

Hormone Replacement Therapy and Cutaneous Manifestations of Systemic Lupus Erythematosus

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ABSTRACT

Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease. Presentation of SLE can range from mild skin symptoms to severe organ damage. Skin manifestations, as one of the most diagnostic signs of SLE, containing a broad range of skin rashes and vascular involvements which can highly be affected by disease flares and medications. Hormone Replacement Therapy (HRT) as a common medication used for infertility treatment and relief of menopausal and postmenopausal symptom can also modify SLE complications. Studies show that the use of oral contraceptives in SLE patients is not recommended but for SLE patients in childbearing age planned pregnancy or the use of assist reproductive technology could be recommended. Receiving HRT can improve menopausal/postmenopausal symptoms and bone mineral density along with increasing thrombotic events and can generally be recommended. Due to the mild increase in SLE flare and its cutaneous manifestations by HRT, after considering the patient specific cost-effectiveness of intended intervention, SLE patients can receive HRT safely. However specific inferences in this area could be done when more related studies are available.

Keywords: Systemic lupus erythematosus; Lupus erythematosus; Hormone replacement therapy; Oral contraceptives; Assisted reproductive technology

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease that tends to affect women in their childbearing years, with an overall 9:1 female to male ratio. SLE can affect every organ in the body, with a particular impact on the central nervous system and kidneys. Its presentation can range from mild skin symptoms to severe organ damage and even death [1]. Hormone Replacement Therapy (HRT) is a recommended approach that has been utilized in some studies for SLE patients. It has the potential to alleviate menopausal and postmenopausal symptoms, including hot flashes, night sweats, sleep disturbances, mood swings, vaginal dryness, and anxiety [2].

HRT replenishes hormones such as estrogen, progesterone, or both, which decline during menopause. HRT may cause side effects such as headaches, breast pain and tenderness, nausea, hair loss, and other symptoms similar to menopause, but in most cases, it does not cause any significant complications [3]. In this regard some previous studies show that HRT increases SLE flares including fatigue, joint pain, rash, fever, and organ inflammation. They also showed that hormonal interventions increase the risk of thrombosis in SLE patients. However, some other studies did not confirm these results and confess that HRT by increasing the level of estrogen and progesterone could only decrease vasomotor symptoms in menopause patients with SLE [1,4,5]. Due to this inconsistency, in this study we aim to have a

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brief review of the effect of HRT on SLE complications with a focus on its cutaneous manifestations.

LITERATURE REVIEW

Cutaneous manifestations of SLE

Skin manifestations, as one of the most diagnostic signs of SLE, contain a broad range of skin complications. There are some conditions that are unique to SLE include chronic Cutaneous Lupus Erythematosus (CLE), subacute CLE, and acute CLE. Specific types of skin lesions for these groups have been mentioned (Table 1) [6].

Cutaneous Lupus Erythematosus (CLE)	Subtypes
Acute CLE	Localized
	Generalized
	TEN-like
Subacute CLE	Annular
	Papulosquamous
	Erythrodermic
Chronic CLE	Discoid Lupus Erythematosus (DLE)
	Hypertrophic mucosal lupus erythematosus
	Panniculitis
	Chilblain Lupus Erythematosus (CHLE)
	Lupus Erythematosus Tumidus (LET)

Table 1: Type of Cutaneous Lupus Erythematosus (CLE).

Besides this SLE presents nonspecific skin lesions (such as palpable purpura, urticarial vasculitis, vasculopathy, degos disease-like lesions, secondary atrophic blanche, periungual telangiectasias, livedo reticularis, thrombophlebitis, raynaud phenomenon, erythromelalgia, sclerodactyly etc.) more commonly, these manifestations occur more often alongside active systemic disease and may also be present in other diseases, such as other connective tissue disorders [6].

DISCUSSION

HRT in SLE patients

HRT is a common treatment for menopausal symptom, osteoporosis, vaginal atrophy, hormone imbalance in PCOS,

premature ovarian failure and many other conditions. It has been the subject of debate for decades, recent studies on non SLE populations suggest that HRT, when initiated soon after menopause, can reduce CHD and mortality, as well as decrease menopausal symptoms and the risk of osteoporotic fractures. In younger, healthy women, the benefits of HRT may outweigh the risks, making it a potential prevention strategy for CHD and all-cause mortality [7].

In female SLE populations, practitioners have been concerned about prescribing hormonal therapy for many years because of the widely held view that these medications may activate the underlying disease. Buyon JP, et al. [5], in one of the largest prospective evaluation of the safety of HRT in postmenopausal women with SLE showed that adding a short course of HRT is associated with a small risk for increasing the natural mild to moderate flares of lupus while no significant differences in severe flares of treatment and control group was found and regardless of hormone therapy overall rate of severe flares was lower in cases with inactive disease or stable active SLE [1].

HRT in premenopausal SLE patients

In premenopausal ages, hormonal therapy can be received in order to prevent pregnancy as Oral Contraceptives (OCP) or as infertility treatment. SLE patients who have conceived a child and have an unplanned pregnancy may experience increased disease activity and skin manifestations such as rash, but these were significantly less common in patients who underwent planned pregnancy or Assisted Reproductive Technology (ART). Prior to Ovulation Induction Therapy (OIT), SLE patients may have experienced discoid and skin lesions, but the incidence of these complications did not increase after OIT. In SLE patients in childbearing age, OCP are rarely prescribed, because of increasing the unnecessary infliction of side effects [1,8,9]. Accordingly, SLE patients who underwent OIT/ART experience fewer dermatological complications compared to those who have an unplanned pregnancy without prior ART/OIT and the use of OCP in premenopausal SLE patients is not recommended.

HRT in perimenopausal SLE patients

The combination of estrogen and progestin has been shown to improve vasomotor symptoms in SLE patients experiencing menopause. However, this combination did not have a significant impact on other menopausal symptoms. HRT was found to increase the risk of thrombotic events, so it should only be used in women with significant vasomotor symptoms. Additionally, HRT did not significantly alter the course of disease activity in SLE patients transitioning through menopause, but it did increase the risk of developing thrombosis. In menopausal patients, there was often a worsening of flares about a year after HRT, but recent studies have not shown any dermatological complications in these patients [9-12]. In summary, HRT can improve vasomotor symptoms but also comes with an increased risk of thrombosis. In regard of dermatological complications more studies should be conducted.

HRT in postmenopausal SLE patients

Latest clinical investigations in different facilities on HRT in postmenopausal women have vividly indicated that it is safe to go on HRT due to the fact that not only it has good tolerability in patients with SLE and reduces the Blatt-Kupperman Index (KI) it also has therapeutic benefits for increasing the Bone Marrow Density (BMD) of patients with osteopenia whom are on regular dose of prednisolone and suffering from its adverse effects [4]. In addition, the risk-benefit balance of using HRT in younger healthy women (aged 50-60 years) is positive and start year of HRT treatment in postmenopausal SLE patients should be considered too.

CONCLUSION

Due to the mild increase in SLE flare and its cutaneous manifestations by HRT, after considering the patient specific cost-effectiveness of intended intervention, SLE patients can receive HRT safely. Besides the heavy burden of SLE in females and wide application of HRT in the treatment of menopausal symptom, osteoporosis, vaginal atrophy, hormone imbalance in PCOS, premature ovarian failure and many other conditions, lack of evidences in this area could be a substantial issue. Thus, we highly recommend to conduct high quality cohort studies or randomized controlled trials in order to clarify the real effect of HRT on SLE patents.

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