Gossypol

Gossypol is a chemical found in the seeds of cotton plants. Cotton plants produce gossypol in order to slow down the reproduction of the insects that eat cotton bolls and seeds; the compound also affects reproduction in mammals. Pressed cakes of cotton seeds, a byproduct of the cotton industry, are sometimes fed to livestock with unintentional contraceptive effects.

The effect of gossypol on human male fertility has been known in China for many years. In 1929, a study of couples who used crude cottonseed oil for cooking showed that they had smaller than average families. Specifically, researchers showed that the oil affected male fertility. Eventually researchers isolated the contraceptive compound gossypol from the cotton seed oil.

This discovery led to large scale testing of gossypol as a male contraceptive in China during the 1970s. The studies involved over 8,000 men, and continued for over a decade. The researchers found that men taking a daily gossypol pill had reliable contraception and no complaints about change in libido. However, the studies revealed two serious flaws: disruption of potassium uptake and incomplete reversibility.

What side effects are expected?

The large-scale trials of gossypol in Chinese men reported an abnormally high rate of hypokalemia among subjects, varying from 1-10%. Hypokalemia is characterized by low levels of potassium in the blood. Potassium is one of the elements used by the muscles and nerves to transmit signals. Symptoms of low blood potassium include fatigue, muscle weakness and at its most extreme, paralysis. Hypokalemia is usually the result of kidney malfunction, and can be caused by excessive consumption of diuretics. Researchers do not understand exactly how gossypol affects the kidneys.

Several studies of gossypol as a contraceptive in male monkeys tried to remedy potassium loss by giving the monkeys a daily potassium supplement. The supplement did not stop the monkeys from losing potassium and the researchers concluded that hypokalemia was an inescapable side effect (Lohiya 1990, Kumar 1997).

However, the dose the monkeys received was higher than the equivalent dose given to men, and there is evidence that the incidence of hypokalemia depends on dosage. Two more studies of gossypol as a low-dose contraceptive in men report no incidences of hypokalemia (Gu 2000, Coutinho 2000). Dr. Elsimar Coutinho (2002) of Brazil contends that previous reports of hypokalemia were the result of “the Chinese diet, which is poor in potassium, and not to the effect of gossypol on the kidneys.”

Regardless of gossypol’s possible causal relationship with hypokalemia, researchers at the World Health Organization (WHO) have other concerns about side effects. Gossypol is a known toxin, and a toxic dose is less than 10 times the contraceptive dose. Some argue that this alone should disqualify it from further study.

How long does it take to reverse?

Lack of complete reversibility was the second major concern raised by the Chinese trials. Some men in those studies remained azoospermic after stopping treatment. The longer the men had taken the gossypol and the higher their overall dosage, the more likely they were to lose part or all of their fertility. Various studies reported between 5 and 25 percent of the men remained infertile up to a year after stopping treatment. A long-term follow up study of men who had taken gossypol showed that 61% of the men regained normal fertility with “a median recovery time of 1.1 years” (Meng 1988). However, 22% remained azoospermic after 3 years.

Dr. Zhi-Ping Gu’s (2000) trial of low-dose gossypol is the only study to report no incidence of lasting infertility. The highest cumulative dosage taken by men in Dr. Gu’s study was 36 grams over 18 months. Dr. Coutinho’s (2000) low-dose trial used a different regimen and found that 20% of the men remained infertile 1 year after stopping treatment. The highest cumulative dosage taken by men in Dr. Coutinho’s trial was 44.8 grams over 14 months. If Dr. Gu’s trial had lasted longer, it is possible that the study participants would have experienced similar rates of lasting infertility.

Where does gossypol stand now?

In the late 1990s, the WHO’s Research Group on Methods for the Regulation of Male Fertility reviewed the studies to date on gossypol and concluded that contraceptive research should be abandoned (Wales 1998). Some researchers have contested this, arguing that the data on hypokalemia were misinterpreted, and that diet and genetic predisposition are responsible for this side effect (Yu 1998). No one has contested the concerns over irreversibility, but gossypol research has continued in China, Brazil, Kenya and Nigeria.

Gossypol as an alternative to vasectomy
Some researchers propose taking advantage of gossypol's lack of reversibility by using it as a non-surgical alternative to vasectomy. Dr. Coutinho (2002) proposes that gossypol "should be prescribed preferably to men who have completed their families or for those who would accept permanent infertility after a few years of use." Even this type of use for gossypol may be controversial unless the WHO changes its stance.

References

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