Original Article

EFFECTS OF D-CHIRO-INOSITOL IN LEAN WOMEN WITH THE POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Objective: To determine whether the administration of D-*chiro*-inositol, a putative insulin-sensitizing drug, would affect the concentration of circulating insulin, the levels of serum androgens, and the frequency of ovulation in lean women with the polycystic ovary syndrome.

Methods: In 20 lean women (body mass index, 20.0 to 24.4 kg/m^2) who had the polycystic ovary syndrome, treatment was initiated with either 600 mg of D-*chiro*-inositol or placebo orally once daily for 6 to 8 weeks. We performed oral glucose tolerance tests and measured serum sex steroids before and after therapy. To monitor for ovulation, we determined serum progesterone concentrations weekly.

Results: In the 10 women given D-*chiro*-inositol, the mean (± standard error) area under the plasma insulin curve after oral administration of glucose decreased significantly from 8,343 ± 1,149 μU/mL per min to 5,335 ± 1,792 μU/mL per min in comparison with no significant change in the placebo group (P = 0.03 for difference between groups). Concomitantly, the serum free testosterone concentration decreased by 73% from 0.83 ± 0.11 ng/dL to 0.22 ± 0.03 ng/dL, a significant change in comparison with essentially no change in the placebo group (P = 0.01). Six of the 10 women (60%) in the D-*chiro*-inositol group ovulated in comparison with 2 of the 10 women (20%) in the placebo group (P = 0.17). Systolic (P = 0.002) and diastolic (P = 0.001) blood pressures, as well as plasma triglyceride concentrations (P = 0.001), decreased significantly in the D-*chiro*-inositol group in comparison with the placebo group, in which these variables either increased (blood pressure) or decreased minimally (triglycerides).

Conclusion: We conclude that, in lean women with the polycystic ovary syndrome, D-*chiro*-inositol reduces circulating insulin, decreases serum androgens, and ameliorates some of the metabolic abnormalities (increased blood pressure and hypertriglyceridemia) of syndrome X. **(Endocr Pract. 2002;8:417-423)**

Abbreviations:
BMI = body mass index; **ISIcomp** = index of composite whole-body insulin sensitivity; **OGTT** = oral glucose tolerance test

INTRODUCTION

The polycystic ovary syndrome is characterized by chronic anovulation and hyperandrogenism. It is the most common cause of female infertility in the United States and affects approximately 6 to 10% of women of childbearing age (1). As many as 50 to 80% of women with the polycystic ovary syndrome are obese, whereas 20 to 50% are lean. Recently, investigators have demonstrated that both obese and nonobese women with the polycystic ovary syndrome exhibit a type of insulin resistance that is intrinsic to the syndrome and poorly understood (2,3). Moreover, obese women with this disorder have an added burden of insulin resistance directly related to their excess adiposity (4).

Previous studies have shown that the use of insulin-sensitizing drugs, such as metformin (5-9), troglitazone (10-13), or D-*chiro*-inositol (14), decreases circulating insulin, reduces serum androgens, and improves ovulation in obese women with the polycystic ovary syndrome. These findings support the idea that hyperinsulinemia has a pathogenic role in both the hyperandrogenism and the anovulation of the polycystic ovary syndrome.

As aforementioned, lean women with the polycystic ovary syndrome have been shown to be insulin-resistant in comparison with age- and weight-matched control subjects (3,15). In these lean women, insulin binding to the insulin receptor is normal, but the insulin-response curve for glucose uptake in adipocytes is shifted to the right (16,17), a finding that is also indicative of insulin resistance. Some studies have suggested that this novel form of insulin resistance in the polycystic ovary syndrome may be linked to abnormal ovarian steroidogenesis by means of altered insulin signal transduction (18,19).

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On the basis of the foregoing observations, one would predict that lean women with the polycystic ovary syndrome would respond favorably to treatment with insulin-sensitizing drugs. Only a single study, however, has tested that hypothesis. In that study, administration of metformin to lean women with the polycystic ovary syndrome reduced circulating insulin and decreased serum total and free testosterone concentrations (8). The effects on ovulation were not assessed in that investigation (8).

A recent study suggests that insulin resistance in obese women with the polycystic ovary syndrome may be related, in part, to a deficiency in a putative D-*chiro*-inositol-containing phosphoglycan mediator of insulin action and that administration of D-*chiro*-inositol reduces circulating insulin, decreases serum testosterone, and enhances ovulation (14). Notably, manifestations of syndrome X (the dysmetabolic syndrome), such as increased blood pressure and hypertriglyceridemia, also improved in that study (14). It is unknown, however, whether the insulin resistance of lean women with the polycystic ovary syndrome is also related, in part, to a deficiency in the putative D-*chiro*-inositol-containing phosphoglycan mediator or whether administration of D-*chiro*-inositol would ameliorate the symptoms of the polycystic ovary syndrome in lean women.

Therefore, we conducted the current study to determine whether the administration of D-*chiro*-inositol to lean women with the polycystic ovary syndrome would decrease serum androgens or improve ovulatory frequency (or both). In a randomized, double-blind study, 20 lean women with the polycystic ovary syndrome were given either D-*chiro*-inositol or placebo.

PATIENTS AND METHODS

Study Subjects

We studied 20 lean women (body mass index, 20.0 to 24.4 kg/m^2), 18 to 40 years of age, with the polycystic ovary syndrome, as defined by the presence of oligomenorrhea (≤6 menstrual periods during the previous year) and hyperandrogenism (high serum free testosterone levels or hirsutism). Although not a criterion for inclusion in the study or for diagnosis, all the women underwent pelvic ultrasonography at baseline and were found to have ovarian morphologic features consistent with the polycystic ovary syndrome (20). The women were recruited from the Hospital de Clinicas Caracas in Caracas, Venezuela. All women had normal results of thyroid function tests and normal serum prolactin concentrations. None of the women had diabetes mellitus, but five had impaired glucose tolerance, as defined by a plasma glucose concentration of more than 140 mg/dL but less than 200 mg/dL 2 hours after oral ingestion of 75 g of dextrose. Among these five women, one was assigned to receive D-*chiro*-inositol and four were assigned to receive placebo after randomization (see subsequent material). None of the women had taken any medications, including insulin-sensitizing agents or oral contraceptives, during the 2 months before the study.

The study was a double-blind trial, and neither the subjects nor the investigators were aware of drug assignment. By randomization, 10 women were assigned to receive D-*chiro*-inositol (Insmed Pharmaceuticals, Richmond, VA), and the other 10 received placebo. A randomization schedule was generated in blocks of 10, and the drug and placebo were packaged at the same time and labeled according to subject number. The study was approved by the institutional review boards of the Hospital de Clinicas Caracas and Virginia Commonwealth University, and each woman gave written informed consent.

Study Design

At the time of entry into the study, all the women were in the equivalent of the follicular phase of the menstrual cycle, as documented by a serum progesterone concentration <2.5 ng/mL. On day 1, the women came to the hospital after a 12-hour overnight fast, at which time their weight, height, waist-to-hip ratio, and blood pressure in the supine position were measured. Blood samples were obtained at 0830, 0845, and 0900 hours, and equal volumes of serum were pooled for the measurement of serum steroids and sex hormone-binding globulin. At 0900 hours, 75 g of dextrose (Glycolab; Relab Laboratory, Caracas, Venezuela) was administered orally. After 30, 60, 90, and 120 minutes, blood samples were collected for measurement of plasma glucose and insulin.

The women were then instructed to take either 600 mg of D-*chiro*-inositol (N = 10) or placebo (N = 10) orally once daily. They were instructed not to alter their usual eating habits, physical activity, or lifestyle during the study, and they were also advised to refrain from sexual intercourse or to use a barrier method of contraception. The women returned to the hospital weekly for measurements of serum progesterone, and ovulation was presumed to have occurred if the value exceeded 8.0 ng/mL.

The women returned for the second study after having taken the drug or placebo for 6 weeks (day 49) if they were confirmed to be in the follicular phase of the menstrual cycle by measurement of a low serum progesterone value (<2.5 ng/mL). At this visit, all the studies performed at baseline were repeated.

Two women in the placebo group and no woman in the D-*chiro*-inositol group were found to be in the postovulatory phase at day 49. Therefore, use of placebo was continued in one of these women for 1 additional week (a total of 7 weeks) and in the other woman for 2 additional weeks (a total of 8 weeks), until their serum progesterone concentrations were <2.5 ng/mL. No side effects were noted in any woman in either study group, and all recruited subjects completed the study.

Assays

Blood samples were centrifuged as soon as they were obtained, and the serum or plasma was stored at −20°C until assayed. The plasma or serum hormones and sex hormone-binding globulin (measured as protein) were assayed in the laboratory of Dr. Nestler as previously described (8), including serum insulin that was assayed by

a commercial kit (Diagnostic Products Corporation, Los Angeles, CA). The serum free testosterone concentration was calculated according to the method of Sodergard et al (21) with use of the concurrently measured serum albumin concentration. For avoidance of variation between assays, all the samples from an individual woman were analyzed in duplicate in a single assay for each hormone. The intra-assay coefficient of variation was 5.5% for the plasma insulin assay and <10% for all serum steroid hormone assays.

Plasma concentrations of cholesterol and triglycerides were measured in the clinical laboratory of the Hospital de Clinicas Caracas. For these determinations, enzymatic colorimetric assays (HUMAN GmbH, Wiesbaden, Germany) were used.

Statistical Analysis

The results are reported as mean values ± standard error. The responses of plasma glucose and insulin to the oral administration of glucose were analyzed by calculating the areas under the response curves by the trapezoidal rule. In addition, insulin sensitivity was determined from the results of the oral glucose tolerance test (OGTT) by using the index of composite whole-body insulin sensitivity (ISIcomp) calculation developed by Matsuda and DeFronzo (22), as follows: ISIcomp = 10,000/square root of ([fasting glucose × fasting insulin] × [mean glucose × mean insulin during OGTT]).

The Fisher exact test was used to analyze the difference in ovulation rates between the women who received D-*chiro*-inositol and those who received placebo. For the other variables, the results were analyzed by comparing the changes from baseline to the end of the study in the D-*chiro*-inositol group with the corresponding changes in the placebo group. The distribution of the changes in the two groups was first tested for normality with use of the Wilks-Shapiro test, and then these distributions were compared with each other by using the Student two-tailed unpaired *t* test or the Wilcoxon rank sum test. For differences between the groups that were of borderline significance, we also report the within-group comparisons, which were analyzed by the Student two-tailed paired *t* test or the Wilcoxon signed rank test. *P* values <0.05 were considered significant.

RESULTS

Baseline Characteristics

The women in the D-*chiro*-inositol and placebo groups did not differ significantly at baseline with respect to age, body mass index (BMI), waist-to-hip ratio, plasma lipids, serum sex steroids, or sex hormone-binding globulin concentrations (Table 1). They also did not differ significantly with respect to fasting plasma insulin, fasting plasma glucose, areas under the curve for insulin and glucose during the OGTT, and frequency of impaired glucose tolerance (10% versus 40%, respectively; $P = 0.30$ by the two-tailed Fisher exact test).

Anthropomorphic Measurements and Plasma Lipids

The BMI did not change significantly within either study group, but when the changes between groups were analyzed, the slight increase in BMI in the D-*chiro*-inositol group differed significantly in comparison with the slight decrease in BMI in the placebo group (Table 2). The waist-to-hip ratio decreased significantly in the D-*chiro*-inositol group in comparison with the degree of change in the placebo group ($P<0.001$), but this decrease was small (0.01) and of questionable clinical significance. The decrease in systolic blood pressure from 128 ± 2 mm Hg to 124 ± 2 mm Hg in the D-*chiro*-inositol group differed significantly ($P = 0.002$) from the increase found in the placebo group. Similarly, the decrease in diastolic blood pressure in the D-*chiro*-inositol group from 85 ± 1 mm Hg to 79 ± 3 mm Hg differed significantly ($P = 0.001$) from the increase in the placebo group.

Plasma triglycerides decreased significantly by 52% in the D-*chiro*-inositol group from 192 ± 20 mg/dL to 92 ± 17 mg/dL ($P = 0.001$) in comparison with the change in the placebo group. Likewise, total cholesterol decreased significantly in the D-*chiro*-inositol group from 208 ± 10 mg/dL to 169 ± 11 mg/dL ($P = 0.001$) in comparison with the change in the placebo group.

Plasma Glucose and Insulin Profiles

The fasting plasma glucose concentration did not change significantly in either study group (Table 3). The area under the plasma glucose curve during the OGTT decreased significantly ($P = 0.02$) in the D-*chiro*-inositol group from 12,109 ± 686 mg/dL per min to 10,052 ± 414 mg/dL per min, and this decrease differed significantly in comparison with the lack of change in the placebo group ($P = 0.04$ for difference between groups). The frequency of impaired glucose tolerance, however, did not differ significantly between groups after therapy (0% versus 30%, respectively; $P = 0.21$).

Similarly, the fasting plasma insulin concentration did not change significantly in either group. The area under the plasma insulin curve decreased by 36% ($P = 0.02$) in the D-*chiro*-inositol group from 8,343 ± 1,149 μU/mL per min to 5,335 ± 1,792 μU/mL per min but remained essentially unchanged in the placebo group ($P = 0.03$ for difference between groups).

Insulin Sensitivity Index

The composite whole-body insulin sensitivity index (ISIcomp) increased by 84% ($P = 0.006$) in the D-*chiro*-inositol group from 2.68 ± 0.35 mg^{-2}/dL^{-2} to 4.92 ± 0.59 mg^{-2}/dL^{-2} but did not change significantly in the placebo group (Table 3). Moreover, the pronounced change in ISIcomp in the D-*chiro*-inositol group differed significantly from the minimal change in the placebo group ($P<0.002$).

Serum Sex Steroid Concentrations

The administration of D-*chiro*-inositol was associated with notable declines in both serum total testosterone and

Table 1
Comparison of Baseline Characteristics
Between Women Treated With D-*chiro*-Inositol and Those Given Placebo

Variable	D-*chiro*-Inositol (N = 10)*	Placebo (N = 10)*	*P* value†
Age (yr)	28.2 ± 1.5	26.5 ± 1.4	0.42
Body mass index (kg/m^2)	22.4 ± 0.3	22.1 ± 0.3	0.39
Waist-to-hip ratio	0.81 ± 0.02	0.80 ± 0.02	0.57
Systolic blood pressure (mm Hg)	128 ± 2.3	125 ± 1.3	0.38
Diastolic blood pressure (mm Hg)	85 ± 1.0	83 ± 7.0	0.91
Menstrual periods/yr	3 ± 1	3 ± 1	0.21
Total testosterone (ng/dL)	98.9 ± 6.9	116.2 ± 14.7	0.30
Free testosterone (ng/dL)	0.83 ± 0.11	0.87 ± 0.12	0.79
Fasting glucose (mg/dL)	86.5 ± 3.5	83.8 ± 5.8	0.70
Fasting insulin (μU/mL)	30.5 ± 4.1	28.8 ± 7.3	0.27
Androstenedione (ng/dL)	264 ± 19	268 ± 21	0.88
DHEAS‡ (μg/dL)	365 ± 47	383 ± 63	0.97
17β-Estradiol (pg/mL)	43 ± 2.5	68 ± 6.7	0.21
Sex hormone-binding globulin (nmol/L)	142.4 ± 18.6	145.0 ± 14.5	0.91
Total cholesterol (mg/dL)	208 ± 10.4	193 ± 7.35	0.26
Triglycerides (mg/dL)	192 ± 20.2	163 ± 20.6	0.35
Glucose AUC§ (mg/dL/min)	12,109 ± 686	12,670 ± 802	0.60
Insulin AUC§ (μU/mL/min)	8,343 ± 1,149	8,703 ± 1,276	0.84
ISIcomp⁄⁄ (mg^{-2}/dL^{-2})	2.68 ± 0.35	3.11 ± 0.48	0.48

*Data are shown as mean values ± standard error.
†Two-sided *P* values comparing baseline mean values for the placebo group versus the treatment group with use of the unpaired Student *t* test.
‡DHEAS = dehydroepiandrosterone sulfate.
§AUC = area under the curve during 2-hour, 75-g oral glucose tolerance test.
⁄⁄ISIcomp = index of composite whole-body insulin sensitivity (see Statistical Analysis in text).

free testosterone concentrations (Table 4). In the D-*chiro*-inositol group, serum free testosterone concentrations decreased significantly by 73% from 0.83 ± 0.11 ng/dL to 0.22 ± 0.03 ng/dL in comparison with the change in the placebo group ($P = 0.01$). The increase in serum sex hormone-binding globulin concentration in the D-*chiro*-inositol group did not differ significantly from the increase in the placebo group ($P = 0.40$)

Although the serum dehydroepiandrosterone sulfate concentration decreased significantly within the D-*chiro*-inositol group ($P = 0.003$), the change from baseline did not differ significantly from the corresponding change in the placebo group ($P = 0.06$). Changes in other serum sex steroid concentrations did not differ significantly between the D-*chiro*-inositol and placebo groups.

Ovulation

Six of the 10 women (60%) in the D-*chiro*-inositol group ovulated, in comparison with 2 of the 10 women (20%) in the placebo group. The difference in ovulation rates between the two groups did not attain statistical significance ($P = 0.17$). The power of the study to exclude a true difference, however, was small (power of 0.26 with $\alpha = 0.05$) because of the limited number of women studied.

The mean peak serum progesterone concentration (defined as the highest progesterone concentration measured for an individual subject during the study) among all women in the D-*chiro*-inositol group was significantly greater than that among all women in the control group (13.1 ± 2.2 ng/mL versus 4.6 ± 1.3 ng/mL, respectively; $P = 0.003$). Furthermore, if only those women who had

Table 2
Anthropomorphic and Lipid Characteristics of Women With Polycystic Ovary Syndrome at Baseline and After Treatment With D-*chiro*-Inositol or Placebo for 6 to 8 Weeks

Characteristic	D-*chiro*-Inositol group (N = 10)*		Placebo group (N = 10)*		*P* value for change comparison†
	Baseline	After treatment	Baseline	After treatment	
Body mass index (kg/m^2)	22.4 ± 0.3	22.5 ± 0.3	22.1 ± 0.3	21.8 ± 0.1	<0.001
Waist-to-hip ratio	0.81 ± 0.02	0.80 ± 0.02	0.80 ± 0.02	0.82 ± 0.01	<0.001
Systolic BP‡ (mm Hg)	128 ± 2	124 ± 2	125 ± 1	127 ± 1	0.002
Diastolic BP‡ (mm Hg)	85 ± 1	79 ± 3	83 ± 7	87 ± 1	0.001
Total cholesterol (mg/dL)	208 ± 10	169 ± 11	193 ± 7	202 ± 9	0.001
Triglycerides (mg/dL)	192 ± 20	92 ± 17	163 ± 21	145 ± 19	0.001

*Data are shown as mean values ± standard error.
†Two-sided *P* values reflect mean or median change from baseline in the placebo group versus the treatment group with use of either the unpaired Student *t* test or the Wilcoxon rank sum test where appropriate.
‡BP = blood pressure.

ovulated were analyzed, the mean peak progesterone level in the ovulating D-*chiro*-inositol-treated women (18.3 ± 0.5 ng/mL; N = 6) was significantly greater than that among the women who had ovulated in the placebo group (12.3 ± 2.8 ng/mL; N = 2) (*P* = 0.004).

DISCUSSION

This randomized, double-blind, placebo-controlled study was conducted to determine the effects of administration of D-*chiro*-inositol on lean women with the polycystic ovary syndrome. In these women, administration of D-*chiro*-inositol improved glucose tolerance and decreased glucose-stimulated insulin release.

Although not directly measured, this effect was likely related to the potential of D-*chiro*-inositol to increase insulin sensitivity, as suggested by the 84% improvement in the ISIcomp. In support of this idea, studies in nonhuman primates (23) and in humans (24) suggest that insulin resistance may be related, in part, to a deficiency in

Table 3
Plasma Glucose and Insulin Profiles and Insulin Sensitivity Index Measurements in Women With Polycystic Ovary Syndrome Before and After Treatment With D-*chiro*-Inositol or Placebo for 6 to 8 Weeks

Characteristic	D-*chiro*-Inositol group (N = 10)*		Placebo group (N = 10)*		*P* value for change comparison†
	Baseline	After treatment	Baseline	After treatment	
Fasting glucose (mg/dL)	86 ± 4	80 ± 4	84 ± 6	87 ± 4	0.12
Fasting insulin (μU/mL)	30 ± 4	24 ± 8	29 ± 7	36 ± 7	0.20
Glucose AUC‡ (mg/dL/min)	12,109 ± 686	10,052 ± 414	12,670 ± 802	12,592 ± 793	0.04
Insulin AUC‡ (μU/mL/min)	8,343 ± 1,149	5,335 ± 1,792	8,703 ± 1,276	8,600 ± 1,162	0.03
ISIcomp§ (mg^{-2}/dL^{-2})	2.68 ± 0.35	4.92 ± 0.59	3.11 ± 0.48	2.68 ± 0.54	<0.002

*Data are shown as mean values ± standard error.
†Two-sided *P* values reflect mean or median change from baseline in the placebo group versus the treatment group with use of either the unpaired Student *t* test or the Wilcoxon rank sum test where appropriate.
‡AUC = area under the curve during 2-hour, 75-g oral glucose tolerance test.
§ISIcomp = index of composite whole-body insulin sensitivity (see Statistical Analysis in text).

Table 4
Serum Sex Hormones in Women With Polycystic Ovary Syndrome Before and After Treatment With D-*chiro*-Inositol or Placebo for 6 to 8 Weeks

Characteristic	D-*chiro*-Inositol group (N = 10)*		Placebo group (N = 10)*		*P* value for change comparison†
	Baseline	After treatment	Baseline	After treatment	
Total testosterone (ng/dL)	99 ± 7	34 ± 4.3	116 ± 15	108 ± 7.5	0.003
Free testosterone (ng/dL)	0.83 ± 0.11	0.22 ± 0.03	0.87 ± 0.12	0.83 ± 0.13	0.01
Progesterone peak value (ng/mL)	…	13.1 ± 2.2	…	4.6 ± 1.3	0.003
SHBG‡ (nmol/L)	142 ± 19	196 ± 24	145 ± 14	161 ± 26	0.40
Androstenedione (ng/dL)	264 ± 19	193 ± 26	268 ± 21	303 ± 41	0.09
DHEAS§ (μg/dL)	365 ± 47	187 ± 24	383 ± 63	319 ± 35	0.06

*Data are shown as mean values ± standard error.
†Two-sided *P* values reflect mean or median change from baseline in the placebo group versus the treatment group with use of either the unpaired Student *t* test or the Wilcoxon rank sum test where appropriate.
‡SHBG = sex hormone-binding globulin.
§DHEAS = dehydroepiandrosterone sulfate.

a putative D-*chiro*-inositol-containing mediator of insulin action and that administration of D-*chiro*-inositol improves insulin sensitivity (25). Whether D-*chiro*-inositol may have decreased gastrointestinal absorption of glucose and thus contributed to an improvement in glucose tolerance was not evaluated in this study and cannot be excluded.

Administration of D-*chiro*-inositol was also associated with a 66% decrease in serum total testosterone concentrations and a 73% decrease in serum free testosterone concentrations. Although threefold as many women ovulated in the D-*chiro*-inositol group in comparison with the placebo group, this difference did not attain statistical significance—most likely because of the limited number of women we were able to study.

The polycystic ovary syndrome has been linked to syndrome X (the dysmetabolic syndrome). Of note, administration of D-*chiro*-inositol was also associated with decreases in diastolic and systolic blood pressures and in plasma triglyceride and total cholesterol concentrations. These findings are similar to those reported previously for obese women with the polycystic ovary syndrome treated with D-*chiro*-inositol (14).

Collectively, the results of this study support the idea that insulin resistance is a feature of the polycystic ovary syndrome in lean women with the disorder and further suggest that insulin resistance has a key role in the pathogenesis of the disorder in these women. This relationship is further corroborated by the only other published study that has assessed the effects of administration of an insulin-sensitizing drug (metformin) specifically to lean women with the polycystic ovary syndrome (8). That investigation also demonstrated a reduction in circulating insulin and decreases in serum androgen concentrations. Ovulation was not monitored in that study.

Although the mechanism of action of D-*chiro*-inositol has not been clearly delineated, the current findings support the premise that insulin resistance in lean women with the polycystic ovary syndrome may be related, in part, to a deficiency in the putative D-*chiro*-inositol-containing inositolglycan mediator of insulin action. Such a deficiency could be due to either decreased production or increased metabolism of D-*chiro*-inositol. Of note, the skeletal muscle of patients with type 2 diabetes mellitus or their first-degree relatives seems to be deficient in D-*chiro*-inositol (26). Further studies to determine whether this deficiency exists in lean women with the polycystic ovary syndrome would be informative.

Administration of D-*chiro*-inositol not only improved glucose tolerance, reduced circulating insulin, and decreased serum androgen concentrations in lean women with the polycystic ovary syndrome but also was associated with decreases in systolic and diastolic blood pressures and in plasma triglyceride concentrations. This outcome would be consistent with the concept that some of the metabolic abnormalities of syndrome X (that is, high blood pressure and dyslipidemia) (27) in lean women with the polycystic ovary syndrome are also related to insulin resistance and can be ameliorated by administration of D-*chiro*-inositol.

CONCLUSION

On the basis of our study of 20 patients, we conclude that D-*chiro*-inositol improves glucose tolerance, reduces circulating insulin, decreases serum androgen concentra-

tions, and ameliorates other metabolic abnormalities associated with insulin resistance in lean women with the polycystic ovary syndrome.

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