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Injectables and Conception: The Intersection of Injectable Obesity Treatments and Pregnancy

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Obesity among women of reproductive age is a significant health problem. Pre-pregnancy overweight or obesity affects approximately 42% of women in the United States, 30% in Europe, and 10% in Asia (1). Excess body weight is linked to issues with fertility and reproduction, and studies show that reducing weight can increase the chances of achieving a successful pregnancy (2). Thus, losing weight before pregnancy has become one of the topics of interest in recent times. Due to the high obesity prevalence and the limited availability of weight management services, including bariatric surgery, which are publicly funded, access to effective treatment options remains a significant challenge. There is an urgent need for well-tolerated and effective pharmacologic therapies for weight loss (2). Only a few medications are currently being used for this purpose, including orlistat, and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) like semaglutide and liraglutide (3). Both medications are self-injected pens available by prescription, typically through specialist clinics with diet and exercise. Though also accessible privately online, many are purchased from unregulated sites, raising safety concerns (3).

Pregnancy is not advised during or shortly after being treated with weight-loss medications due to the potential risk of teratogenic effects (3). Animal studies conducted with GLP-1 RAs have demonstrated toxicity on reproduction, although the potential risk to humans remains unknown (4). Therefore, contraception is advised during any period when treatment and the potential for pregnancy may overlap. It is recommended for semaglutide to wait about two months after stopping treatment before attempting conception (3). Nevertheless, it was also reported that liraglutide 1.2 mg QD s.c. (COMBI) in low-dose for a period of 12 weeks and then starting the protocol of ovarian stimulation after a medication-free period of 4 weeks was found to be a safe and effective strategy in patients who underwent in vitro fertilization cycles (5). Notably, the number of studies that have been conducted regarding GLP-1 RAs use is limited, suggesting that limited information exists about the perspectives and needs of women using these drugs for managing overweight, obesity, or fertility issues (3). It was observed that administering orlistat before fertility treatment did not increase the live birth rates, despite its effectiveness in promoting weight loss. The obstetric and perinatal complications were also comparable between the groups. It has been shown that women did not want to postpone infertility treatment despite receiving orlistat therapy. This indicates that, in real-life practice, orlistat and/or another injectable weight loss method would be more feasible and acceptable for patients aiming to conceive, provided it fits within more reasonable time constraints (6). Nevertheless, women with obesity who are referred for assisted reproductive treatments may encounter limitations or delays in access to care until they have lost weight (7). Women of reproductive age often experience intersecting forms of stigma, stemming from both their weight and their struggles with infertility (8). These factors may drive financially able individuals to buy GLP-1 RAs online without prescriptions, raising concerns about a lack of medical supervision. Such users likely do not receive guidance on contraception (3).

Animal studies show GLP-1 RAs cause fetal harm, including low fetal weight, poor survival, and skeletal defects, linked to reduced maternal food intake (4). Since it's unclear if liraglutide and semaglutide affect humans similarly or cross the placenta, contraception is recommended during their use, though the exact duration is not well defined (3,4). In the United States

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and Europe, GLP-1 RAs are included in "category C" during pregnancy, meaning women planning pregnancy should stop them first. Due to semaglutide's long half-life, an 8-week washout is recommended before conception. No formal guideline exists for liraglutide, but providers usually suggest stopping it 10–14 days prior, given its shorter half-life (3).

It remains unclear whether these medications benefit women with overweight or obesity planning pregnancy, especially regarding when to start treatment. Their use is prohibited during pregnancy, making it difficult to assess safety and effectiveness among these women. Even so, with thorough and timely contraceptive guidance, reproductive-aged women should still have equitable access to proven weight-loss therapies. Further investigation is needed to understand how these medications affect reproductive health and pregnancy, both in the immediate term and over the long run, spanning the preconception, gestational, and postpartum periods.

Competing Interests
None declared.

Ethical Issues
Not applicable.

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