Myoma (A Review)

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Abstract

Myoma or fibroids are benign, smooth uterine muscle, composed of a large amount of external cellular matrix including collagen, fibronectin, and protoglichane. Searches were conducted by two independent researchers in international (PubMed, Web of science, Scopus and Google scholar) and national (SID, Magiran) databases for related studies from the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned. The specific search strategies were created by a Health Sciences Librarian with expertise in systematic review search using the MESH terms and free terms according to the PRESS standard. The occurrence of myoma is very common among women. Although the main cause of myoma is still unknown, there have been recent advances in understanding the hormonal, genetic, growth and molecular morphology of these complications. These factors are likely to trigger genetic changes in the myoma cells and cause abnormalities in the smooth muscle of the uterus.

Introduction:

Myoma or fibroids are benign, smooth uterine muscle, composed of a large amount of external cellular matrix including collagen, fibronectin, and protoglichane (1).

Methods:

1.1. Search strategy:

Searches were conducted by two independent researchers in international (PubMed, Web of science, Scopus and Google scholar) and national (SID, Magiran) databases for related studies from the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned. The specific search strategies were created by a Health Sciences Librarian with expertise in systematic review search using the MESH terms and free terms according to the PRESS standard. After the MEDLINE strategy was finalized, it was adapted to search in other databases. Accordingly, PROSPERO was searched for ongoing or recently related completed systematic reviews. The key words used in the search strategy were “Myoma” which were combined with Boolean operators including AND, OR, and NOT.

1.2. Study selection:
Results of the Literature review were exported to Endnote. Prior to the formal screening process, a calibration exercise was undertaken to pilot and refine the screening. Formal screening process of titles and abstracts were conducted by two researchers according to the eligibility criteria, and consensus method was used for solving controversies among the two researchers. The full text was obtained for all titles that met the inclusion criteria. Additional information was retrieved from the study authors in order to resolve queries regarding the eligibility criteria. The reasons for the exclusion criteria were recorded. Neither of the review authors was blinded to the journal titles, the study authors or institutions.

Prevalence:
The occurrence of myoma is very common among women. A randomized study was conducted on the prevalence of myoma between 35 to 49 year old white-American Indigo-American women and African-American black women. The mortality rate among black women at age 35 was 60% and increased to 80% by age 50. In white women, the prevalence was 40% at age 35 and increased to 70% by age 50 (2).

Etiology:
Although the main cause of myoma is still unknown, there have been recent advances in understanding the hormonal, genetic, growth and molecular morphology of these complications. These factors are likely to trigger genetic changes in the myoma cells and cause abnormalities in the smooth muscle of the uterus.

These changes include increased estrogen receptors in the uterus, hereditary changes, hormonal changes, or in the absence of blood to the tissue in the uterine wall during the menopause (3).

Genetic structure:
Myomas have a monoclonal structure and about 40% of them have been chromosomally altered to other uterine walls (4). These changes include the movement of chromosomes 12 and 14, the removal of chromosome 7 and an additional chromosome at the chromosome 12 position; chromosomal changes are seen mainly in large and symptomatic myoma. The remaining 60% have unidentified mutations (5).

More than 100 genes have been identified that increase or decrease receptors at the level of myoma cells; these receptors include estrogen receptor alpha and beta, and progesterone A and B receptors, growth hormone receptor, prolactin and collagen genes and extracellular matrix. Many of these genes regulate cell growth, differentiation, proliferation and cell division (6).

Hormones:
Both estrogen and progesterone appear to be the driving force behind the development of the myoma. Myoma are rarely seen in adulthood, and their formation rates increase after puberty at reproductive age and decrease again after menopause.

Factors that increase long-term estrogen levels include obesity and early menstruation.

Factors such as exercise and couples' sexual intercourse reduce the level of progesterone and protect the body against the formation of myoma.

Although blood levels of estrogen and progesterone are the same in women who have myoma and those who do not have these complications, the blood levels of estradiol are much more pronounced in those with myoma.

Estrogen production occurs with increasing levels of aromatase in the myoma tissue. The aromatase is an enzyme that converts androgen into estrogen. In the cells of the myoma, there is a decrease in the level of enzymes that convert estradiol to estrogen, which causes the accumulation of estradiol in the cells. This increase in estradiol leads to increased expression of estrogen and progesterone receptors in the cell and increases the response to estrogen and myoma growth.

In addition to this theory, myoma of menstrual cycle shows more proliferation than other cells in the uterine wall (7).

Biochemical, clinical, and pharmacological research also confirms that progesterone is important in the pathogenesis of myoma. In the cells of the myoma, the number of progesterone receptors A and B increases compared to other cells (8). The highest mitosis has been observed during the secretion phase of the progesterone production peak, and the number of mitoses in the women treated with medroxyprogesterone acetate was much higher than that of the other subjects in the control group (9).

GNRH agonists reduce the size of the myoma, but simultaneous administration of progestin and
GNRH prevents the myoma size from falling. A study showed that the use of progestin-contraceptives alone would increase the risk of developing myoma (10).

Functioning as a progesterone receptor modulus, mifepristone decreases the size of myoma (11).

Growth factors, proteins, and polypeptides made in the form of smooth muscle cells and fibroblasts seem to stimulate the growth of myoma by increasing the extracellular matrix.

Some myoma-related growth factors include TGF-β, EGF, PDGF, VEGF, IGF, and prolactin. The expression of many of these growth factors increases in myoma and increases the proliferation of smooth muscle cells (12).

Types of fibroids

The uterine fibroids are divided into several categories according to the location of the uterus wall:

- **Intramural myoma:**
  
  These types of myoma are located inside the uterus. They may be so enlarged that they are drawn to the uterine cavity or the serosa surface and some of the serous can be transmitted to the mucosal surface.

- **Sub-mucosal myoma:**
  
  These types of myoma are derived from myometrium cells located just below the uterine endometrium (uterine cavity cover). These neoplasms move toward the uterus.

  **The scope of this extension is divided into three types according to the International Federation of Obstetrics and Gynecology (FIGO):**

  Zero Type: Fully contained within the uterine endometrium

  Type One: Less than 50% having gone into myometrium

  Type two: 50% or more in the middle of myometrium

- **Sub serosa myoma:**
  
  These myoma are caused by the myometrium surface of the erythrocytes of the uterus. They may have a flat or solid state and are located in the muscle.

- **Cervical:**

  These myoma are more in the cervix than in the trunk. (13 and 14)

**Figure 1- A view of the position of various fibroids in the uterine tissue**

**References:**


