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Fractional Vaginal Laser for management of GSM– Review of recent published data and FDA warning

Symptoms of vaginal dryness and discomfort during sexual activity are common in postmenopausal women. The current gold standard treatment is vaginal estrogen which reduces vaginal dryness in most cases and may be more effective than systemic estrogen for vaginal symptoms [1]. Despite progress in the development and evaluation of non-hormonal treatment for vasomotor symptoms [2], there has been relatively little progress in non-hormonal treatments for vaginal symptoms. Ospemifene, a selective estrogen receptor modulator is available in some countries but carries the same restrictions for use as vaginal estrogen and has not been shown to be superior to vaginal estrogen in comparative studies. For women who wish to avoid exogenous estrogen there is an unmet need for safe and effective non-hormonal treatments for the genitourinary symptoms of menopause (GSM). Laser therapies have long been used in cosmetic surgery to provide skin resurfacing, improve tone, texture and pigmentation. More recently, fractional laser to the vaginal mucosa via a purpose-designed probe has been promoted as a novel therapy for a wide range of gynaecological symptoms including vaginal dryness, pain during sexual activity, orgasm, stress incontinence, pelvic floor dysfunction, and other GSMs [3]. Exactly how vaginal lasers might achieve these outcomes is uncertain, but purported mechanisms are through activation of heat shock proteins and tissue growth factors as well as stimulation of epithelial remodelling and collagen synthesis. Currently, evidence to support the safety and efficacy of vaginal laser is lacking. The safety of fractional CO2 laser has been investigated in a small number of observational studies and case series [4]. All of these studies had small sample sizes and short durations of follow up. Efficacy is implied but not demonstrated in small studies using objective and subjective scales of GSM symptoms compared to pre-treatment, but without a placebo or sham control group. In January 2018, Cruz et al. [5] published a three-armed randomised trial of fractional CO2 laser compared to vaginal estrogen, or vaginal laser plus vaginal estrogen in symptomatic postmenopausal women. There were only 15 women in each arm and the study was not powered for multiple comparisons (including non-inferiority). Whilst the authors concluded that vaginal laser appeared to be effective, this conclusion was not supported by the data as presented. This trial had significant methodological concerns raised in commentary by other authors [6,7]. Namely, that the placebo effect required to truly determine clinical efficacy was not appropriately investigated. Although the authors used sham laser in the estrogen arm and sham estrogen in the laser arm, estimating the placebo effect required a sham estrogen and sham laser treatment arm which was not included. Randomised clinical trials of the treatment effect on GSM symptoms have previously reported placebo effects of up to 20%. Furthermore, the baseline characteristics of the patients entered into the study were significantly different, with less bothersome burning and sexual complaints in the vaginal estriol arm compared to the other two arms. Although their findings included a reduction in the Vaginal Health Index (VHI) in the laser arm compared to the other two arms at 20 weeks, the authors do not discuss this finding or speculate the mechanism underlying this observation. Alarmingly, they reported an increase in pain associated with vaginal penetration following vaginal laser treatment compared to estrogen treatment. Given the recent disastrous outcomes following vaginal mesh insertion for prolapse without adequate evidence addressing long-term adverse outcomes such as pain, it would be very disappointing if gynaecologists promoted another

vaginal treatment without first investigating the potential short and long-term adverse events. Comment Concerns about the widespread promotion of vaginal laser without adequate supporting literature and the considerable costs to patients in the absence of high-quality data lead the FDA, in July 2018, to issue a warning to several firms to state that their marketing was "deceptive" and that using these devices may have serious risks without adequate evidence to support their use [5]. The manufacturers were requested to alter their marketing to reflect this and that the devices are yet to be approved for management of GSM, pending the publication of high-quality safety and efficacy data [6]. Eight other randomized controlled trials, internationally, are currently evaluating the efficacy and safety of vaginal laser [9, 10]. Only one of these is a phase 3 clinical trial and recruitment has been currently suspended. It will not be long before high quality evidence indicating the risks and benefits of vaginal laser is available. In the meanwhile, clinicians and women should be very wary of claims that the procedure is either safe or effective. Vaginal estrogen therapy remains the gold standard for the management of GSM.

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