

Low-molecular-weight heparin (LMWH) in recurrent reproductive failures (RRF)

단국의대 제일병원 박찬우

Considering the association between thrombophilia and pregnancy loss, the efficacy of antithrombotic therapy, heparin in particular, for women with recurrent reproductive failures (RRF) including recurrent pregnancy loss (RPL) and repeated implantation failure (RIF).

The mechanism of action of heparin is mostly attributed to binding to and potentiating the action of antithrombin (Hirsh et al., 2001). This anticoagulant activity may reduce thrombosis in the (micro) vasculature of the placenta. Furthermore, heparin promotes extravillous trophoblast differentiation in placental tissue in vitro (Quenby et al., 2004). Low-molecular-weight heparin (LMWH) reduces antiphospholipid antibody binding to trophoblast cells in vitro (Di Simone et al., 1999).

Despite the uncertainty of mechanisms of action, physicians frequently prescribe antithrombotic agents in pregnancy. These studies have been performed in various subgroups of women: (i) women with antiphospholipid syndrome; (ii) women with recurrent pregnancy loss and inherited thrombophilia; and (iii) women with unexplained recurrent pregnancy loss.

(i) For women with antiphospholipid syndrome clinicians worldwide have adopted practice to prescribe antithrombotic agents. (ii) Results from several small retrospective and prospective cohort studies in women with inherited thrombophilia, with or without previous pregnancy complications, suggest a beneficial effect of antithrombotic therapy to reduce pregnancy complications. (iii). Based on the available evidence (de Jong et al., 2014), various guidelines now recommend against the use of antithrombotic agents in women with unexplained recurrent pregnancy loss.

To provide a solid base for clinical practice, further studies on the role of LMWH in reproduction, as well as randomized controlled trials of antithrombotic therapy in women with RRF are needed.

References

- Hirsh J, Warkentin TE, Shaughnessy SG, Anand SS, Halperin JL, Raschke R, Granger C, Ohman EM, Dalen JE. Heparin and low-molecular-weight heparin: mechanisms of action, pharmacokinetics, dosing, monitoring, efficacy, and safety. *Chest* 2001;119:64S–94S.
- Quenby S, Mountfield S, Cartwright JE, Whitley GS, Vince G. Effects of low-molecular-weight and unfractionated heparin on trophoblast function. *Obstet Gynecol* 2004;104:354–361.
- Di Simone N, Caliandro D, Castellani R, Ferrazzani S, De CS, Caruso A. Lowmolecular weight heparin restores in-vitro trophoblast invasiveness and differentiation in presence of immunoglobulin G fractions obtained from patients with antiphospholipid syndrome. *Hum Reprod* 1999;14:489–495.
- de Jong PG, Kaandorp S, Di Nisio M, Goddijn M, Middeldorp S. Aspirin and/or heparin for women with unexplained recurrent miscarriage with or without inherited thrombophilia. *Cochrane Database Syst Rev.* 2014 Jul 4;(7):CD004734.