabolic profile of PCOS women, therefore, reducing the cardiovascular risk.

PMID: 23467955 [PubMed - indexed for MEDLINE]

## **The combined therapy myo-inositol plus D-chiro-inositol, rather than D-chiro-inositol, is able to improve IVF outcomes: results from a randomized controlled trial.**

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### **Abstract**

**PURPOSE:** The present study aims to investigate the effects of the combined therapy myo-inositol (MI) plus D-chiro-inositol (DCI) or D-chiro-inositol treatment in oocyte quality.

**METHODS:** Polycystic ovary syndrome (PCOS) women undergoing IVF-ET were treated with myo-inositol combined with D-chiro-inositol in the physiological ratio (1.1 g myo-inositol plus 27.6 mg of D-chiro-inositol; INOFOLIC combi Lo.Li.pharma) or D-chiro-inositol alone (500 mg; Interquim, s.a., Barcelona, Spain) to evaluate the number of morphological mature oocytes, total International Units (IU) of recombinant FSH administered and the number of grade 1 embryos.

**RESULTS:** The data clearly showed that only the combined therapy was able to improve oocyte and embryo quality, as well as pregnancy rates, in PCOS women undergoing IVF-ET.

**CONCLUSION:** The present paper further supports the hypothesis that MI plays a crucial role in the ovary in PCOS women. In particular, due to the physiological role played by MI and DCI, the combined therapy should represent a better choice.

PMID: 23708322 [PubMed - in process]

## **The rationale of the myo-inositol and D-chiro-inositol combined treatment for polycystic ovary syndrome.**

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### **Abstract**

PCOS is one of the most common endocrine disorders affecting women and it is characterized by a combination of hyper-androgenism, chronic anovulation, and insulin resistance. While a significant progress has recently been made in the diagnosis for PCOS, the optimal infertility treatment remains to be determined. Two inositol isomers, myo-inositol (MI) and D-chiro-inositol (DCI) have been proven to be effective in PCOS treatment, by improving insulin resistance, serum androgen levels and many features of the metabolic syndrome. However, DCI alone, mostly when it is administered at high dosage, negatively affects oocyte quality, whereas the association MI/DCI, in a combination reproducing the plasma physiological ratio (40:1), represents a promising alternative in achieving better clinical results, by counteracting PCOS at both systemic and ovary level.

**KEYWORDS:** embryo; infertility; inositol; oocyte; polycystic ovarian syndrome

PMID: 25042908 [PubMed - in process]

## **Inositol: history of an effective therapy for Polycystic Ovary Syndrome.**

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### **Abstract**

Inositol is a physiological compound belonging to the sugar family. The two inositol stereoisomers, myo-inositol and D-chiroinositol are the two main stereoisomers present in our body. Myo-inositol is the precursor of inositol triphosphate, a second messenger regulating many hormones such as TSH, FSH and insulin. D-chiroinositol is synthesized by an insulin dependent epimerase that converts myo-inositol into D-chiroinositol. Polycystic Ovary Syndrome (PCOS) is a metabolic and hormonal disorder and a common cause of infertility. Insulin resistance and the consequent hyperinsulinaemia contribute to hyperandrogenism development, typical marker of PCOS. In these patients myo and/or D-chiro-inositol administration improves insulin sensitivity while only myo-inositol is a quality marker for oocytes evaluation. Myo-inositol produces second messengers for FSH and glucose uptake, while D-chiroinositol provides second messengers promoting glucose uptake and glycogen synthesis. The physiological ratio of these two isomers is 40:1 (MI/DCI) and seems to be an optimal approach for the treatment of PCOS disorders.

PMID: 25010620 [PubMed - in process]

## **Results from the International Consensus Conference on Myo-inositol and d-chiro-inositol in Obstetrics and Gynecology: the link between metabolic syndrome and PCOS.**

Facchinetti F, Bizzarri M, Benvenga S, D'Anna R, Lanzone A, Soulage C, Di Renzo GC, Hod M, Cavalli P, Chiu TT, Kamenov ZA, Bevilacqua A, Carlomagno G, Gerli S, Oliva MM, Devroey P.

### **Abstract**

In recent years, interest has been focused to the study of the two major inositol stereoisomers: myo-inositol (MI) and d-chiro-inositol (DCI), because of their involvement, as second messengers of insulin, in several insulin-dependent processes, such as metabolic syndrome and polycystic ovary syndrome. Although these molecules have different functions, very often their roles have been confused, while the meaning of several observations still needs to be interpreted under a more rigorous physiological framework. With the aim of clarifying this issue, the 2013 International Consensus Conference on MI and DCI in Obstetrics and Gynecology identified opinion leaders in all fields related to this area of research. They examined seminal experimental papers and randomized clinical trials reporting the role and the use of inositol(s) in clinical practice. The main topics were the relation between inositol(s) and metabolic syndrome, polycystic ovary syndrome (with a focus on both metabolic and reproductive aspects), congenital anomalies, gestational diabetes. Clinical trials demonstrated that inositol(s) supplementation could fruitfully affect different pathophysiological aspects of disorders pertaining Obstetrics and Gynecology. The treatment of PCOS women as well as the prevention of GDM seem those clinical conditions which take more advantages from MI supplementation, when used at a dose of 2g twice/day. The clinical experience with MI is largely superior to the one with DCI. However, the existence of tissue-specific ratios, namely in the ovary, has prompted researchers to recently develop a treatment based on both molecules in the proportion of 40 (MI) to 1 (DCI).

PMID: 26479434

## **A Combined Therapy with Myo-Inositol and D-Chiro-Inositol Improves Endocrine Parameters and Insulin Resistance in PCOS Young Overweight Women.**

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### **Abstract**

**Introduction.** We evaluated the effects of a therapy that combines myo-inositol (MI) and D-chiro-inositol (DCI) in young overweight women affected by polycystic ovary syndrome (PCOS), characterized by oligo- or anovulation and hyperandrogenism, correlated to insulin resistance. **Methods.** We enrolled 46 patients affected by PCOS and, randomly, we assigned them to two groups, A and B, treated, respectively, with the association of MI plus DCI, in a 40:1 ratio, or with placebo (folic acid) for six months. Thus, we analyzed pretreatment and posttreatment FSH, LH, 17-beta-Estradiol, Sex Hormone Binding Globulin, androstenedione, free testosterone, dehydroepiandrosterone sulphate, HOMA index, and fasting glucose and insulin. **Results.** We recorded a statistically significant reduction of LH, free testosterone, fasting insulin, and HOMA index only in the group treated with the combined therapy of MI plus DCI; in the same patients, we observed a statistically significant increase of 17-beta-Estradiol levels. **Conclusions.** The combined therapy of MI plus DCI is effective in improving endocrine and metabolic parameters in young obese PCOS affected women.

PMID: 27493664 PMC: 4963579

## **The Effectiveness of Myo-Inositol and D-Chiro Inositol Treatment in Type 2 Diabetes.**

Pintaudi B, Di Vieste G, Bonomo M.

### **Abstract**

Inositol has been used as a supplement in treating several pathologies such as PCOS, metabolic syndrome, and gestational diabetes. Both myo-inositol and its isomer d-chiro-inositol showed insulin mimetic effects in conditions of insulin resistance. Type 2 diabetes (T2DM) is a condition typically caused by insulin resistance. There is a lack of evidence of inositol use in T2DM. We evaluated the effectiveness and safety of myo-inositol and d-chiro-inositol treatment in T2DM. This was a pilot study involving a consecutive sample of patients with T2DM with suboptimal glycemic control (HbA1c 7.0-10.0%) already treated with glucose-lowering agents. Patients (23.1% males, mean age of  $60.8 \pm 11.7$  years) took for three months a combination of myo-inositol (550 mg) and d-chiro-inositol (13.8 mg) orally twice a day as add-on supplement to their glucose-lowering drugs. Possible occurrence of side effects was investigated. After three months of treatment fasting blood glucose ( $192.6 \pm 60.2$  versus  $160.9 \pm 36.4$ ;  $p = 0.02$ ) and HbA1c levels ( $8.6 \pm 0.9$  versus  $7.7 \pm 0.9$ ;  $p = 0.02$ ) significantly decreased compared to baseline. There was no significant difference in blood pressure, lipid profile, and BMI levels. None of the participants reported side effects. In conclusion, a supplementation with a combination of myo- and d-chiro-inositol is an effective and safe strategy for improving glycemic control in T2DM.

PMID: 27807448 PMCID: PMC5078644



# **Comparison of Myo-inositol to Metformin**

## **Insulin sensitiser agents alone and in co-treatment with r-FSH for ovulation induction in PCOS women.**

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### **Abstract**

**OBJECTIVE:** The aim of this study was to compare the effectiveness of myo-inositol (MYO) and metformin, in monotherapy or in association with recombinant follicle stimulating hormone (r-FSH), in the treatment of menstrual irregularities, chronic anovulation, and female infertility in patients with polycystic ovary syndrome (PCOS).

**MATERIALS AND METHODS:** One hundred twenty patients were randomly treated with metformin 1500 mg/day orally (n = 60), or 4 g MYO plus 400 microg folic acid daily (n = 60), continuously. If no pregnancy occurred, r-FSH (37.5 units/day) was added to the treatment for a maximum of three attempts.

**RESULTS:** Fifty percent of the patients who assumed metformin restored spontaneous ovulation, 18.3% of these obtained pregnancy. The remaining 42 patients were treated with metformin plus r-FSH. Pregnancy occurred in a total of 11 women (26.1%). The total pregnancy rate was 36.6%. Sixty-five percent of the patients treated with MYO plus folic acid restored spontaneous ovulation activity, 30% of these obtained pregnancy. The remaining 38 patients were treated with MYO, folic acid plus r-FSH. Pregnancy occurred in a total of 11 women (28.9%). The total pregnancy rate was 48.4%.

**CONCLUSIONS:** Both metformin and MYO, can be considered as first line treatment for restoring normal menstrual cycles in most patients with PCOS, even if MYO treatment seems to be more effective than metformin.

PMID: 20222840 [PubMed - indexed for MEDLINE]

## **Inositol versus Metformin administration in polycystic ovary syndrome patients: a case-control study**

Abdel Hamid, Amr Mohamed S. Ismail Madkour, Wael A.; Borg, Tamer F.

### **Abstract**

**Aim of the study:** The aim of this case-control study is to evaluate the clinical and biochemical efficiency of Inositol versus Metformin in polycystic ovary syndrome.

**Patients and methods:** The 128 patients who completed the study were divided into group A, which included 62 patients prescribed myo-inositol+D-chiro-inositol, two tabs per day, and group B, which included 66 patients prescribed Metformin 1500 mg per day for 3 months. Then, both groups were followed up for 3 months after the end of the treatment period. All patients underwent the following: baseline vaginal ultrasound, BMI and weight evaluation, Anti mullerian hormones (AMH) evaluation, serum progesterone, and Homeostasis Model of Assessment-Insulin Resistance (HOMA-IR), and were evaluated according to clinical and biochemical outcomes.

**Results:** Spontaneous menstruation and spontaneous pregnancy rate were significantly higher in group A than in group B: 46.7 and 11.2% in the Inositol group compared with 13.6 and 3.0% in the Metformin group. In terms of weight loss, the difference between both groups was significant in favor of the Inositol group. A significant difference was also detected in terms of a higher progesterone level in group A, whereas AMH and HOMA-IR showed insignificant differences in both groups.

**Conclusion:** Myo-inositol+D-chiro-inositol showed significantly better results in terms of weight reduction, resumption of spontaneous ovulation, and spontaneous pregnancy than Metformin in polycystic ovary syndrome patients. However, the effects of both drugs were comparable in decreasing either AMH or HOMA-IR.



# **Myo-inositol and Hormone, Metabolic, & Ovulation Induction Effects**

## **Randomized, double blind placebo-controlled trial: effects of myo-inositol on ovarian function and metabolic factors in women with PCOS.**

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### **Abstract**

Oligomenorrhea and polycystic ovaries in women are one of the most important causes of the high incidence of ovulation failure. This is linked, perhaps, to insulin resistance and related metabolic features. A small number of reports show that myo-inositol improves ovarian function, but in these trials the quality of evidence supporting ovulation is suboptimal. Furthermore, few of them have been placebo-controlled. The aim of our study was to use a double-blind, placebo-controlled approach with detailed assessment of ovarian activity (two blood samples per week) to assess the validity of this therapeutic approach in this group of women. Of the 92 patients randomized, 47 received 400 mcg folic acid as placebo, and 45 received myo-inositol plus folic acid (4 g myo-inositol plus 400 mcg folic acid). The ovulation frequency assessed by the ratio of luteal phase weeks to observation weeks was significantly ( $P < 0.01$ ) higher in the treated group (25%) compared with the placebo (15%), and the time to first ovulation was significantly ( $P < 0.05$ ) shorter [24.5 d; 95% confidence interval (CI), 18, 31; compared with 40.5 d; 95% CI, 27, 54]. The number of patients failing to ovulate during the placebo-treatment period was higher ( $P < 0.05$ ) in the placebo group, and the majority of ovulations were characterized by normal progesterone concentrations in both groups. The effect of myo-inositol on follicular maturation was rapid, because the E2 circulating concentration increased over the first week of treatment only in the myo-inositol group. A significant increase in circulating high-density lipoprotein was observed only in the myo-inositol-treated group. Metabolic risk factor benefits of myo-inositol treatment were not observed in the morbidly obese subgroup of patients (body mass index  $> 37$ ). After 14-wk myo-inositol or placebo therapy, no change in fasting glucose concentrations, fasting insulin, or insulin responses to glucose challenge was recorded. There was an inverse relationship between body mass and treatment efficacy. In fact a significant weight loss (and leptin reduction) ( $P < 0.01$ ) was recorded in the myo-inositol group, whereas the placebo group actually increased weight ( $P < 0.05$ ). These data support a beneficial effect of myo-inositol in women with oligomenorrhea and polycystic ovaries in improving ovarian function.

PMID: 18074942 [PubMed - indexed for MEDLINE]

## **Metabolic and hormonal effects of myo-inositol in women with polycystic ovary syndrome: a double-blind trial.**

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### **Abstract**

To investigate the effects of treatment with Myo-inositol (an insulin sensitizing drug), on circulating insulin, glucose tolerance, ovulation and serum androgens concentrations in women with the Polycystic Ovary Syndrome (PCOS). Forty-two women with PCOS were treated in a double-blind trial with Myo-inositol plus folic acid or folic acid alone as placebo. In the group treated with Myo-inositol the serum total testosterone decreased from 99.5 +/- 7 to 34.8 +/- 4.3 ng/dl (placebo group: from 116.8 +/- 15 to 109 +/- 7.5 ng/dl; P = 0.003), and serum free testosterone from 0.85 +/- 0.1 to 0.24 +/- 0.33 ng/dl (placebo group: from 0.89 +/- 0.12 to 0.85 +/- 0.13 ng/dl; P = 0.01). Plasma triglycerides decreased from 195 +/- 20 to 95 +/- 17 mg/dl (placebo group: from 166 +/- 21 to 148 +/- 19 mg/dl; P = 0.001). Systolic blood pressure decreased from 131 +/- 2 to 127 +/- 2 mmHg (placebo group: from 128 +/- 1 to 130 +/- 1 mmHg; P = 0.002). Diastolic blood pressure decreased from 88 +/- 1 to 82 +/- 3 mmHg (placebo group: from 86 +/- 1 to 90 +/- 1 mmHg; P = 0.001). The area under the plasma insulin curve after oral administration of glucose decreased from 8.54 +/- 1.149 to 5.535 +/- 1.792 microU/ml/min (placebo group: from 8.903 +/- 1.276 to 9.1 +/- 1.162 microU/ml/min; P = 0.03). The index of composite whole body insulin sensitivity (ISI comp) increased from 2.80 +/- 0.35 to 5.05 +/- 0.59 mg(-2)/dl(-2) (placebo group: from 3.23 +/- 0.48 to 2.81 +/- 0.54 mg(-2)/dl(-2); P < 0.002). 16 out of 23 women of Myo-inositol group ovulated (4 out of 19 in placebo group). Treatment of PCOS patients with Myo-inositol provided a decreasing of circulating insulin and serum total testosterone as well as an improvement in metabolic factors.

PMID: 19499845 [PubMed - indexed for MEDLINE]

## **Endocrine and clinical effects of myo-inositol administration in polycystic ovary syndrome. A randomized study.**

Artini PG<sup>1</sup>, Di Bernardino OM, Papini F, Genazzani AD, Simi G, Ruggiero M, Cela V.

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### **Abstract**

**OBJECTIVE:** To evaluate the effects the administration of myo-inositol (MYO) on hormonal parameters in a group of polycystic ovary syndrome (PCOS) patients.

**DESIGN:** Controlled clinical study.

**SETTING:** PCOS patients in a clinical research environment.

**PATIENTS:** 50 overweight PCOS patients were enrolled after informed consent.

**INTERVENTIONS:** All patients underwent hormonal evaluations and an oral glucose tolerance test (OGTT) before and after 12 weeks of therapy (Group A (n¼10): MYO 2 g plus folic acid 200 mg every day; Group B (n¼10): folic acid 200 mg every day). Ultrasound examinations and Ferriman-Gallwey score were also performed.

**MAIN OUTCOME MEASURES:** Plasma LH, FSH, PRL, E2, 17OHP, A, T, glucose, insulin, C peptide concentrations, BMI, HOMA index and glucose-to-insulin ratio.

**RESULTS:** After 12 weeks of MYO administration plasma LH, PRL, T, insulin levels and LH/FSH resulted significantly reduced. Insulin sensitivity, expressed as glucose-to-insulin ratio and HOMA index resulted significantly improved after 12 weeks of treatment. Menstrual cyclicality was restored in all amenorrheic and oligomenorrheic subjects. No changes occurred in the patients treated with folic acid.

**CONCLUSIONS:** MYO administration improves reproductive axis functioning in PCOS patients reducing the hyperinsulinemic state that affects LH secretion.

PMID: 23336594 [PubMed - indexed for MEDLINE]

## **Myo-inositol modulates insulin and luteinizing hormone secretion in normal weight patients with polycystic ovary syndrome.**

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### **Abstract**

**AIM:** To investigate hormonal dynamics in a group of non-obese polycystic ovary syndrome (PCOS) patients under myo-inositol (MYO) administration.

**METHODS:** Hormonal profiles, insulin response to oral glucose tolerance test (OGTT) and luteinizing hormone (LH) response to gonadotropin-releasing hormone (GnRH) stimulation test before and after the administration of a preparation of MYO (3 g p.o. daily) mixed with lactoferrin and bromelin, in a group (n = 24) of normal weight PCOS patients.

**RESULTS:** After the treatment interval, body mass index (BMI) did not change while LH, LH/follicle-stimulating hormone, 17-hydroxy-progesterone and androstenedione decreased significantly. Insulin response to OGTT was significantly reduced after the treatment interval ( $P < 0.05$ ) as well as GnRH-induced LH response ( $P < 0.05$ ). High-sensitivity C-reactive protein decreased significantly after the treatment interval.

**CONCLUSION:** MYO administration positively modulates insulin sensitivity in non-obese PCOS patients without compensatory hyperinsulinemia, improving hormonal parameters. The presence of bromelin in the formulation modulated the pro-inflammatory state that characterizes PCOS, independently of BMI.

**KEYWORDS:** C-reactive protein; hyperinsulinism; insulin resistance; myo-inositol; polycystic ovary syndrome

PMID: 24606639 [PubMed - in process]

## **Ovulation induction with myo-inositol alone and in combination with clomiphene citrate in polycystic ovarian syndrome patients with insulin resistance.**

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<sup>1</sup>Clinic of Endocrinology, Alexandrovska University Hospital, Medical University, Sofia, Bulgaria.

### **Abstract**

**BACKGROUND:** Insulin resistance plays a key role in the pathogenesis of polycystic ovarian syndrome (PCOS). One of the methods for correcting insulin resistance is using myo-inositol.

**AIM:** The aim of the present study is to evaluate the effectiveness of myo-inositol alone or in combination with clomiphene citrate for (1) induction of ovulation and (2) pregnancy rate in anovulatory women with PCOS and proven insulin resistance.

**PATIENTS AND METHODS:** This study included 50 anovulatory PCOS patients with insulin resistance. All of them received myo-inositol during three spontaneous cycles. If patients remained anovulatory and/or no pregnancy was achieved, combination of myo-inositol and clomiphene citrate was used in the next three cycles. Ovulation and pregnancy rate, changes in body mass index (BMI) and homeostatic model assessment (HOMA) index and the rate of adverse events were assessed.

**RESULTS:** After myo-inositol treatment, ovulation was present in 29 women (61.7%) and 18 (38.3%) were resistant. Of the ovulatory women, 11 became pregnant (37.9%). Of the 18 myo-inositol resistant patients after clomiphene treatment, 13 (72.2%) ovulated. Of the 13 ovulatory women, 6 (42.6%) became pregnant. During follow-up, a reduction of body mass index and HOMA index was also observed.

**CONCLUSION:** Myo-inositol treatment ameliorates insulin resistance and body weight, and improves ovarian activity in PCOS patients.

**KEYWORDS:** Anovulation; PCOS; clomiphene citrate; insulin resistance; myo-inositol

PMID: 25259724 [PubMed - in process]

# **Myo-inositol and Egg Quality, Fertility**

## **Myo-inositol may improve oocyte quality in intracytoplasmic sperm injection cycles. A prospective, controlled, randomized trial.**

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### **Abstract**

**OBJECTIVE:** To determine the effects of myo-inositol on oocyte quality in polycystic ovary syndrome (PCOS) patients undergoing intracytoplasmic sperm injection (ICSI) cycles.

**DESIGN:** A prospective, controlled, randomized trial.

**SETTING:** Assisted reproduction centers.

**PATIENT(S):** Sixty infertile PCO patients undergoing ovulation induction for ICSI.

**INTERVENTION(S):** All participants underwent standard long protocol. Starting on the day of GnRH administration, 30 participants received myo-inositol combined with folic acid (Inofolic) 2 g twice a day and 30 control women received folic acid alone, administered continuously.

**MAIN OUTCOME MEASURE(S):** Primary end points were number of morphologically mature oocytes retrieved, embryo quality, and pregnancy and implantation rates. Secondary end points were total number of days of FSH stimulation, total dose of gonadotropin administered, E(2) level on the day of hCG administration, fertilization rate per number of retrieved oocytes, embryo cleavage rate, live birth and miscarriage rates, cancellation rate, and incidence of moderate or severe ovarian hyperstimulation syndrome.

**RESULT(S):** Total r-FSH units (1,958 +/- 695 vs. 2,383 +/- 578) and number of days of stimulation (11.4 +/- 0.9 vs. 12.4 +/- 1.4) were significantly reduced in the myo-inositol group. Furthermore, peak E(2) levels (2,232 +/- 510 vs. 2,713 +/- 595 pg/mL) at hCG administration were significantly lower in patients receiving myo-inositol. The mean number of oocytes retrieved did not differ in the two groups, whereas in the group cotreated with myo-inositol the mean number of germinal vesicles and degenerated oocytes was significantly reduced (1.0 +/- 0.9 vs. 1.6 +/- 1.0), with a trend for increased percentage of oocytes in metaphase II (0.82 +/- 0.11% vs. 0.75 +/- 0.15%).

**CONCLUSION(S):** These data show that in patients with PCOS, treatment with myo-inositol and folic acid, but not folic acid alone, reduces germinal vesicles and degenerated oocytes at ovum pick-up without compromising total number of retrieved oocytes. This approach, reducing E(2) levels at hCG administration, could be adopted to decrease the risk of hyperstimulation in such patients.

PMID: 18462730 [PubMed - indexed for MEDLINE]

## **Effects of myo-inositol supplementation on oocyte's quality in PCOS patients: a double blind trial.**

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<sup>1</sup>Microbiological and Gynecological Science Department, Gynecology Section Santo Bambino Hospital (Catania), University of Catania, Italy.

### **Abstract**

**BACKGROUND:** Polycystic ovary syndrome is the most common cause of chronic anovulation infertility in women in fertile period, and it's characterized by an increased production of androgens and estrogens. The administration of myo-inositol, a B complex vitamin, was associated with a decreased of serum testosterone and simultaneously, due to its ability to increase insulin sensitivity, women who received myo-inositol showed a great improvement of the ovulatory function. Besides, the supplementation of inositol improves the oocytes' quality and increase the number of oocytes collected after ovarian stimulation in patients undergoing IVF (in vitro fertilization).

**AIM:** The aim of this study is to determine the effects of myo-inositol on oocyte's quality on a sample of women with polycystic ovary syndrome.

**MATERIAL AND METHODS:** The patients were divided into two groups: patients of Group A in-took 2 g of myo-inositol + 200 microg of folic acid (Inofolic, LO.LI. Pharma, Rome, Italy) while Group B only 200 microg of folic acid, both groups took the treatment twice a day, continuously for 3 months.

**RESULTS:** At the end of treatment, the number of follicles of diameter > 15 mm, visible at ultrasound during stimulation, and the number of oocytes recovered at the time of pick-ups were found to be significantly greater in the group treated with myo-inositol, so as the average number of embryos transferred and embryo Score S1. Significantly reduced was the average number of immature oocytes (vesicles germ and degenerated oocytes) too.

**CONCLUSIONS:** These data suggest that myoinositol may be useful in the treatment of PCOS patients undergoing ovulation induction, both for its insulin-sensitizing activity, and its role in oocyte maturation.

PMID: 21744744 [PubMed - indexed for MEDLINE]

## **Myo-inositol rather than D-chiro-inositol is able to improve oocyte quality in intracytoplasmic sperm injection cycles. A prospective, controlled, randomized trial.**

Unfer V<sup>1</sup>, Carlomagno G, Rizzo P, Raffone E, Roseff S.

<sup>1</sup>AGUNCO Obstetrics and Gynecology Centre, Rome, Italy. vunfer@gmail.com

### **Abstract**

**OBJECTIVE:** Polycystic ovary syndrome (PCOS) is the most common cause of infertility due to menstrual dysfunction, and the most promising treatments for this disease are insulin sensitising agents. Myo-inositol and D-chiro-inositol are insulin sensitizing agents used in PCOS treatment. In the present paper, we aimed to compare the effects myo-inositol and D-chiro-inositol on oocyte quality in euglycemic PCOS patients.

**MATERIALS AND METHODS:** Eighty-four euglycemic PCOS patients, undergoing ovulation induction for ICSI, were recruited for this study. Forty-three participants received MyoInositol 2 g twice a day and forty-one patients received D-chiro inositol 0.6 g twice a day.

**RESULTS:** The results of our study showed that the total number of oocytes retrieved did not differ in the two treatments groups. However, the number of mature oocytes was significantly increased in the myo-inositol group compared to D-chiro-inositol. Concurrently, the number of immature oocytes decreased in myo-inositol treated patients. Furthermore, the myo-inositol-treated group showed an increase in the mean number of top quality embryos and in the total number of pregnancies compared to the D-chiro-inositol-treated group.

**CONCLUSIONS:** Our data show that, in PCOS patients having a normal insulin response, myo-inositol treatment rather than D-chiro-inositol is able to improve oocyte and embryo quality during ovarian stimulation protocols.

PMID: 21608442 [PubMed - indexed for MEDLINE]

## **Pretreatment with myo-inositol in non polycystic ovary syndrome patients undergoing multiple follicular stimulation for IVF: a pilot study.**

Lisi F<sup>1</sup>, Carfagna P, Oliva MM, Rago R, Lisi R, Poverini R, Manna C, Vaquero E, Caserta D, Raparelli V, Marci R, Moscarini M.

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### **Abstract**

**BACKGROUND:** Aim of this pilot study is to examine the effects of myo-inositol administration on ovarian response and oocytes and embryos quality in non PolyCystic Ovary Syndrome (PCOS) patients undergoing multiple follicular stimulation and in vitro insemination by conventional in vitro fertilization or by intracytoplasmic sperm injection.

**METHODS:** One hundred non-PCOS women aged <40 years and with basal FSH <10 mIU/ml were down-regulated with triptorelin acetate from the mid-luteal phase for 2 weeks, before starting the stimulation protocol for oocytes recovery. All patients received rFSH, at a starting dose of 150 IU for 6 days. The dose was subsequently adjusted according to individual response. Group B (n=50) received myo-inositol and folic acid for 3 months before the stimulation period and then during the stimulation itself. Group A (n=50) received only folic acid as additional treatment in the 3 months before and through treatment.

**RESULTS:** Total length of the stimulation was similar between the two groups. Nevertheless, total amount of gonadotropins used to reach follicular maturation was found significantly lower in group B. In addition, the number of oocytes retrieved was significantly reduced in the group pretreated with myo-inositol. Clinical pregnancy and implantation rate were not significantly different in the two groups.

**CONCLUSIONS:** Our findings suggest that the addition of myo-inositol to folic acid in non PCOS-patients undergoing multiple follicular stimulation for in-vitro fertilization may reduce the numbers of mature oocytes and the dosage of rFSH whilst maintaining clinical pregnancy rate. Further, a trend in favor of increased incidence of implantation in the group pretreated with myo-inositol was apparent in this study. Further investigations are warranted to clarify this pharmacological approach, and the benefit it may hold for patients.

PMID: 22823904 [PubMed - indexed for MEDLINE]

## **Prospective Randomized Study on the Influence of Myoinositol in PCOS Women Undergoing IVF in the Improvement of Oocyte Quality, Fertilization Rate, and Embryo Quality.**

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### **Abstract**

Polycystic ovarian syndrome (PCOS) is one of the pathological factors involved in the failure of in vitro fertilization (IVF). The aim of the present study was to investigate if the combination of myoinositol + folic acid was able to improve the oocyte quality, the ratio between follicles and retrieved oocytes, the fertilization rate, and the embryo quality in PCOS patients undergoing IVF treatments. 29 patients with PCOS underwent IVF protocols for infertility treatment and were randomized prospectively into two groups. Group A (placebo) with 15 patients and group B (4000 mg myoinositol + 400 µg folic acid per day) with 14 patients. The patients of group B used for two months myoinositol + folic acid before starting the IVF protocol and data were obtained concerning number of follicles, number of oocytes, quality of oocytes, fertilization rates, and embryo quality in both groups. The ratio follicle/retrieved oocyte was better in the myoinositol group (= group B). Out of the 233 oocytes collected in the myoinositol group 136 were fertilized, whereas only 128 out of 300 oocytes in the placebo group were fertilized. More metaphase II and I oocytes were retrieved in relation to the total amount of oocytes in the myoinositol. More embryos of grade I quality were obtained in the myoinositol. The duration of stimulation was 9,7 days ( $\pm 3,3$ ) in the myoinositol group and 11,2 ( $\pm 1,8$ ) days in the placebo group and the number of used FSH units was lower in the myoinositol group: 1750 FSH units (mean) versus 1850 units (mean). Our evidence suggests that myoinositol therapy in women with PCOS results in better fertilization rates and a clear trend to a better embryo quality. As the number of retrieved oocytes was smaller in the myoinositol group, the risk of hyper stimulation syndrome can be reduced in these patients.

PMID: 27635136, PMCID: PMC5011206

## **Myo-inositol therapy for poor-responders during IVF: a prospective controlled observational trial.**

Caprio F, D'Eufemia MD, Trotta C, Campitiello MR, Ianniello R, Mele D, Colacurci N.

### **Abstract**

**BACKGROUND:** The overall incidence of poor ovarian response in IVF cycles has been reported to be between 9 and 24%. The management of these patients remains a significant challenge in assisted reproduction. The aim of the present study was to evaluate the effect of myo-inositol (MI) on ovarian function in poor responders undergoing ICSI.

**METHODS:** The study is a prospective controlled observational trial, that involved 72 poor responders included in an ICSI program and divided into two groups; group A: 38 patients who have been assuming MI (4 g) + folic acid (FA) (400 µg) for the previous 3 months before the enrollment day; group B: 38 patients assuming FA (400 µg) alone for the same period. COH was carried out in the same manner in the two groups. The main goal was the assessment of oocytes retrieved number and quality; secondary endpoints were the Ovarian Sensitivity Index (OSI: n° oocytes retrieved/total Gonadotropins units × 1000), oestradiol levels on the day of hGC, fertilization rate, implantation rate, ongoing pregnancy rate.

**RESULTS:** There was no significant difference between the two groups regarding oestradiol level, but total rec-FSH units were significantly lower ( $p = 0.004$ ) and M2 oocytes rate significantly higher ( $p = 0.01$ ) in group A. The ovarian sensitivity index was higher, reaching a statistical significance ( $p < 0.05$ ), in the group of patients pre-treated with MI, showing an improvement in ovarian sensibility to gonadotropin.

**CONCLUSIONS:** Our results suggest that MI therapy in poor responders results in an increased of the number of oocytes recovered in MII and of the gonadotropin Ovarian Sensitivity Index (OSI), suggesting a MI role in improving ovarian response to gonadotropins. Therefore MI seems to be helpful in "poor responders" undergoing IVF cycles.

PMID: 26067283 PMCID: PMC4464995

## **Inositol Treatment and ART Outcomes in Women with PCOS.**

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### **Abstract**

Polycystic ovary syndrome (PCOS) affects 5-10% of women in reproductive age and is characterized by oligo/amenorrhea, androgen excess, insulin resistance, and typical polycystic ovarian morphology. It is the most common cause of infertility secondary to ovulatory dysfunction. The underlying etiology is still unknown but is believed to be multifactorial. Insulin-sensitizing compounds such as inositol, a B-complex vitamin, and its stereoisomers (myo-inositol and D-chiro-inositol) have been studied as an effective treatment of PCOS. Administration of inositol in PCOS has been shown to improve not only the metabolic and hormonal parameters but also ovarian function and the response to assisted-reproductive technology (ART). Accumulating evidence suggests that it is also capable of improving folliculogenesis and embryo quality and increasing the mature oocyte yield following ovarian stimulation for ART in women with PCOS. In the current review, we collate the evidence and summarize our current knowledge on ovarian stimulation and ART outcomes following inositol treatment in women with PCOS undergoing in vitro fertilization (IVF) and/or intracytoplasmic sperm injection (ICSI).

# **Myo-inositol and Gestational Diabetes**

## **Myo-Inositol supplementation and onset of gestational diabetes mellitus in pregnant women with a family history of type 2 diabetes: a prospective, randomized, placebo-controlled study.**

D'Anna R<sup>1</sup>, Scilipoti A, Giordano D, Caruso C, Cannata ML, Interdonato ML, Corrado F, Di Benedetto A.

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### **Abstract**

**OBJECTIVE:** To check the hypothesis that myo-inositol supplementation may reduce gestational diabetes mellitus (GDM) onset in pregnant women with a family history of type 2 diabetes.

**RESEARCH DESIGN AND METHODS:** A 2-year, prospective, randomized, open-label, placebo-controlled study was carried out in pregnant outpatients with a parent with type 2 diabetes who were treated from the end of the first trimester with 2 g myo-inositol plus 200 µg folic acid twice a day (n = 110) and in the placebo group (n = 110), who were only treated with 200 µg folic acid twice a day. The main outcome measure was the incidence of GDM in both groups. Secondary outcome measures were as follows: the incidence of fetal macrosomia (>4,000 g), gestational hypertension, preterm delivery, caesarean section, shoulder dystocia, neonatal hypoglycemia, and neonatal distress respiratory syndrome. GDM diagnosis was performed according to the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommendations.

**RESULTS:** Incidence of GDM was significantly reduced in the myo-inositol group compared with the placebo group: 6 vs. 15.3%, respectively (P = 0.04). In the myo-inositol group, a reduction of GDM risk occurrence was highlighted (odds ratio 0.35). A statistically significant reduction of fetal macrosomia in the myo-inositol group was also highlighted together with a significant reduction in mean fetal weight at delivery. In the other secondary outcome measures, there were no differences between groups.

**CONCLUSIONS:** myo-Inositol supplementation in pregnant women with a family history of type 2 diabetes may reduce GDM incidence and the delivery of macrosomia fetuses.

PMID: 23340885 PMCID: PMC3609506

## **Effect of dietary myo-inositol supplementation in pregnancy on the incidence of maternal gestational diabetes mellitus and fetal outcomes: a randomized controlled trial.**

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### **Abstract**

**OBJECTIVE:** To test the hypothesis that dietary myo-inositol may improve insulin resistance and the development of gestational diabetes mellitus (GDM) in women at high risk of this disorder.

**DESIGN:** A prospective, randomized, double-blind, placebo controlled clinical trial, pilot study.

**PARTICIPANTS:** Non-obese singleton pregnant women with an elevated fasting glucose in the first or early second trimester were studied throughout pregnancy.

**INTERVENTION:** Supplementation with myo-inositol or placebo during pregnancy.

**MAIN OUTCOME MEASURE:** Development of GDM on a 75 g oral glucose tolerance test at 24-28 weeks' gestation. Secondary outcome measures were increased in BMI, need for maternal insulin therapy, macrosomia, polyhydramnios, neonatal birthweight and hypoglycemia.

**RESULTS:** Thirty-six women were allocated to receive myo-inositol and 39 placebo. The incidence of GDM in mid-pregnancy was significantly reduced ( $p = 0.001$ ) in women randomized to receive myo-inositol compared to placebo (relative risk 0.127). Women randomized to receive myo-inositol also required less insulin therapy, delivered at a later gestational age, had significantly smaller babies with fewer episodes of neonatal hypoglycemia.

**CONCLUSIONS:** Myo-inositol supplementation in pregnancy reduced the incidence of GDM in women at high risk of this disorder. The reduction in incidence of GDM in the treatment arm was accompanied by improved outcomes.

PMID: 23327487

## **Myo-inositol Supplementation for Prevention of Gestational Diabetes in Obese Pregnant Women: A Randomized Controlled Trial.**

D Anna R<sup>1</sup>, Di Benedetto A, Scilipoti A, Santamaria A, Interdonato ML, Petrella E, Neri I, Pintaudi B, Corrado F, Facchinetti F.

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### **Abstract**

**OBJECTIVE:** To evaluate whether myo-inositol supplementation, an insulin sensitizer, reduces the rate of gestational diabetes mellitus (GDM) and lowers insulin resistance in obese pregnant women.

**METHODS:** In an open-label, randomized trial, myo-inositol (2 g plus 200 micrograms folic acid twice a day) or placebo (200 micrograms folic acid twice a day) was administered from the first trimester to delivery in pregnant obese women (prepregnancy body mass index 30 or greater). We calculated that 101 women in each arm would be required to demonstrate a 65% GDM reduction in the myo-inositol group with a statistical power of 80% ( $\alpha=0.05$ ). The primary outcomes were the incidence of GDM and the change in insulin resistance from enrollment until the diagnostic oral glucose tolerance test.

**RESULTS:** From January 2011 to April 2014, 220 pregnant women at 12-13 weeks of gestation were randomized at two Italian university hospitals, 110 to myo-inositol and 110 to placebo. Most characteristics were similar between groups. The GDM rate was significantly reduced in the myo-inositol group compared with the control group, 14.0% compared with 33.6%, respectively ( $P=.001$ ; odds ratio 0.34, 95% confidence interval 0.17-0.68). Furthermore, women treated with myo-inositol showed a significantly greater reduction in the homeostasis model assessment of insulin resistance compared with the control group,  $-1.0\pm 3.1$  compared with  $0.1\pm 1.8$  ( $P=.048$ ).

**CONCLUSION:** Myo-inositol supplementation, started in the first trimester, in obese pregnant women seems to reduce the incidence in GDM through a reduction of insulin resistance.

**CLINICAL TRIAL REGISTRATION:** ClinicalTrials.gov, [www.clinicaltrials.gov](http://www.clinicaltrials.gov), NCT01047982.

PMID: 26241420

## **Antenatal dietary supplementation with myo-inositol in women during pregnancy for preventing gestational diabetes.**

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### **Abstract**

**BACKGROUND:** Gestational diabetes, glucose intolerance with onset or first recognition during pregnancy, is a rising problem worldwide. Both non-pharmacological and pharmacological approaches to the prevention of gestational diabetes have been, and continue to be explored. Myo-inositol, an isomer of inositol, is a naturally occurring sugar commonly found in cereals, corn, legumes and meat. It is one of the intracellular mediators of the insulin signal and correlated with insulin sensitivity in type 2 diabetes. The potential beneficial effect on improving insulin sensitivity suggests that myo-inositol may be useful for women in preventing gestational diabetes.

**OBJECTIVES:** To assess if antenatal dietary supplementation with myo-inositol is safe and effective, for the mother and fetus, in preventing gestational diabetes.

**SEARCH METHODS:** We searched the Pregnancy and Childbirth Group's Trials Register, ClinicalTrials.gov, WHO ICTRP (2 November 2015) and reference lists of retrieved studies.

**SELECTION CRITERIA:** We sought published and unpublished randomised controlled trials, including conference abstracts, assessing the effects of myo-inositol for the prevention of gestational diabetes mellitus (GDM). Quasi-randomised and cross-over trials were not eligible for inclusion, but cluster designs were eligible. Participants in the trials were pregnant women. Women with pre-existing type 1 or type 2 diabetes were excluded. Trials that compared the administration of any dose of myo-inositol, alone or in a combination preparation were eligible for inclusion. Trials that used no treatment, placebo or another intervention as the comparator were eligible for inclusion.

**DATA COLLECTION AND ANALYSIS:** Two review authors independently assessed trials for inclusion, risk of bias and extracted the data. Data were checked for accuracy.

**MAIN RESULTS:** We included four randomised controlled trials (all conducted in Italy) reporting on 567 women who were less than 11 weeks' to 24 weeks' pregnant at the start of the trials. The trials had small sample sizes and one trial only reported an interim analysis. Two trials were open-label. The overall risk of bias was unclear. For the mother, supplementation with myo-inositol was associated with a reduction in the incidence of gestational diabetes compared with control (risk ratio (RR) 0.43, 95% confidence interval (CI) 0.29 to 0.64; three trials; n = 502 women). Using GRADE methods this evidence was assessed as low with downgrading due to unclear risk of bias for allocation concealment in two of the included trials and lack of generalisability of findings. For women who received myo-inositol supplementation, the incidence of GDM ranged from 8% to 18%; for women in the control group, the incidence of GDM was 28%, using International Association of Diabetes and Pregnancy Study Groups Consensus Panel 2010 criteria to diagnose GDM. Two trials reported on hypertensive disorders of pregnancy, a primary maternal outcome of this review. There was no clear difference in risk of hypertensive disorders of pregnancy between the myo-inositol and control groups (average RR 0.43, 95% CI 0.02 to 8.41; two trials; n = 398 women; Tau(2) = 3.23; I(2) = 69%). Using GRADE methods, this evidence was assessed as very low, with downgrading due to

wide confidence intervals with very low event rates, a small sample size, and lack of blinding and unclear allocation concealment methods, and a lack of generalisability. For women who received myo-inositol the risk of hypertensive disorders of pregnancy ranged from 0% to 33%; for women in the control group the risk was 4%. For the infant, none of the included trials reported on the primary neonatal outcomes of this systematic review (large-for-gestational age, perinatal mortality, mortality or morbidity composite). In terms of this review's secondary outcomes, there was no clear difference in the risk of caesarean section between the myo-inositol and control groups (RR 0.95, 95% CI 0.76 to 1.19; two trials; n = 398 women). Using GRADE methods, this evidence was assessed as low, with downgrading due to unclear risk of bias in one trial and lack of generalisability. For women who received myo-inositol supplementation, the risk of having a caesarean section ranged from 34% to 54%; for women in the control group the was 45%. There were no maternal adverse effects of therapy in the two trials that reported on this outcome (the other two trials did not report this outcome). Two trials found no clear difference in the risk of macrosomia between infants whose mothers received myo-inositol supplementation compared with controls (average RR 0.35, 95% CI 0.02 to 6.37; two trials; n = 398 infants;  $\tau^2 = 3.33$ ;  $I^2 = 73\%$ ). Similarly, there was no clear difference between groups in terms of neonatal hypoglycaemia (RR 0.36, 95% CI 0.01 to 8.66) or shoulder dystocia (average RR 2.33, 95% CI 0.12 to 44.30,  $\tau^2 = 3.24$ ;  $I^2 = 72\%$ ). There was a lack of data available for a large number of maternal and neonatal secondary outcomes, and no data for any of the long-term childhood or adulthood outcomes, or for health service cost outcomes.

**AUTHORS' CONCLUSIONS:** Evidence from four trials of antenatal dietary supplementation with myo-inositol during pregnancy shows a potential benefit for reducing the incidence of gestational diabetes. No data were reported for any of this review's primary neonatal outcomes. There were very little outcome data for the majority of this review's secondary outcomes. There is no clear evidence of a difference for macrosomia when compared with control. The current evidence is based on small trials that are not powered to detect differences in outcomes including perinatal mortality and serious infant morbidity. All of the included studies were conducted in Italy which raises concerns about the lack of generalisability of the evidence to other settings. There is evidence of inconsistency and indirectness and as a result, many of the judgements on the quality of the evidence were downgraded to low or very low quality (GRADEpro Guideline Development Tool). Further trials for this promising antenatal intervention for preventing gestational diabetes are encouraged and should include pregnant women of different ethnicities and varying risk factors and use of myo-inositol (different doses, frequency and timing of administration) in comparison with placebo, diet and exercise or pharmacological interventions. Outcomes should include potential harms including adverse effects.

PMID: 2667825

## **Myo-inositol may prevent gestational diabetes onset in overweight women: a randomized, controlled trial.**

Santamaria A, Di Benedetto A, Petrella E, Pintaudi B, Corrado F, D'Anna R, Neri I, Facchinetti F.

### **Abstract**

**OBJECTIVE:** To evaluate whether myo-inositol supplementation may reduce gestational diabetes mellitus (GDM) rate in overweight women.

**METHODS:** In an open-label, randomized trial, myo-inositol (2 g plus 200 µg folic acid twice a day) or placebo (200 µg folic acid twice a day) was administered from the first trimester to delivery in pregnant overweight non-obese women (pre-pregnancy body mass index  $\geq 25$  and  $< 30$  kg/m<sup>2</sup>). The primary outcome was the incidence of GDM.

**RESULTS:** From January 2012 to December 2014, 220 pregnant women were randomized at two Italian University hospitals, 110 to myo-inositol and 110 to placebo. The incidence of GDM was significantly lower in the myo-inositol group compared to the placebo group (11.6% versus 27.4%, respectively,  $p = 0.004$ ). Myo-inositol treatment was associated with a 67% risk reduction of developing GDM (OR 0.33; 95% CI 0.15-0.70).

**CONCLUSIONS:** Myo-inositol supplementation, administered since early pregnancy, reduces GDM incidence in overweight non-obese women.

PMID: 26698911

