

Ten Reasons why You Should not Use Clomid for Fertility Treatment

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Not the Way your Using it Anyway

Ten Reasons why You Should not Use Clomid for Fertility Treatment, Not the Way your Using it Anyway. Clomiphene citrate (clomid) was the first medication introduced for fertility treatment (1960s). It works through masking of estrogen receptors in the brain. The brain, blind to estrogen in the blood, starts pouring FSH, the protein that drives development of dormant follicles in the ovary.

When one considers a fertility treatment: not only the pregnancy and delivery rates per cycle is considered, but also the time to conceive (TTC) and the complication rate especially multiple pregnancy. Clomid is a very attractive medicine to women and gynecologists, alike. It is an oral medication, easy to use for both general gynecologists and women seeking fertility treatment. It is also cheap. It is successful in inducing ovulation in 90% women that do not regularly ovulate e.g. polycystic ovary syndrome. Response to clomid is modest in most cases (1-2 follicles).

In spite of all these advantages, there are many other disadvantages. It, most likely, will not improve the odds of conception in regularly ovulating women. Its indiscriminate use, in The US and worldwide (without ultrasound monitoring of ovarian response), probably makes clomid the drug responsible for multiple pregnancies over all other forms of fertility treatment. Although clomid is successful in inducing ovulation

in 80-90% of well selected patients, only 20% become pregnant. This discrepancy happens because of undesirable effects of clomid on the lining of the uterus (thin) and cervical mucus (thick). In my opinion though, many clomid cycles fail due to its in women that are not destined to benefit from it. Those are older and regularly ovulating women with unexplained infertility as opposed to suitable candidates: younger non-ovulating women. Clomid offers little help to women with unexplained infertility (ovulating) because in these women, the majority do not conceive because of chromosomal abnormalities in the eggs. Clomid commonly does not induce superovulation (many follicles) to partially compensate for abnormalities in the eggs.

Do Not Use Clomid Unless

1. Preconception labs are normal. Many patients are prescribed clomid without a complete fertility workup, including genetic screening. If you and your partner are carriers of cystic fibrosis or sickle cell anemia gene abnormalities, for example, you are at risk of transmitting these diseases to your future children (1:4). Genetic screening should be performed BEFORE starting fertility treatment. It does not help you to detect these abnormalities after pregnancy ensues. Decline clomid or any other fertility treatment without proper preconception history and lab tests.

2. Evidence of patent tubes. After ovulation induction, using clomid, the eggs has to be picked up by the fallopian tubes. Sperm also has to enter the fallopian tube to allow fertilization. Completely blocked fallopian tube may prevent the egg and sperm to meet. Partially blocked fallopian tube may allow fertilization but the the embryo may become stuck in the tube leading to ectopic pregnancy.

3. Near normal sperm analysis. A sperm concentration of < 15 million per mL and movement < 50% may reduce the odds for fertilization and reduce the chance of pregnancy after clomid

treatment.

4. If you ovulate regularly. Together with normal sperm analysis and open tubes, that indicates you have unexplained infertility. The most likely cause for not conceiving is chromosomal abnormalities in the eggs. We cannot fix chromosomal abnormalities in the egg but we can induce the ovaries to produce more eggs. More mature eggs means more chance of producing a normal egg. Clomid induces the ovary to produce 1-2 eggs in most cycles, thus does not address effectively egg abnormalities. On the other hand, if you are young and do not regularly ovulate, clomid is able to induce ovulation and potentially solve your problem.

5. Without monitoring. Some women are more sensitive to the effects of clomid. They respond by producing a large number of follicles. The safest approach here is to cancel the cycle and restart another treatment with a lower dose. Although the risk of multiple pregnancy with clomid is about 10%, women that respond with producing a large number of follicles are at a much higher risk. Careful monitoring of response, using vaginal ultrasound, is required in all clomid cycles.

6. Use the lowest dose that leads to ovulation (start with one tablet per day). Do not increase the dose if ovulation took place at a lower dose. Most patients get pregnant at doses of 50 to 150 mg (1-3 tablets) per day. Increasing the dose does not increase the chance for pregnancy and increases the side effects of clomid e.g thin endometrium, thick cervical mucus..

7. Do not use clomid more than 3 months (6 months life time max). The majority of women get pregnant in the first three months of treatment. If you are younger and ovulate on clomid and would like to try few more months, then 6 months is the maximum amount of time you should use clomid in your life time.

8. Clomid less likely to lead to pregnancy delivery in women

>38y. In women 38 or older with unexplained infertility, there is good evidence that clomid-IUI is inferior to IVF. The vast majority of women in that age group that start on clomid end up switching to IVF to achieve pregnancy.

9. Expertise with optimizing clomid cycles: clomid cycles should be supervised by a physician with expertise in clomid dosing, use of repeat courses, use of adjuvant treatments as estradiol and IUI. This enables maximizing the benefits of fertility treatment and tailoring treatment to individual woman.

10. Use letrozole before using clomid. Accumulating evidence from many studies, including randomized clinical trials, indicates that letrozole is superior to clomid in terms of achieving pregnancy. Applying the same principals above, letrozole should be considered as the initial treatment for anovulatory infertility.

On tailoring Fertility Treatment to Specific Patient's Needs

In too many times, the use of clomid for fertility treatment is a stark example of tailoring patients to treatments familiar to general gynecologists, rather than individualizing fertility treatment to women biology and fertility needs, citing ease of use, perceived safety and familiarity. Cheap treatments that appear safe can quickly become aggressive and unsafe if they lead to low pregnancy rate and high multiple pregnancy. The time lost treating older patients with clomid for a prolonged periods can be detrimental to their ovarian reserve and can minimize the chance for eventually achieving pregnancy and delivery.

On men and clomid

There is no proof that men benefits from the use of clomid and similar treatment to improve sperm parameters. Specifically, there is no evidence that female partners of men that were

prescribed clomid conceive at higher rates. With very few exceptions, clomid should not be used to treat male factor infertility.

Idiopathic Infertility Treatment: what do you need to know

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Idiopathic infertility (unexplained infertility) is defined as inability to conceive after trying for 6 months in women 35y or older and one year for women younger than 35, with no tubal, ovarian or male factor infertility. This diagnosis of idiopathic infertility is established after open fallopian tubes are detected in HSG or laparoscopy, regular ovulation is detected from history, lab tests and ultrasound and sperm is near normal on sperm analysis. These fertility tests can be performed within few days. Note that good health and physical fitness..etc are not factors here. Many women with terrible general health do conceive. On the other hand, many women in excellent physical fitness and sound health have extreme difficulty conceiving even with fertility treatment. Having difficulty getting pregnant without an apparent cause applies to a large category of the sub-fertile population and is puzzling to couples trying to conceive. The consensus of opinion among reproductive endocrinologist can divide the underlying factors for unexplained infertility into

1. Chromosomal abnormalities in the egg (low egg quality)

Abnormal eggs are present in every woman, albeit to a varying degree. Older women has more abnormal eggs. In addition, the fewer eggs you have the higher the proportion of abnormal eggs. There is no *non-invasive test* for egg quality and history, age, blood tests for ovarian reserve and antral follicle count detected on vaginal ultrasound are the most used methods.

Factors that point to low egg quality

1. Advanced maternal age,
2. Diminished ovarian reserve (e.g high FSH, low AMH), also prior surgery in the ovaries, smoking, family history of early menopause and exposure to chemotherapy
3. Early pregnancy loss before a fetal heart activity is detected (chemical pregnancy, blighted ovum),
4. Abnormal chromosomes of the products of conception and
5. Abnormal chromosome configuration of male or female partner e.g chromosome translocation. Less than 5% of couples miscarry due to a translocation in the male or female partner.

2. Other factors: may be more prevalent in younger patient and include mild endometriosis, immunological factors as anti-sperm antibodies, abnormality in cervical mucus, abnormalities in the cavity of the uterus and endometrial lining. Generally, these are not considered major factors in idiopathic infertility. Mostly oral medication produce few or only one follicles, thus they do not increase te chance that one or more eggs are healthy leading to a pregnancy.

Treatment Options for Idiopathic Infertility

Oral medication – IUI or expectant treatment (intercourse)

Oral medications are either clomid (clomiphene citrate) or an aromatase inhibitor (mostly letrozole) are used. This is followed by intercourse or intrauterine insemination (IUI). The pregnancy rate is about 5% to 7% per treatment cycle. There is no evidence that oral medications followed by IUI are superior to just intercourse in treatment of unexplained infertility. The risk for multiple pregnancy is about 8%. However, because oral medication (clomid) widespread use, mostly without ultrasound monitoring, they are probably responsible for more multiple pregnancy than any other fertility treatment.

Injection medications – IUI

This **treatment** should probably be avoided in the majority of couples because of a. No added benefit: Pregnancy rate is not significantly higher than Clomid-IUI cycles; 9% pregnancy rate per treatment cycle and drops to 5% in women >38y. b. Risks: notably multiple pregnancy (two or more babies; 30%) and higher order multiple pregnancy (three or more babies; 3 to 8%). Multiple pregnancy has significant risks to the mother and babies. Preterm delivery can be associated with permanent neurological and intellectual defects in the babies. This risk can be minimized with careful stimulation under supervision of a reproductive endocrinologist, but cannot be completely prevented.

In Vitro Fertilization (IVF)

a. The pregnancy rate per an IVF treatment cycle is approximately 30% on average, three times that of IUI. The specific pregnancy rate is dependent on female age. The time to conception is also shorter than any other fertility treatment modality. The higher success rate can be further extended through the use of frozen embryos in couples that have good quality embryos available for freezing. The

cumulative pregnancies resulting from fresh transfer and subsequent frozen-thaw embryo transfer can result in a very high odds for pregnancy. Frozen embryos can be used years after their creation, when ovarian reserve has considerably diminished. The contribution of IVF to treatment success becomes more pronounced in older women >38 years as the success of ovarian stimulation – IUI drops considerably. b. The risk for twins and higher order multiple pregnancy can be greatly minimized through single embryo transfer (1% twins and no higher order multiple pregnancy). In other words *if you want to get pregnant faster, with one baby and at higher chance for success per treatment cycle strongly consider IVF with single embryo transfer.*

Infertility Treatment Strategy for Idiopathic Infertility

Conventional [fertility treatment](#): “expectant management → clomid / letrozole- IUI x2 to 3 cycles → gonadotropin – IUI x3 cycles → IVF ” is the old method of treatment for unexplained infertility Modern treatment of Unexplained infertility: ” expectant management or oral medication – IUI → IVF preferably with single embryo transfer “. Women 38 years and older modern treatment strategy suggests Immediate IVF as the initial fertility treatment. The modern paradigm for fertility treatment will lead to pregnancy faster, is more successful, minimize multiple pregnancy and is more cost effective (lower dollar cost per baby). The majority of women (>70%) with unexplained infertility especially women with normal ovarian reserve will succeed in delivering a baby.