**Abstract**

**Objective:** Endometriosis is a bothersome disease affected women worldwide, the mechanism of disease development is still under investigation. Several inflammatory responses after clinical hyaluronic acid (HA) use were reported. Cyclooxygenase (COX)-2 mediated inflammation pathway is involved in the pathogenesis of endometriosis. Thus, we tried to investigate the inflammatory role of hyaluronic acid in endometriosis.

**Materials and methods:** Peritoneal fluid was collected in endometriosis and disease-free patients for the measurement of HA. Endometriotic stromal cells were treated with IL-1β and HA and expression of COX-2 was evaluated. Mice model of endometriosis was established and treated with fluid or gel form of HA. Endometriotic lesion size and weight were recorded and level of COX-2 was evaluated by immunohistochemistry staining.

**Results:** The level of HA in the peritoneal fluid had no statistically significant difference between normal, early and advanced stage endometriosis patients. The overexpression of COX-2 protein was detected when treating endometriotic stromal cell with HA in the presence of IL-1β (P < 0.001). The endometriotic lesion size was reduced in mice model when treated with higher concentration gel form HA. It further showed less proportion of strong COX-2 expression compare of gel form HA to fluid form treatment in COX-2 expression score of endometriosis lesion.

**Conclusion:** Both proinflammatory evidence, elevated COX-2 expression, and anti-inflammatory result, reduced endometriosis lesion size and COX-2 expression score, were noted in our study after treating HA in in vivo and in vitro models. We hypothesized it is possible that HA may induce an acute proinflammatory response followed by chronic anti-inflammatory reaction in the formation of endometriosis.