Inositols for PCOS: An Update

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Overview

- Understanding the role of insulin in PCOS
- The relationship between inositols and insulin
- Inositols for PCOS: Published studies
- Practical considerations
Understanding the role of insulin
Understanding the role of insulin

- A hormone produced by the pancreas that regulates glucose metabolism
GLUCOSE

CELL

INSULIN RECEPTOR
GLUCOSE

SECOND MESSENGERS

CELL
GLUCOSE
SECOND MESSENGERS
GLUCOSE
SECOND MESSENGERS
Energy production

CELL
GLUCOSE
SECOND MESSENGERS
Energy production
Energy storage
CELL
So, what can go wrong??
Type 1 diabetes
Understanding the role of insulin

- A hormone produced by the pancreas that regulates glucose metabolism

- Insulin resistance (IR) is present in 70-80% of women with PCOS
  - Increased blood sugar (“hyperglycemia“)
  - Increased serum insulin levels (“hyperinsulinemia“)

- Increased serum insulin levels then cause the ovary to produce increased amounts of testosterone

- Increased serum insulin and testosterone interfere with ovulation
Metformin and PCOS
Metformin and PCOS

- Metformin is an insulin sensitizing drug
- Improves function of second messengers, and reduces insulin resistance
- Reduces hyperinsulinemia and testosterone overproduction
- Common side effects:
  - Bloating
  - Nausea
  - Diarrhea
  - Loss of appetite
Overview

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Inositols
Inositols

- 6-carbon sugars - similar to mannitol and sorbitol
- 9 different types of inositols - “stereoisomers”
Myo-Inositol

D-chiro-Inositol
Inositols

- 6-carbon sugars - similar to mannitol and sorbitol
- 9 different types of inositols - “stereoisomers”
- Myo-inositol (MYO) and d-chiro inositol (DCI) are key components of the “second messengers”
Insulin resistance
GLUCOSE
SECOND MESSENGERS
Insulin resistance
CELL
GLUCOSE
SECOND MESSENGERS
Insulin resistance
Inositols

- 6-carbon sugars - similar to mannitol and sorbitol
- 9 different types of inositols - “stereoisomers”
- The insulin receptor’s “second messengers” contain myo-inositol (MYO) and d-chiro inositol (DCI)
- Supplementing with MYO and DCI will improve insulin receptor “signaling” and reduce insulin resistance
- First inositol/PCOS clinical trial published in 1999 by Nestler, et al, using DCI alone
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- 30% of patients had disappearance of hirsutism
- 53% of patients had resolution of acne

- 155 women with PCOS
- Randomized to treatment with either BCP+MYO or BCP alone

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<table>
<thead>
<tr>
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<th>Birth Control Pill</th>
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<th>P&lt;.05</th>
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<tbody>
<tr>
<td>Reduction in testosterone</td>
<td>29%</td>
<td>44%</td>
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<tr>
<td>Reduction in insulin resistance</td>
<td>7%</td>
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- 42 women with PCOS
- Randomized to either 4 grams MYO daily or placebo

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- 70% of subjects in MYO group ovulated during study, compared to 21% in the placebo group

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<td>Letrozole (Legro, 2014)</td>
<td>62%</td>
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Colazingari, et al, “The combined therapy MYO plus DCI, rather than DCI, is able to improve IVF outcomes: results from a randomized controlled trial”, Arch Gyn Obstet, 2013, 288: 1405-1411

- 100 women with PCOS and undergoing IVF
- Randomized to treatment with either MYO+DCI, or, DCI alone
- Combined treatment group had better embryo quality and higher fertilization and pregnancy rate
MYO and DCI play different roles

- MYO and DCI are both inositol derivatives, but are very different molecules.
- Each produces a different second messenger.
- MYO improves ovarian function.
- DCI improves metabolic function in the peripheral tissues.
- Combined treatment with MYO and "low-dose" DCI together appears to be more effective than either alone.
Inositols for PCOS: Practical Concerns

- The combination of myo-inositol and d-chiro inositol is an effective treatment for PCOS
  - 2-4 grams of MYO/day
  - 50-100 mg of DCI/day

- Safe, inexpensive and completely free of side effects

- Available without prescription, as OTC dietary supplements
Questions?