

New Research Development 1

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

Costantino D, Minozzi G, Minozzi E, Guaraldi C.

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 +/- 7.0 to 34.8 +/- 4.3 ng/dl (placebo group: from 116.8 +/- 15.1 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 156 +/- 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 83 +/- 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 8.57 +/- 1.149 to 6.355 +/- 1.732 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 2.837 +/- 0.35 to 5.05 +/- 0.59 mg/2ydl/2 (placebo group: from 3.23 +/- 0.48 to 2.81 +/- 0.54 mg/2ydl/2); P < 0.002). 16 out of 23 women of Myo-inositol group ovulated (4 out of 19 in placebo group). Treatment with Myo-inositol provided a decreasing of circulating insulin and serum total testosterone as well as an improvement in metabolic factors.

Pictorial Depiction, 2nd Women Health Convention 2012 (3rd to 4th Oct., Lahore)



New Research Development 2

hMG and idiopathic oligoasthenozoospermia (OAT): effects on seminal fluid parameters and on results in ICSI cycles.

Beretta G, Fino E, Sicilio L, Dilena M.

Abstract
Many studies on gonadotropin treatment in idiopathic OAT have produced inconsistent (75 IU FSH + 75 IU LH) at the dosage of 3 ampoules a week for 30 days in 18 patients with idiopathic OAT and testicular volume 12-15 ml. At the end of the cycle seminal fluid parameters and testicular volume were reassessed, comparing them with a homologous control group including 13 subjects awaiting ICSI, who were not given any kind of pharmacological treatment. Treatment with a statistically significant improvement in spermatozoa concentration (p = 0.016) and reduction in atypical forms (p = 0.040). We assessed also the impact on oocyte fertilization and pregnancy rates after the use of assisted reproduction techniques in a more restricted group of 8 patients, who had already undergone ICSI cycles before pharmacological therapy. Treatment with menotropin (hMG) appears to improve embryo quality.

Sparkling updates...

Gonadotropin administration after gonadotropin-releasing-hormone agonist: a therapeutic option in severe testiculopathies.

Foresta C, Solico R, Moretti A, Pati MA, Carraro M, Engl B, Garolla A.

Abstract
OBJECTIVE: To evaluate the effect of recombinant human follicle-stimulating hormone (rFSH) plus human chorionic gonadotropin (hCG) on seminal parameters and pregnancy rate in severe testiculopathies after high FSH plasma concentrations have been suppressed.
DESIGN: Prospective, controlled, randomized clinical study.
SETTING: Infertility center at a university hospital.
PATIENT(S): Eighty-seven men affected by severe testiculopathy.
INTERVENTION(S): We treated 57 men with a gonadotropin-releasing hormone agonist (GnRH-a) and then with recombinant human FSH and hCG, and 30 patients did not receive any treatment. Seminal parameters and sperm aneuploidies were evaluated during and after the treatment period. Couples did not achieve a spontaneous pregnancy received assisted reproduction treatment.
MAIN OUTCOME MEASURE(S): Seminal parameters, sperm aneuploidies, testicular cytologic analysis, FSH, luteinizing hormone, testosterone, inhibin B concentrations, and pregnancy rate.
RESULT(S): After the therapy period, the treated group showed statistically significant improvement in sperm parameters and sperm aneuploidies. No changes were observed in the untreated group. A trend toward an increase in pregnancy rate also was observed among treated couples (cumulative pregnancy rates 31.6% treated vs. 20.0% untreated), although the increase was not statistically significant. The improvement of seminal parameters in the treated group allowed some patients to undergo in vitro fertilization-embryo transfer instead of intracytoplasmic sperm injection.
CONCLUSION(S): Results from this controlled, randomized clinical trial show that FSH therapy improves sperm parameters in severe male factor infertility when endogenous high FSH plasma levels are suppressed. In cases of severely impaired testes, a rational treatment of male infertility is mandatory to improve the outcome of assisted reproduction techniques.

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Effects of inositol on oocyte quality in patients affected with polycystic ovary syndrome.

Ciotta L, Stracquadanio M, Pagano I, Carbonaro A, Palumbo M, Guino F.

Abstract
AIM: Polycystic ovary syndrome is the most common cause of chronic anovulation infertility in women in fertile period. The supplementation of inositol, due to its ability to increase insulin sensitivity, improves the oocytes' quality and increase the number of oocytes collected after ovarian stimulation in patients undergoing IVF (In Vitro Fertilization). The aim of our study is to determine the effects of myo-inositol on oocyte's quality on a sample of women with polycystic ovary syndrome.
METHODS: The patients were divided into two groups: patients of Group A took 2 g of myo-inositol + 400mcg of folic acid 2 times a day, continuously for 3 months, while Group B only 400mcg of folic acid.
RESULTS AND CONCLUSION: 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 Grade G1. Significantly reduced was the average number of immature oocytes (ies) too.

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The role of melatonin as an antioxidant in the follicle

Hiroshi Tamura, Akirisa Takasaki, Toshiaki Takotani, Manabu Tanabe, Fumio Kizuka, Lilia Lee, Isao Tamura, Ryo Maekawa, Hiromi Aasada and Yoshiaki Yamagata.

Abstract
Melatonin (N-acetyl-5-methoxytryptamine) is secreted during the dark hours at night by pineal gland, and it regulates a variety of important central and peripheral actions related to circadian rhythms and reproduction. It has been believed that melatonin regulates ovarian function by the regulation of gonadotropin release in the hypothalamus-pituitary-gonadal axis via its specific receptors. In addition to the receptor-mediated action, the discovery of melatonin as a direct free radical scavenger has greatly broadened the understanding of melatonin's mechanisms which benefit reproductive physiology. Higher concentrations of melatonin have been found in human preovulatory follicular fluid compared to serum, and there is growing evidence of the direct effects of melatonin on ovarian function especially oocyte maturation and embryo development. Many scientists have focused on the direct role of melatonin on oocyte maturation and embryo development as an antioxidant to reduce oxidative stress induced by reactive oxygen species, which are produced during ovulation process. The beneficial effects of melatonin administration on oocyte maturation and embryo development have been confirmed by in vitro and in vivo experiments in animals. This review also discusses the first application of melatonin to the clinical treatment of infertile women and confirms that melatonin administration reduces intrafollicular oxidative damage and increase fertilization rates. This review summarizes our recent works and new findings related to the reported beneficial effects of melatonin on reproductive physiology in its role as a reducer of oxidative stress, especially on oocyte maturation and embryo.

Pycnogenol alleviates pain associated with pregnancy.

Kohama T, Inoue M.

Abstract
The effect of Pycnogenol was studied in women in the third trimester of pregnancy, complaining of lower back pain, hip pain, pain, pelvic pain, and/or calf cramps. The women were supplemented with Pycnogenol at a dose of 30 mg/day without any other therapy. Alleviation of pain was evaluated by pain scores until delivery. A significant reduction of pain could be obtained compared with the control group, where no decrease in pain scores in any symptoms was reported. No unwanted effects were observed in the Pycnogenol group. These results indicate the potential of Pycnogenol to reduce pain associated with pregnancy.

Progesterone and the Risk of Preterm Birth among Women with a Short Cervix

Eduardo B. Fonseca, M.D., Ebru Celik, M.D., Mauro Pierra, M.D., Mandip Singh, M.D., and Kypros H. Nicolaides, M.D.

BACKGROUND: Previous randomized trials have shown that progesterone administration in women who previously delivered prematurely reduces the risk of recurrent premature delivery. Asymptomatic women found at midgestation to have a short cervix are at greatly increased risk for spontaneous early preterm delivery, and it is unknown whether progesterone reduces this risk in such women.
METHODS: Cervical length was measured by transvaginal ultrasonography at a median of 22 weeks of gestation (range, 20 to 25) in 24,620 pregnant women seen for routine prenatal care. Cervical length was 15 mm or less in 413 of the women (1.7%). These 413 (60.5%) of these 413 women were randomly assigned to receive vaginal progesterone (200 mg each night) or placebo from 24 to 34 weeks of gestation. The primary outcome was spontaneous delivery before 34 weeks.
RESULTS: Spontaneous delivery before 34 weeks of gestation was less frequent in the progesterone group than in the placebo group (19.2% vs. 34.4%; relative risk, 0.56; 95% confidence interval [CI], 0.36 to 0.89). Progesterone was associated with a nonsignificant reduction in neonatal morbidity (8.1% vs. 13.8%; relative risk, 0.59; 95% CI, 0.29 to 1.25; P=0.17). There were no serious adverse events associated with the use of progesterone.
CONCLUSIONS: In women with a short cervix, treatment with progesterone reduces the rate of spontaneous early preterm delivery.

Treating Male Infertility

Prelox improves Sperm Parameters

Nikolaova V, Stanislavov R, Vatev I, Nabanski B, Punovska K.

Abstract
The diagnosis of male infertility is determined after assessment of sperm quality and clinical study. In nearly 30% of the cases nevertheless detailed clinical and laboratory study it can't be discovered the cause and on the bases of exclusion criteria set the diagnosis idiopathic infertility. The object of our study was investigation of the group patients (n=50) with idiopathic infertility treated with Prelox. To be studied the effects on spermatozoa parameters.
METHODS AND RESULTS: The study design was double-blind, placebo-controlled, cross-over, randomized study including 50 patients (each one of 1 month) separated with 1 month wash out period and concluding period of 1 month. There was applied a new method for treatment with mechanism of action stimulation the production c/MP of spermatozoa endothelial nitric oxide synthase (eNOS). This is not surprising achieving results show improvement of sperm quality.
The methods of the study were:
1. Assessment of the conventional semen analysis (according the criteria of WHO, 1999).
2. Spermatozoa functional tests.
3. Spermatozoa cervical mucus penetration tests.
RESULTS: The obtained results showed improvement of sperm quality, in the middle-aged men the therapeutic answers were better than in younger. In conclusion the therapy with Prelox improve sperm parameters in men with idiopathic infertility. Pycnogenol (one of the constituents of Prelox) has powerful antioxidative influence ameliorating spermatozoa function.

Stimulating Spermatogenesis

Stimulation of Spermatogenesis with Recombinant Human Follicle-Stimulating Hormone: long-term treatment in azoospermic men with hypogonadotropic hypogonadism.

Matsumoto AM, Snyder PJ, Bhasin S, Martin K, Wober T, Winters S, Spratt D, Brantzel J, O'Dea L.

Abstract
OBJECTIVE: To demonstrate the efficacy and safety of follitropin administered with hCG on spermatogenesis in adult male hypogonadotropic hypogonadism (HH) patients.
DESIGN: Phase III, multicenter, open-label, noncomparative.
SETTING: Seven U.S. medical centers.
PATIENT(S): A total of 36 adult males with severe HH.
INTERVENTIONS: A total of 36 adult males on alternate days for 3 to 6 months, with dose adjustments after 2 months, if necessary, to normalize LH levels, followed by follitropin 150 IU and hCG on the same alternate days for 18 months, with dose adjustments as necessary.
MAIN OUTCOME MEASURE(S): Proportion of patients with sperm density > or = 1.5 x 10(6)/mL. Pubertal advancement and long-term safety and tolerability were also evaluated.
RESULT(S): In total, 22 of 29 patients (75.9%) who received > or = 1 dose of follitropin and 20 of 25 patients (80%) who completed 18 months of hCG + follitropin treatment achieved a sperm concentration > or = 1.5 x 10(6)/mL. A sperm concentration > 20 x 10(6)/mL was achieved by 8 of 29 men (27.5%). Median sperm concentration at 18 months was 5.2 x 10(6)/mL. Pubertal development continued during the study, and testis volumes increased. Five clinical pregnancies were achieved. Azoospermia was the most common side effect, and gynecomasia was reported in 10% of patients.
CONCLUSION(S): Long-term treatment of azoospermic HH men using follitropin and hCG is effective for stimulating spermatogenesis and is well-tolerated.

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Induction of Spermatogenesis in a man with NOA

Use of the aromatase inhibitor letrozole to treat male infertility.

Patry G, Jarvi K, Grober ED, Lo KC.

Abstract
OBJECTIVE: Report the case of induction of spermatogenesis with the aromatase inhibitor letrozole.
DESIGN: Case report.
SETTING: University infertility center.
PATIENT(S): A 31-year-old man with primary infertility, normal volume azoospermia, normal follicle stimulating hormone (FSH) levels and pattern of nonobstructive azoospermia (NOA) on a testicular biopsy.
INTERVENTIONS: The patient was given the aromatase inhibitor letrozole for 4 months and had repeated FSH, testosterone, LH levels, semen analyses, and finally a testicular biopsy.
MAIN OUTCOME MEASURE(S): Results of a testis biopsy.
RESULT(S): Testis biopsy showed normal spermatogenesis following 4 months of letrozole therapy.
CONCLUSION(S): This is the first case report on the use of letrozole to treat male infertility and the first case report on the induction of spermatogenesis in a man with NOA using any aromatase inhibitor.

Ease in Ovulation Induction

Role of aromatase inhibitor in ovulation induction in patients with poor response to clomiphene citrate.

Begum MR, Quadir E, Begum A, Begum RA, Begum M.

Abstract
AIM: To examine the efficacy of aromatase inhibitor in the induction of ovulation.
METHODS: This prospective clinical trial in patients with infertility and poor response to clomiphene citrate for induction of ovulation in a tertiary referral infertility clinic. Thirty-five infertile patients, who were treated by clomiphene citrate for several cycles and referred to the infertility clinic, were the target population. The response of CC was assessed by same dose of CC that the patient had in her last cycle. The patients who did not respond adequately were treated by aromatase inhibitor 2.5-5 mg/day from day 3-7 of the menstrual cycle. The main outcome measures were the number of mature follicles, ovulation rate, endometrial thickness and pregnancy rate.
RESULTS: Twenty-seven (90%) patients developed mature follicles by day 12. The majority (77.7%) developed single follicle. Except for one cycle of one patient, the follicles of all patients were ruptured in all cycles and seven (25.94%) got pregnant and sixteen (59.26%) got pregnant.
CONCLUSION: The aromatase inhibitor letrozole is effective for ovulation induction in anovulatory infertility in patients that failed to ovulate by CC.

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Good News for Poor Responders...

Addition of dehydroepiandrosterone (DHEA) for poor-responder patients before and during IVF treatment improves the pregnancy rate: a randomized prospective study.
Wiser A, Gonon O, Gheller Y, Shavit T, Berkovitz A, Shulman A.
Abstract
BACKGROUND: The aim of this study was to evaluate the effect of dehydroepiandrosterone (DHEA) supplementation on IVF data and outcomes among poor-responder patients.
METHODS: A randomized, prospective, controlled study was conducted. All patients received the long-protocol IVF. Those in the study group received 75 mg of DHEA once a day before starting the next IVF cycle and during treatment.
RESULTS: Thirty-three women with significantly diminished ovarian reserves were enrolled: 17 in the DHEA group and 16 in the control group. The 33 patients underwent 51 IVF cycles. The DHEA group demonstrated a non-significant improvement in estradiol levels on day of hCG (P = 0.09) and improved embryo quality during treatment (P = 0.04) between first and second cycles. Patients in the DHEA group also had a significantly higher live birth rate compared with controls (23.1% versus 4.0%; P = 0.05), respectively. Six of seven deliveries were among patients with secondary infertility (P = 0.006).
CONCLUSION: Dehydroepiandrosterone supplementation can have a beneficial effect on ovarian reserves for poor-responder patients on IVF treatment.