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Considerations on Concurrent Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists and Isotretinoin

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INTRODUCTION

We read with interest the numerous recent publications regarding adverse dermatologic events related to glucagon-like peptide-1 receptor agonists (GLP-1RA).[1,2,3] We hope to highlight some additional considerations related to the use of GLP-1RAs concurrently with isotretinoin.

Isotretinoin is a highly effective medication commonly used for acne vulgaris (along with many other dermatologic conditions), but it is also extremely teratogenic. As such, it is a requirement in the United States for females with childbearing potential to remain on at least 2 forms of contraceptives while on treatment.[4] Despite these well-known risks, some data suggest roughly a third of individuals may not be fully adherent to pregnancy prevention guidelines (eg, intercourse with <2 forms of contraception, failure to remain abstinent, missing doses of oral contraceptives, or in some cases, having completely unprotected intercourse).[4]

Likely due to weight loss and direct effects on the hypothalamic-pituitary-ovarian axis,[5] GLP1-RAs may also increase fertility, along with the possibility of pregnancy. Women with obesity have a higher risk of infertility, both due to anovulatory disorders, such as polycystic ovarian syndrome (PCOS), and co-existing metabolic syndrome, including insulin resistance.

As women lose weight while taking the GLP1-RAs, they often regain regulatory ovulatory cycles and have improved insulin sensitivity, both of which positively affect fertility. A recent meta-analysis demonstrated an increased rate of unassisted pregnancy in individuals with PCOS taking GLP1RAs compared to controls (Relative risk 1.72, 95% confidence interval 1.22-2.43, P=0.002).[5] This analysis also found significantly increased sex hormone binding globulin levels, decreased androgenetic sex hormone levels, and increased menstrual cyclicity in these patients.[5] In patients with a prior history of infertility related to metabolic syndrome taking GLP1-RAs, it may be salient to emphasize strict adherence to contraceptive methods, as these patients may see increased fertility as a result of subsequent weight loss and hormonal changes. In addition, this class of medications is contraindicated in those currently pregnant and should ideally be stopped 2 months in advance.

Interactions between GLP1-RAs and isotretinoin are also possible. A key function of GLP1-RAs is the delay of gastric emptying, which has been shown to reduce the absorption of oral medications. For example, the absorption rate of acetaminophen and atorvastatin was shown to be reduced by 50 to 90% when administered with the GLP1-RA semaglutide compared to controls.[6] This effect was also shown to be accentuated with increased body weight.[6] Thus, isotretinoin may also not be absorbed as readily in patients taking GLP1-RAs. This may also reduce the potency of oral contraceptive pills, potentially contributing to the increased likelihood of pregnancy during treatment. Dermatologists may consider advocating for more reliable forms of contraceptives, including long-acting reversible contraceptives, including intrauterine devices or implants.

The data on adolescents, a demographic commonly using isotretinoin, suggest increased usage of GLP1-RAs.[7] To date, there are no clinical data on GLP1-RAs used concurrently with isotretinoin. However, due to the potential for increased rates of pregnancy and confirmed decreased absorption of some oral medications, we advocate for continued study and vigilance when initiating isotretinoin in patients on GLP1-RAs.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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