CHAPTER II

REVIEW OF LITERATURES

Radiotherapy (intracavitary and pelvic irradiation) with or without chemotherapy (concurrent radio-chemotherapy) is the standard treatment of advanced stage cervical cancer (*2*), and the average total radiation dose was 8,000-8,500 cGy(*2*). The effects of irradiation therapy are not only on the cervical tumor but also the surrounding pelvic structures and vagina. This treatment causes some changes in vaginal anatomy and its functions. Many studies investigated the short and long-term effects of pelvic radiotherapy and/or brachytherapy on the vagina and sexual function of women treated for cervical cancer (*3-8*). Using questionnaires assessment prior to radiotherapy, at completion of radiotherapy, and at 6 weeks and 14 weeks after radiotherapy, significant changes in sexual activity and satisfaction had been demonstrated. Dyspareunia, bleeding and concern of recurrence were all significant factors. A feeling of vaginal shortening was the most frequent reason (*6,7*). Bruner et al.(*6*) showed that at least 6 months follow-up post-radiation treatment, vaginal length was decreased, which compared to the normal vaginal length of 8 to 9 cm, documented by Masters and Johnson. Katz et al.(*8*) showed that vaginal shortening could occur during the course of intracavitary and external irradiation. Vaginitis and vaginal shortening occurred early(*8*). The distal vaginal mucosa has a poorer radiation tolerance than the mucosa in the upper vagina. With the maximal extension of the vaginal cylinder above the pubis, Katz et al.(*8*) found that the difference in mean values of vaginal length between two intracavitary insertions (2.27 ± 1.14 versus 1.72 ± 1.14 cm.) was highly statistically significant ($p < 0.0001$) in cervical cancer patients treated with both brachytherapy and pelvic irradiation(*8*).

The patient's distress due to vaginal changes was not only direct from radiation effect, but also because of estrogen deprivation from radiation castration, especially in pre-menopausal patients. It caused thinning of vaginal epithelium, loss of rugae, then it became early shortening, agglutination and lately turned to vaginal occlusion/stenosis according to loss of elasticity of vaginal connective tissue from radiation fibrosis. The vagina appeared insufficient lubrication and elasticity which resulted in unsatisfactory in sexual activity. A comprehensive approach to detect and management of postmenopausal vaginal atrophy with local hormonal support was

reviewed systematically. Application of vaginal moisturizers as local hormone replacement was recommended for the treatment of local urogenital symptoms such as vaginal itching, irritation, and dyspareunia, and it yielded a good efficacy. This application should be offered to women who want to avoid systemic hormone replacement therapy. For menopausal women experiencing vaginal atrophy, any of the following effective vaginal estrogens should be offered: conjugated equine estrogen cream (CEE) , low dose estradiol tablet, or intravaginal estrogen ring (*9,10*).

To prevent or decrease vaginal occlusion and restoration of vaginal function that have changed after complete radiation treatment, the application of digital pressure with local vaginal estrogenic cream for six weeks was suggested by Poma (*5*). According to systematic review, to avoid systemic estrogen absorption when using conjugated equine estrogen cream, the dose of estradiol should not be greater than 0.5 mg/daily (*9*). However, in the radiated patients the absorption of estrogen and maturation of epithelium of the radiated vagina were significantly slower than in the non-irradiated group(*11*). Regarding patient's safety, the side effects of conjugated equine estrogen cream included breast pain , perineal pain. And the incidence of endometrial hyperplasia was 4% in natural menopausal patients, but no data available in radiated patients(*9*). Until now there is no strong evidence to support that estrogen aggravates cervical cancer, especially squamous cell type(*12*).