



Benefit of Add-Back Therapy in Total Laparoscopic Hysterectomy for Benign Uterus Disease

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ABSTRACT

Total Laparoscopic Hysterectomy (TLH) is already the standard procedure for benign uterine disease such as fibroids and adenomyomas and is the first choice in many centres in Japan. The number of nulliparous women is increasing, as is the weight of the uterus removed due to the expanding range of indications. The strain on the vaginal wall during specimen extraction is therefore greater than in the past. Preoperative Gonadotropin-Releasing Hormone analogue (GnRHa) therapy facilitates TLH for uterine fibroids and adenomyomas reduces the size of the uterus, resulting in less intraoperative blood loss and operating time. However, GnRHa use can cause vaginal atrophy, making transvaginal procedures difficult. We were the first in the world to evaluate the association between efficacy of preoperative vaginal estriol use as add back therapy for TLH with GnRHa therapy and intraoperative and postoperative outcomes.

Keywords: Add-back therapy; Estriol; Gonadotropin releasing hormone analogue; Total laparoscopic hysterectomy

DESCRIPTION

We retrospectively assessed 2,571 patients who underwent TLH with transvaginal specimen extraction, of whom 2505 was postmenopausal or GnRHa-treated. The patients were divided into two groups according to the administration with vaginal estriol [1]. The patient characteristics, surgical and postoperative outcomes were compared between the groups. In the analysis of surgical outcomes, the rate of colpoperineal laceration was significantly lower in the estriol group than in the non-estriol group ($p < 0.01$), while operative time, blood loss and specimen extraction time were similar in both groups. Furthermore, we were the first in the world to assessed postoperative outcome, i.e. hemorrhage from the vaginal stump required hospitalization and outpatient treatment for suture or pressure hemostasis and found no significant group differences.

The vaginal effects of estrogen replacement therapy include improved vaginal mucosal flexibility, vaginal wall extensibility and elasticity, restoration of vaginal self-cleaning and increased resistance to inflammation by promoting keratinisation of vaginal mucosal cells [2]. In our study, preoperative administration of

vaginal estriol was found to reduce the risk of colpoperineal laceration, which may be mainly due to improved vaginal flexibility and extensibility [1]. Clinically, it has long been known that transvaginal administration of estrogen prior to surgery for pelvic organ prolapse accelerates wound healing at the vaginal suture site. Rahn et al., reported that vaginal estrogen application preoperatively increased synthesis of mature collagen, decreased degradative enzyme activity and increased thickness of the vaginal wall, suggesting this intervention improves vaginal wound healing in patients undergoing surgery for pelvic organ prolapse [3]. In total vaginal hysterectomy, there are also reports that preoperative and postoperative estrogen therapy in postmenopausal women promotes vaginal wound healing [4]. A systematic review of the effects of estrogen therapy in vaginal surgery, including total hysterectomy, has a benefit effect on vaginal healing [5]. Estrogen administration improves neovascularization, microscopic wound closure, collagen synthesis and tissue strength. Estrogen decreases the inflammatory response and reduces levels of Transforming Growth Factor (TGF)- $\beta 1$. In addition, these factors also promoted gross and microscopic wound healing and collagen synthesis in a statistically significant manner.

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CONCLUSION

As described above, even if GnRHa administration makes vaginal manipulation difficult in TLH, vaginal wound healing is facilitated by preoperative estrogen. Short-term local low-dose estrogen therapy does not require concomitant progestin [6] and self-administration of preoperative vaginal estriol appears to be relatively easy and safe for the patient. Add-back therapy may allow both benefitting from GnRHa and reduction of disadvantage of GnRHa. In present data, we were able to confirm that vaginal estriol reduced intraoperative colpoperineal lacerations, but no association with postoperative hemorrhage was observed. There have been no reports of an association between add-back therapy and postoperative complications and further research is needed.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest associated with this manuscript

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