

MEDICAL TREATMENT OF MALE INFERTILITY

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TREATMENT

- ◉ Surgical

- ◉ Non surgical

specific therapy

nonspecific therapy

NON SURGICAL

- ◉ Once the etiology has been identified and surgical treatment has been ruled out
- ◉ nonsurgical problems usually fall into either pretesticular or intratesticular causes

MEDICATIONS RESPONSIBLE FOR MALE-FACTOR INFERTILITY

- ◉ Cimetidin
- ◉ Ca channel blockers
- ◉ Spironolactone
- ◉ Androgen Excess

ILLICIT DRUGS, ALCOHOL, AND TOBACCO

- Marijuana

HPG axis, decrease serum testosterone,

spermatotoxic effect

cannabinoid Receptors, sperm motility, the acrosome reaction, mitochondrial activity

ALCOHOLISM

hepatotoxic-induced estrogenic effects
including:

- ⊙ depressed libido, and erectile dysfunction
- ⊙ inhibits male fertility

Vit C

motility



smoking

count

morphology

INFECTIONS

- ◉ Chlamydia trachomatis
- ◉ Most common STD
- ◉ Asymptomatic 50%
- ◉ Enter sperm head count motility
- ◉ Azithromycin Minocycline Doxycycline
- ◉ Pyospemia
- ◉ Active urethral symptoms
- ◉ Unexplained asthenospermia

UREAPLASMA UREALYTICUM

- ◉ Lower seminal PH
- ◉ Lower viscosity
- ◉ Count

ANTISPERM ANTIBODY

- ◉ 10% of male infertility
- ◉ serum and seminal plasma sperm surface
- ◉ Immobilization- agglutination of spermatozoa
-sperm-egg interaction
- ◉ Oral corticoids
- ◉ ICSI is considered to be the treatment of choice
- ◉ antisperm antibodies and earlier failed fertilization during IVF or ICSI

HYPOGONADOTROPIC HYPOGONADISM

- ⊙ HCG 2000-5000IU 1- 3/week 6m
- ⊙ hMG 75IU 3/week 12m
- ⊙ FSH 100-150 IU
- ⊙ GnRH 5-20 μ g /2 hour SQ 4m
- ⊙ rare infertile male with HH may benefit from clomiphene

HYPOGONADOTROPIC HYPOGONADISM

- Therapy initiated with 2000-5000 IU of hCG administered subcutaneously three times per week for six months
- FSH therapy: hMG, at 75 units SQ three times weekly
- Testis size
- GnRH pulse: 5-20 μg every two hours

CLOMIPHENE CITRATE

- ◉ stimulates secretion of gonadotropin-releasing hormone (GnRH)
- ◉ release of gonadotropins from the anterior pituitary.
- ◉ Increasing levels of intratesticular testosterone

NONOBSTRUCTIVE AZOOSPERMIA

- ⊙ biopsy : maturation arrest & hypospermatogenesis
- ⊙ dosing of 25-75 mg
- ⊙ 3-9 months
- ⊙ 64.3% of men demonstrated sperm in their ejaculate with a mean density of 3.8 million/mL
- ⊙ Positive TESE
- ⊙ a well-tolerated, relatively inexpensive oral medication.

HYPERPROLACTINEMIA

- ⊙ GT
- ⊙ LH receptor in leydig cell
- ⊙ Microadenoma <1cm 50 μ g /L
- ⊙ Cabergoline 0.5 mg /week 2mg/week 6m
- ⊙ Bromocriptine

THYROID DYSFUNCTION

- ◉ Hypo > hyper
- ◉ Hypo: semen volume & motility
- ◉ Hyper: count & motility > morphology

CONGENITAL ADRENAL HYPERPLASIA

- ◉ 21 hydroxylase
- ◉ Cortisone synthesis
- ◉ ACTH
- ◉ Androgen excess
- ◉ GT
- ◉ Treatment : glucocorticoid + clomiphen

SPERM DNA DAMAGE MECHANISMS

- ◉ *First, DNA damage could be the result of increasing apoptosis during spermatogenesis*
- ◉ *Second, DNA breaks could be induced by chromatin remodelling during the process of spermiogenesis*
- ◉ *Third oxygen radicals could lead to sperm DNA fragmentation during transport through the seminiferous tubules and the epididymis*
- ◉ *Fourth endogenous caspases and endonucleases could cause DNA damage*
- ◉ *Fifth, exogenous factors, such as radiotherapy, chemotherapy and environmental toxicants*

DNA FRAGMENTATION

- ◉ 75-150 IU of recombinant human FSH, given three times a week for at least 3 months
- ◉ improves sperm DNA integrity in hypogonadotropic hypogonadism and idiopathic oligoasthenoteratozoospermia men with DFI >15 %
- ◉ Giovanni Ruvolo & Maria Carmela Roccheri
- ◉ New York 2013

THE EFFECT OF ANTIOXIDANTS ON DFI

- ◉ DNA fragmentation >25%
- ◉ 500 mg of vitamin C, 400 mg of vitamin E, 0.20 mg of selenium, 1,000 mg of L-carnitine, 20 mg of zinc, 1,000 mg of folic acid, 10 mg of lycopene
- ◉ not improve DNA integrity
- ◉ Nine fertility centers in the United States from December 2015 to December 2018

IMPACT OF ANTIOXIDANT TREATMENT ON DNA FRAGMENTATION INDEX

- ◉ 77 men from infertile couples, with normal testosterone, LH and FSH levels and DFI $\geq 25\%$
 - ◉ vitamin C 30 mg, vitamin E 5 mg and vitamin B12 0.5 lg, antioxidants (l-carnitine 750 mg, coenzyme Q10 10 mg and folic acid 100 lg) and zinc 5 mg and selenium 25 lg
 - ◉ DFI did not change during the 6 months of antioxidant therapy
-
- ◉ Stenqvist Lund University, Malmo, Sweden
 - ◉ started in June 2015 and ended in August 2016

EMPIRIC MEDICAL THERAPY

- ◉ Idiopathic male infertility 25%
- ◉ Empeirikos
- ◉ Uncorrectable cause
- ◉ Prior to firm diagnosis
- ◉ Specific treatment unavailable
failed

EFFICACY

- ◉ Semen variation
- ◉ Heterogeneous group (etiology & baseline infertility patient selection)
- ◉ Partner evaluation
- ◉ Dosing regimen
- ◉ Treatment period
- ◉ Follow up

ANTIESTEROGEN THERAPY

- ◉ Negative feedback of steroid in HPG
- ◉ Clomiphene citrate 12.5-50 mg /d
- ◉ Trans > Cis
- ◉ FSH & LH & Testosterone rise
- ◉ Semen parameter +/- sc 70%
- ◉ Pregnancy rate 0-40%
- ◉ Follow up : SA FSH Testosterone /m

CLOMIPHENE

- ◉ Elevated GT is contraindicated
- ◉ Side effect
 - visual disturbance
 - weight gain
 - HTN
 - gynecomastia

TOMOXIFEN CITRATE

- ◉ Metastatic breast cancer
- ◉ Less estrogenic activity than clomiphene
- ◉ 20 mg/ d / 6-11m
- ◉ SC> motility & morphology
- ◉ Pregnancy rate 20% -
- ◉ NL base line gonadotropin
- ◉ One week stimulation test: 40mg test
FSH cte SC 50% rise

AROMATASE INHIBITOR

- ◉ Metastatic breast cancer
- ◉ Testosterone T/E GT Estradiol
- ◉ T/E <10
- ◉ Obese man
- ◉ Testolactone 100-200 mg /d
- ◉ Anastrozole 1mg/d
- ◉ SC 80% motility NL morph
- ◉ Pregnancy rate 30%

GONADOTROPINS

- ◉ Sub fertile men :NL or elevated gonadotropins
- ◉ Defective or inefficient bioactive FSH & LH
- ◉ Idiopathic oligospermia or NOA
 - HCG 5000IU 2-3/week 4m SA60% PR35%
 - hMG 75IU 2-3/week 1-3m SA19% PR15%
- ◉ Anabolic 3m wait
 - HCG10000IU 2/w +/- hMG 75IU/d
- ◉ IVF failure FSH 150IU 3/w 3m

GNRH

- ◉ Idiopathic oligospermia mod> severe
- ◉ Intranasal SQ pump
- ◉ Semen parameters 67%
- ◉ Pregnancy rate 24%

ANDROGENS

- ⊙ Testosterone is 50 fold of serum
- ⊙ Epididymal function
- ⊙ Low dose T easily metabolised by liver
- ⊙ Extraordinary high dose of animal model
- ⊙ Floxymesterone 20mg/d 6w

TESTOSTERONE REBOUND THERAPY

- ⦿ High dose testosterone for pituitary inhibition
- ⦿ Withdrawal for rebound testosterone
- ⦿ Oligospermia semen parameter 20-67%
pregnancy rate 14-41%
- ⦿ Azoo
- ⦿ Chemotherapeutic agent

KALLIKEREIN

- ◉ Polypeptide enzyme
- ◉ Source : pancreas
- ◉ Oral & parenteral
- ◉ Regulation & stimulation of sperm motility
- ◉ 600 KU/d
- ◉ Semen parameter & pregnancy rate +/-
- ◉ Inflammation of epididyme & prostate

INDOMETHACIN

- ◉ PG steroidogenesis & spermatogenesis
sperm motility
- ◉ 75 mg/d
- ◉ Oligospermia
- ◉ Pyospermia
- ◉ ASA
- ◉ FSH & LH & Testosterone
- ◉ Motility & Count
- ◉ Pregnancy rate 35%
- ◉ Gastritis

PHOSPHODIESTERASE INHIBITOR

- ◉ Petoxyfylline 400-800mg/d
- ◉ Sildenafil
- ◉ Motility invitro+
 invivo-
- ◉ CAMP
- ◉ Micro circulation

ZINC

- ◉ Semen rich in zinc
- ◉ Prostate
- ◉ Deficiency
- ◉ High dose detrimental sperm function
- ◉ 66mg/d

L-CARNITINE

- ◉ intracellular energy metabolism as well as spermatozoa
- ◉ membrane stabilization
- ◉ Carnitine also has an antioxidant capacity
- ◉ Epididymal secretions
- ◉ Motility
- ◉ 1-2 g/ d

VIT A

- ◉ Sperm maturation

- ◉ 25000IU

VIT E

- ◉ Sperm count , motility , morphology
- ◉ Acrosome reaction
- ◉ ICSI
- ◉ 400 IU/d

A AGONIST

- Retrograde ejaculation
- Emission disorder
- Phenylpropanolamin 75mg BD
- Psuedoephedrine 60mg QID
- Imipramine 25mg BD

LICOPEN

- ◉ Testis & semen
- ◉ Idiopathic OAT
- ◉ 2mg BD
- ◉ 3m

FOLIC ACID

- ◉ Morphology
- ◉ Motility
- ◉ Count
- ◉ 5mg
- ◉ 3-6m

ARGININ

- ◉ Aminoacid

- ◉ Count

- ◉ Motility

COQ10

- ⦿ Antioxidant
- ⦿ Sperm energy