CoQ10 and Ovarian Function

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January 30, 2012   www.medigogy.com
Overview

- A Chinese medicine view of mitochondria
- Mitochondria and ovarian function
- Understanding CoQ10 and mitochondrial function
- Research on CoQ10 and ovarian function
- Dosages and Forms of CoQ10
- Questions
Overview of Qi production
Mitochondria in Chinese Medicine

- Mt are an aspect of Yuan qi
- Yuan qi is transported to organs via TH mechanism
- Yuan qi has both structural (quantity) and functional aspects
- Note: Yuan Qi cannot create a significant amount of Zhen Qi without sufficient Gu and Da Qi
  - CoQ10 helps to regulate Da Qi
Working with Mt

- Kd qi the CM analogue to ovarian Mt
- Assess what aspect of kd function is having the problem.
  - If kd yin deficiency – coQ10 won’t help
  - If kd qi deficiency – coQ10 may help
  - If kd yang deficiency – coQ10 may help
  - If fire, or sufficiency of kd qi or yang, coq10 may damage the ovaries or other organs
- Acupuncture can greatly improve efficacy of CoQ10 by targeting it to the reproductive system
Acupuncture perspective

- Kd3 is very beneficial to mitochondrial function of the reproductive system
  - Can be used as a source point to increase number of mt
    - Combine with CV4 and St 36. Connect to CV 4. E stim 3 hz for 10-20 minutes 2-3x/week.
    - Note: “Restoring Fertility” yoga designed to increase both number and function of mitochondria in appropriate algorithm (phase dependent). http://www.eccmpc.com/restoringfertility
  - Can be used as a shu stream point to modulate energy production and distribution
- Kd 7 has more intrinsic properties directly related to CoQ10 when tonified
Acupuncture perspective

- Radial or other pulses are very useful for monitoring the effects or need of CoQ10
  - Look for inappropriate excess or deficiency
Mt and Fertility

- A fully grown human oocyte contains approximately 500,000 mitochondria.
  - A heart cell contains about 3,000 mitochondria.

- Even minor mitochondrial disorders can lead to infertility. Human Reproduction, Vol. 16, No. 5, 909-917, May 2001

- Mitochondria not only provide energy but are necessary for active transport of nutrients into the blood.
  - E.g., glucose, amino acids, iron, calcium, potassium, magnesium, sodium, uric acid, vitamin C
    - E.g., vitamin C is very important for implantation, prevention of miscarriages, protection against atresia and to help facilitate ovulation. Molecular Human Reproduction, Vol. 5, No. 4, 299-302, April 1999

*Taken from: Optimizing Ovarian Reserve Course*

http://www.prodseminars.net/product/optimizing-ovarian-reserve

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Mt and Fertility (cont’d)

- Loss of efficiency in mt respiration and subsequent impairment of ATP production may be a major factor in age related oocyte quality issues. **Human Reproduction, Vol. 16, No. 5, 909-917, May 2001**

- The transfer of cytoplasm containing mt from young donors to older recipient oocytes improved embryo quality. **Human Reproduction, Vol. 16, No. 5, 909-917, May 2001**

- “**Ovarian insufficiency** [defined as day 3 fsh > 8IU/L or < 4 antral follicles per ovary] *is clearly associated with specifically low mt DNA content.*” May-Panloup, et al. Human Reproduction Vol.20, No.3 pp. 593–597, 2005.

- Therefore mt function is an issue of both quality and quantity.

*Taken from: Optimizing Ovarian Reserve Course*

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mtDNA and Ovarian Insufficiency

- Oocytes have highest mtDNA content of all cells (kidney qi)
- Ovarian insufficiency (high FSH, low antral count) is clearly associated with low mtDNA
  - Oogenesis through the process of follicular growth requires a great deal of energy production
  - ATP content of oocytes has been associated with the viability of embryos
  - Once embryo is formed, ATP production depends on oxidative phosphorylation

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Simplified aerobic energy production

- 1. Glycolosis – produces pyruvate
- 2. Krebs Cycle – generate NADH and FADH2
- 3. ETC (CoQ) – pumps protons
- 4. Chemiosmosis
- 5. ATP
Overview of Aerobic ATP Production

Glycolysis

Pyrurate (2 molecules)

Aerobic (oxidized)
Acetyl CoA
NADH

Krebs Cycle (2 ATP Generated) + NADH, FADH2

ETC (Fe-S, CoQ,)

Chemiosmosis (drives ATP Synthase)

HMG-CoA (Reductase/Statin)

Cholesterol

CoQ10

ATP

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Simplified ETC Overview

- 1. NADH (Niacin Dependent) donates electrons to FMN (Riboflavin dependent)
- 2. FMN transfers electrons to Fe – S complexes
- 3. Fe-s complexes transfer electrons to ubiquinone (coq10 fully oxidized)
- 4. Ubiquinone is reduced to ubiquinol
  - Note: intermediary is semiquinone*
- 5. The reduction of ubiquinone pumps protons across the membrane driving chemiosmosis.

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Overview of ETC – Complex I

- NADH (Vitamin B3 - Niacin Dependent)
- FMN (Vitamin B2 - Riboflavin dependent)
- Ubiquinone
  - Ubiquinol (Reduction of Ubiquinone creates proton gradient)
- Fe - S Complexes
- Chemiosmosis
  - ATP

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Oxidative Stress: ROS, RNS

- **ROS (Reactive Oxygen Species)**
  - Including: Superoxide ($O_2^-$, e.g., from ETC leakage), hydrogen peroxide ($H_2O_2$, e.g., when SOD acts on superoxide), hydroxyl (OH, highly active-modifies purines, pyrimidines, causes strand breaks in DNA)
  - Note: SOD changes $O_2^-$ into $H_2O_2$ and $O_2$. If $H_2O_2$ reacts with $O_2^-$ it forms OH$^-$

- **RNS (Reactive Nitrogen Species)**
  - Including: Nitric Oxide (synthesized during conversion of L-arginine to L-citrulline via NOS).
  - Highly reactive, damages proteins, CHO, nucleotides, lipids resulting in cell and tissue damage
Oxidative Stress and Oocytes


- However, ROS and RNS are important players in ovulation, folliculogenesis, implantation and ovarian steroidogenesis. *Reproductive Biology and Endocrinology* 2005, 3:28

- Delicate balance between ROS/RNS and antioxidant enzymes.

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CoQ10 supplementation improves ovarian response in aged mice (Bentov,. et al. Sep 2009)

- Materials and methods: **Aged mice** were randomized to receive Co Q10, Resveratrol, R-ALA via injection for 18 weeks (The dosage is not specified). The mice were later subjected to superovulation with gonadotropins. Oocytes were then analyzed for membrane potential and ROS accumulations. Mitochondrial DNA copy was also obtained.

- Results: Co Q10 significantly increased the number of oocytes ovulated, while the other nutrients had no effect. Oocyte MMP was reduced and **ROS levels were increased**. Mitochondrial DNA copy was lower in mice treated with Co Q10, albeit it was significantly higher than in younger mice.
Quantity may be more important

Compared with other cell types in the body, germ cell mitochondria are unique. The number of cristae in a mitochondrion has been directly correlated to the level of ATP production (Jansen & de Boer 19998), as such, the germ cell mitochondria with their limited number of cristae and denser matrices have diminished ability to generate ATP.

In aged mitochondrial oocytes the number of mitochondrial cristae is even lower compared to younger oocytes, which may compromise development. A relationship between oocyte mtDNA copy number and oocyte quality/fertility was observed (Yesody et al., 2002) and fertilized oocytes present a higher mtDNA copy number than unfertilized oocytes (Almeida-Santos et al., 2006).

This may suggest that it is not primarily OXPHOS dysfunction that contributes to diminished fertility, but rather reduced mitochondrial/mtDNA copy number that leads to the OXPHOS dysfunction observed and subsequently to poor quality oocytes or reduced fertility (Jacobs et al., 2006)
Mitochondrial migration

- During oocyte maturation and in early embryos, mitochondria are relocated to different regions, probably in response to localized energy demands (Vavister and Squirell, 2000).

- Impaired redistribution of mitochondria may compromise fertilization and embryo development (Au est al., 2005) and blastomeres that received an insufficient amount of mitochondria remain undivided and undergo fragmentation (Van Blerkom et al., 2000)
Downregulation also important

- At the morula stage, mitochondrial and metabolic changes occur gradually and a shift in ATP production to glycolysis is evident (Leese, 1995; Van Blerkom et al., 1995). Glucose is the predominant substrate that supports later embryo development (Biggers et al., 1997).

- Mature oocytes and early embryos maintain an overall low-level metabolism, thus minimizing oxidative stress, but generating the necessary ATP to fulfill cellular functions (Lees, 2002; Leese et al., 2007).
Forms and Dosage
Different forms of CoQ10

- **Ubiquinone**
  - Oxidized form of CoQ10
  - Needs to be reduced in order for it to act as an antioxidant
  - Most studies have been conducted with Ubiquinone

- **Ubiquinol**
  - Reduced form
  - Immediate antioxidant effects
  - Less hydrophobic – better absorption?
  - Unclear whether benefits would be the same, better or worse for fertility than Ubiquinone
Absorption of CoQ10

- Powder < 1% absorption
- Crystalline ~2% absorption
  - Melted ~5%
- Liposomal forms ~3%
- Nanoparticles ~3.5%
- Monoglyceride ~8% (e.g., Designs for Health, Thorne Q Best)
Potential Side effects

- Inhibits TNF alpha and integrins
  - May increase cancer risk

- May increase clotting
  - Counteracts Warfarin

- Lowers blood pressure

- Can cause GI upset
Additional Information

- Optimizing Ovarian Reserve
  [http://www.prodseminars.net/product/optimizing-ovarian-reserve](http://www.prodseminars.net/product/optimizing-ovarian-reserve)

- Yoga for fertility
  - Available on amazon.com or call 323-551-5962 for wholesale pricing

- Acupuncture strategies to significantly improve IVF success

- Upcoming Seminar: Understanding and application of the 8 Extraordinary Channels