Nutraceutical Management Of Male Subfertility: An Update

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Abstract

INTRODUCTION

Male subfertility is an important aspect of medicine, with major public health and personal/social ramifications. Unfortunately, because of the lack of trained specialists, and want of appropriate guidelines for interested physicians, patients are being exploited by unqualified doctors.

The review relies on the CONGRUENT guidelines, issued this year, by the ALLIANCE National Advisory Board on Nutraceuticals in Health and Disease, of which the authors are expert members.(1)

DEFINITION OF MALE INFERTILITY/ SUBFERTILITY

'Subfertility is the inability of a sexually active, non-contracepting couple to achieve pregnancy in one year' (2)

This definition implies that the management of infertility should involve both partners, including the male. The concept of unilateral care of the female partner, which has gained momentum in the reproductive health community, especially with the advent of in vitro fertilization and intracytoplasmic sperm injection, is counterproductive, and should be discouraged.

ETIOLOGY OF MALE SUBFERTILITY

Reduced male fertility can be the result of congenital and acquired urogenital abnormalities, infections of the genital tract, increased scrotal temperature (varicocoele), endocrine disturbances, genetic abnormalities and immunological factors. No causal factor is found in 60-75% of cases (idiopathic male subfertility). These men present with no previous history associated with fertility problems and have normal findings on physical examination and endocrine laboratory testing. Semen analysis reveals a decreased number of spermatozoa (oligozoospermia), decreased motility (asthenozoospermia) and many abnormal forms on morphological examination (teratozoospermia). These abnormalities usually occur together and are described as the oligoastheno- teratozoospermia (OAT) syndrome.

Heritable forms of nonsyndromic male infertility can arise from single-gene defects as well as chromosomal abnormalities.(3)

However, the commonest cause of male infertility is idiopathic, and may be related to environmental factors. Endocrine disruptor chemicals (EDCs) are exogenous agents which interfere with the synthesis, secretion, transport, binding, action or elimination of natural hormones in the body, which are responsible for the maintenance of homeostasis, reproduction, development or behaviour, including male fertility.

They may be either natural or synthetic chemicals.

EDCs are chemicals which are usually present in

- Plastic & plastic components, e.g., phthalates
- Pesticides, including fungicides, herbicides, eg, organochlorine pesticides, atrazine, trifluralin, permethrin.
- Industrial chemicals, eg polychlorinated dioxins, polychlorinated biphenyls
- Paints, eg, organotins, found in antifoultants used to paint hulls of ship: tributylin.
- Detergents, eg, alkylphenolics (surfactant) : nonylphenol
- Heavy metals e.g. mercury, cadmium and lead.
- Natural products
- Phytoestrogens e.g. genistein, equol

- Fungal estrogens e.g. zearalenone

Exposure to EDCs occurs through food, ground water, combustion sources, contaminated consumer products, pesticides (including agricultural and domestic use of chemicals) and plastic.

A hypothesis was put forwarded by Sharpe and Skakkeback in 1993 that agents which interfere with normal development of the reproductive system could be linked to the increase in human male reproductive system disorders, all of which were expressions of the testicular dysgenesis syndrome (3).

While there is controversy regarding the temporal trends in sperm count, metaanalysis reported in 1980, and again in 1992, 1997 and 2000, have shown significant declines in semen quality. Whether this is due to endocrine disruptor chemicals alone, or due to other factors, is debatable.

Studies however, have demonstrated negative correlation between sperm count and motility, and PCB (polychlorinated biphenyls) concentrations in men.

Studies are also available on the adverse effect of EDCs on fertility and fecundity. Reduced fertility has been noted in male fruit growers exposed to pesticides . Similar findings have been seen in men exposed to aromatic solvents , and men with high intake of sport fish containing PCBs and mercury .

CLINICAL EVALUATION

Clinical evaluation includes a detailed history-taking and examination.

FERTILITY HISTORY

- marital history
- history of female partner
- sexual history
- previous evaluation|
- general medical/ surgical history
- occupation/ drug abuse/ stress
- exposure to heat/tight clothing

PHYSICAL EVALUATION

- body habitus
- secondary sexual characters
- genital examination- testicular volume
- Per rectal examination

SEMEN ANALYSIS

COLLECTION

Generally at least two semen analyses are needed to establish a baseline for a patient. If a discrepancy exists, a third or perhaps even a fourth specimen may be required. Each semen analysis is collected after 2-3 days of abstinence. The specimen is generally collected by masturbation into a clean, dry container and examined within 1 hour. If the specimen is collected at home, it should be kept near body temperature during transportation to the laboratory (shirt pocket). The patient should avoid lubricants during specimen collection. If needed, silicone condom devices are available.

MINIMAL STANDARDS OF ADEQUACY

Although there is no absolute measure of fertility on semen analysis, minimal standards of semen adequacy have been defined by the World Health Organization (2)(Table)

Figure 1

Table: Semen Analysis - Minimal Standards of Adequacy

Nutritional Factors	Mitochondrial Energizers	Free Radical Scavengers
Zinc	L-Carnitine	Lycopene
L-Arginine	Coenzyme Q10	Selenium
Folic Acid	Acetyl Carnitine	Vitamin E
Vitamin B12		Vitamin C
		Glutathione

Seen on at least two occasions:

Ejaculate volume 1.5-5.0 ml

Sperm density >20 millions/ml

Motility >50% motile

Forward progression >2.0 (scale 0-4)

Morphology (WHO) >30% normal morphology

(Strict) >14% normal morphology

And:

No significant sperm agglutination

No significant pyospermia

No hyperviscosity

OTHER LABORATORY TESTS

Urinalysis, to rule out infection

Endocrine evaluation: LH, FSH, testosterone, prolactin, thyroid function.

90% of endocrine conditions can be detected by initial measurement of FSH and testosterone.

Genetic testing

Karyotyping analysis is critical for all men with azoospermia and severe oligospermia (<10 million sperm/ml) who are planning IVF/ICSI

Sperm function tests

Sperm morphology

Sperm chromatin assay

- COMET assay

- TUNNEL assay

- Flow cytometry (acridine orange)

- Toluidine blue test

c. Hamster egg penetration test

Antisperm antibodies

- ELISA

- Immunobead binding assay

Imaging, in specific cases

TRUS (transrectal ultrasound)

Vasography

Scrotal ultrasound

NUTRACEUTICAL MANAGEMENT OF MALE SUBFERTILITY

This section does not cover ART and surgical management of infertility

Medical management is usually empirical and is indicated in idiopathic male infertility.

The infertile couple should be counselled, with empathy, and in privacy, about the aetiology and management of infertility. They should be informed that infertility and sexual function are two separate issues, and need not be associated with each other.

Nutraceuticals (5) are diet supplements that deliver a concentrated form of a presumed bioactive agent from a food, presented in a non-food matrix, and used with the purpose of enhancing health in dosages that exceed those that could be obtained from normal foods.

Based on their prime mechanism of action in improving sperm parameters, following classification of nutraceuticals for male fertility has been proposed.

(a) L-Carnitine

L-carnitine provides an energy substrate for spermatozoa in the epididymis, and is necessary for transport of fatty acids into the mitochondria. Epididymal sperm use fatty acid oxidation as the main source of energy. Hence, L-carnitine contributes to sperm motility and may be involved in sperm maturation as well.

L-carnitine improves sperm count, sperm density and sperm motility, and the gains in sperm motility are sustained. (6, 7)

The recommended dose range of L-carnitine is 1 gram to 3 grams daily.

Consensus guidelines recommend the use of L-carnitine in the management of oligo-asthenospermia.

(b) Zinc

Zinc ensures proper sperm production and motility, and zinc deficiency is associated with low testosterone levels. Zinc increases sperm count, and progressive motility, and we suggest the use of the trace mineral in the management of oligospermia (8, 9). Zinc is a micronutrient present in meat and seafood, and we suggest its use in vegetarians with sub fertility.

The recommended dose range of Zinc is 24 mg to 500 mg daily.

(c) Coenzyme Q -10

Co Q 10 is concentrated in the midpiece of the sperm, and is involved in energy generation. It is also an antioxidant, preventing lipid per oxidation and damage of sperm membranes.

Co Q 10 has been shown to improve sperm count, sperm

motility and fertilization rates (10, 11). Experts recommend the use the Co Q10 in the treatment of oligo-asthenospermia.

The recommended dose range of Co Q-10 is 60 mg to 200 mg daily.

(d) Lycopene

Lycopene is a naturally synthesized carotenoid found in fruits and vegetables. It is also a component of the human redox mechanism that scavenges free radicals including ROS. It is found in high concentrations in seminal plasma.

Various studies indicate that lycopene can protect against membrane and DNA damage and possibly play a protective role against oxidative damage. Lycopene therapy shows improvement in sperm concentration, motility and improvement in sperm morphology. In a trial pregnancy occurred in 23% patients on lycopene therapy (12).

CONGRUENT guidelines recommend use of lycopene in management of male sub fertility.

The recommended dose range of Lycopene is 4000 mcg to 22.6 mg.

CONCLUSION

Male infertility needs a complete clinical workup, including history-taking, clinical examination, and investigations, for optimal treatment. Medical treatment with nutraceuticals helps improve sperm parameters, and even if the response is not adequate, increases the response to assisted reproductive technology.

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