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Analysis of medication data of women with uterine fibroids based on data mining technology

Jianyan Xuan [a,1], Guangfei Deng [b,1], Rui Liu [a], Xiangdong Chen [a], Yuhua Zheng [a,*]

[a] Department of Gynaecology, Maternal and Child Health Hospital of Foshan, No. 11 Renmin West Road, Chancheng District, Foshan City, 528000, Guangdong Province, China
[b] School of Basic Medical Sciences, Guangzhou Medical University, Jingxiu Road, Panyu District, Guangzhou City, 511436, Guangdong Province, China

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ABSTRACT

The purpose of this study was to analyze the characteristics of the diagnosis and treatment of female uterine fibroids based on data mining technology and the medication rule. Clinical literature related to the treatment of uterine fibroids by Chinese National Knowledge Infrastructure (CNKI) from 2004 to 2018 were searched, and the literature meeting the requirements were selected according to the inclusion criteria and exclusion criteria. The contents of the prescription were recorded into the database, and the results of drug frequency, common drugs and core rules, etc. were obtained by the rule analysis of the software, so as to analyze the medication rules of modern doctors in treating uterine fibroids. Through research and analysis, it showed that common clinical drugs include leuprorelin (GnRH-a), danazol (androgen), gestrinone (progestin), mifepristone (progesterone receptor antagonist), and some cases of combination therapy. Based on the analysis of the frequency of drug, treatment effect and adverse drug reactions, it was found that the clinical application of mifepristone in the treatment of uterine fibroids was relatively common, with significant drug effect and mild adverse reactions, which was worthy of clinical promotion and application. Therefore, the results of this study provide a new basis for the clinical and basic research of traditional Chinese medicine in the treatment of uterine fibroids, but it still needs the verification of expert interpretation, experimental research and other methods.

Introduction

Uterine fibroids are one of the most common benign tumors in women and are derived from the monoclonal proliferation of uterine smooth muscle cells. Uterine fibroids are more common in women of childbearing age and are greatly affected by estrogen and progesterone. The incidence of uterine fibroids is related to race, with the highest incidence among African Americans, accounting for 80% [1]. In addition, the high-risk factors of fibroids also include age, early menarche, late childbirth, coffee, alcohol abuse, gene mutation, obesity and other problems [2]. There are a variety of clinical manifestations of uterine fibroids, including menorrhagia, prolonged menstruation, pain, anemia, abortion, infertility, abnormal band, bladder and rectal compression symptoms. Uterine fibroids will not only affect the fertility of patients, but also affect the quality of life and psychological status of patients. In terms of infertility, infertility caused by uterine fibroids alone accounts for less than 3% of all infertile patients [3,4].

Studies have shown that normal tissue around the uterus in patients with uterine fibroids contains significantly less estrogen and progesterone receptors than fibroids. In patients with uterine fibroids, the normal tissue surrounding the uterus contains significantly reduced estrogen and progesterone receptors than in fibroid tissue. In 2014, the state food and drug administration has approved Mifepristone (RU486), gonadotropin-releasing hormone agonist (GnRH-a), gossypol and some traditional Chinese medicines for the treatment of uterine fibroids [5,6]. Recent studies have shown that mifepristone not only directly inhibits follicular development and secretion in the ovary, but also may inhibit the secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH). Therefore, the drugs commonly used in the clinical treatment of uterine fibroids are drugs that can reduce the level of estrogen and progesterone. For example, the use of gonadotropin receptor agonists

and antagonists, danazol, gestrinone, cabergoline, and mifepristone can reduce the uterine volume and tumor size, so as to improve the symptoms associated with this disease [7].

Data mining (DM) refers to the method and technology of discovering and extracting hidden, previously unknown and potentially useful information and knowledge from a large amount of Data, which is also known as database knowledge discovery (KDD) [8]. At present, there is no unified definition of data mining, which is generally accepted as "a non-trivial process of effective, novel, potentially useful and ultimately understandable patterns from a large amount of data" [9–11]. Since the 1990s, data mining technology has been applied in the Chinese medicine industry [12,13]. Up to now, DM has been applied in almost all researches in the field of traditional Chinese medicine, such as ancient books of traditional Chinese medicine, modern literature, diagnosis of traditional Chinese medicine, syndrome differentiation and treatment, traditional Chinese medicine, science of prescription, experience inheritance of traditional Chinese medicine practitioners, etc., which has effectively promoted the development of traditional Chinese medicine [14,15]. In this study, the research method of data mining was adopted to establish the recipe database of uterine fibroids, and then the data was derived. Statistical software SPSS20.0 and SPSS Modeler14.1 were used to mine the data, so as to explore the characteristics of the diagnosis and treatment of female uterine fibroids and the medication rule.

Research contents

Source of literature

The main page of CNKI was opened and the advanced search was selected. The search term "full text" was selected, the search words "uterine fibroids" and "medicine" were selected, the matching term "fuzzy" was selected, and the sequencing method "time" was selected. The search term was from January 1, 2004 to December 31, 2018, and the rest was the default. From 2004 to 2018, 1152 clinical literatures related to the treatment of uterine fibroids by western medicine on CNKI were collected. According to the inclusion criteria and exclusion criteria, a total of 328 literatures meeting the requirements were selected.

Inclusion criteria: Clinical report or clinical trial on the treatment of uterine fibroids with integrated Chinese and western medicine or traditional Chinese medicine; expert experience (with complete prescription); and the literature of prescribed drugs in specific dosages. *Exclusion criteria*: Literature on prevention of recurrence of uterine fibroids after surgery; literature in which prescribed drug doses are not indicated or published or where prescribed drugs are lacking; literature review and animal experiments; literature of enema and external application for the treatment of TCM; literature of the same prescription appears repeatedly; and literature reports on the treatment of uterine fibroids without traditional Chinese medicine.

Establishment of the database

According to the above screening conditions, the prescription that meets the requirements were screened. Excel was used to enter and establish a database of prescriptions for uterine fibroids. A total of two groups of databases were established. The first database was the general database, containing five items of prescription number, prescription name, prescription source and symptoms, and traditional Chinese medicine. The second database was a prescription database composed of traditional Chinese medicine, which was recorded according to whether a certain medicine was in a certain prescription, the presence of which was set as T, and the absence of which was set as F. This library could be imported into SPSS20.0 for descriptive statistics, and it could also be imported into SPSS Modeler14.1 for association rule analysis.

Statistical software and data mining methods

First, descriptive research methods: The frequency analysis in the descriptive analysis method of SPSS20.0 software is used to process the data of drugs and syndromes. The descriptive analysis of this study mainly refers to the analysis of drug frequency.

Second, the association rule method: The relationship between drugs and drugs is analyzed by the Apriori method of SPSS Modeler 14.1. Association rules are used to discover the correlation between different items that occur in the same event, that is, to find out the correlation between all subsets of items and attributes that occur frequently in the transaction and between items. In the study of traditional Chinese medicine, it is mainly used to analyze the correlation between drugs and symptoms, drugs and pathogenesis, and symptoms and pathogenesis. In this study, association rules are mainly used to explore the relationship between drugs and drugs and between drugs and symptoms. The task of association rule mining is to find the rules in the transaction database that the support degree and confidence degree meet the minimum and minimum confidence levels specified by the user. The strength between its items is represented by support degree, confidence degree and promotion degree, among which confidence degree can better represent the strength of their association rules.

Research results

Drug statistics

In this study, the Western medicines in the 328 literature on the treatment of uterine fibroids by Western medicine in the past 15 years were classified. The selected literature mainly included leuprolide (GnRH-a), danazol (androgen), gestrinone (progesterone), mifepristone (progesterone receptor antagonist) and so on. When the data of all literature were summarized, it was found that the treatment of uterine fibroids with western medicine was mainly used in the following situations: patients with uterine fibroids and no clinical symptoms confirmed by gynecological examination and B-ultrasound examination; patients aged between 25 and 49 years; patients with a normal menstrual cycle and a range of 22–34 days; patients with uterine body size less than 10 weeks of pregnancy, tumor diameter greater than 2 cm and less than 5 cm and without menopause; patients without contraindications for cardio-cerebral vascular, liver and kidney dysfunction, and coagulopathy; patients who were not treated with other drugs for half a year and were excluded from malignant lesions of endometrium and cervical duct; and patients who can adhere to oral medication during observation.

Among the 328 references selected, there were 52 cases (15.9%) of leuprorelin, 60 cases (18.4%) of danazol, 44 cases (13.4%) of gestrinone, and 78 cases (23.8%) of mifepristone. In addition, there were 47 cases (14.3%) of mifepristone combined with danazol, and 47 cases (14.3%) of mifepristone combined with guizhifuling capsule and Gong Liu Xiao Jiao Nang, which were represented by A–F respectively, as shown in Figs. 1 and 2.

Analysis of drug effects

Gestrinone has moderate anti-estrogen progesterone action and anti-gonadal effects. It can increase the content of free testosterone in serum, reduce the level of gonadal binding globulin, inhibit pituitary function, decrease FSH and LH, decrease estrogen, so that the ectopic lesion loses hormone support and shrinks, and the pelvic
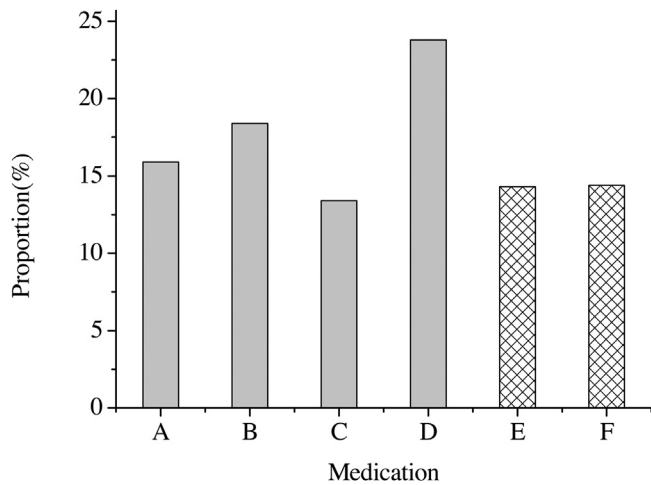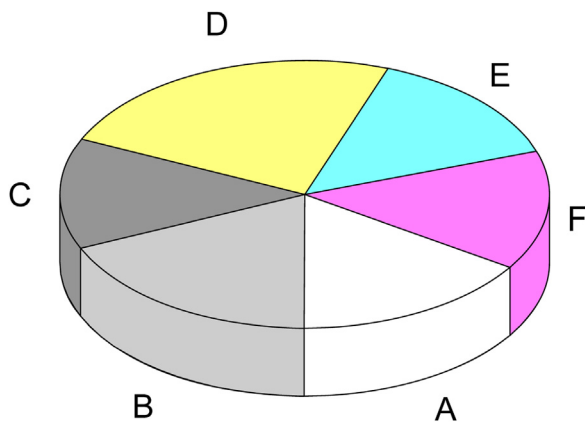
Fig. 1. Drug statistics.

Fig. 2. Statistics on drug selection.

Table 1
Analysis of adverse drug reactions.

Medicine	Liver damage	Gastrointestinal reaction	Vertigo	Endometrial thickening	Total incidence rate
A	0	4	5	0	17.3%
B	1	3	4	0	13.3%
C	0	3	1	0	11.3%
D	2	3	3	2	12.8%
E	1	2	2	1	12.8%
F	0	0	2	1	6.4%

Fig. 3. Comparison of adverse drug reactions.

environment is improved. The pharmacological effects of danazol are relatively complex, which can directly inhibit the release of GnRH, reduce FSH and LH, thereby inhibiting the generation of estrogen and progesterone in the ovary, and increasing the metabolism of estrogen and progesterone.

Mifepristone and leuprolide are the main drugs used in the treatment of uterine fibroids at present. The long-term application of mifepristone can inhibit ovarian function, cause amenorrhea, and reduce estrogen progesterone levels. Leuprolide is a highly active analog of luteinizing hormone releasing hormone produced by the lower part of the hypothalamus. It can effectively inhibit pituitary production and release of the gonadal hormone, and then reduce the level of endogenous estrogen and progesterone, so as to promote tumor atrophy.

After many studies, it has been found that the treatment of uterine fibroids with mifepristone can achieve good results no matter how large or small the dose of drugs is used. Mifepristone can reduce the level of estrogen and progesterone in the body, thereby reducing the uterine volume and fibroid volume and improving clinical symptoms. Meanwhile, in the treatment of uterine fibroids, mifepristone can effectively reduce the level and concentration of estrogen and progesterone in patients. In particular, long-term use of small doses of mifepristone can significantly reduce the size of fibroids and is safer. Studies have shown that taking 25 mg/d of high-dose mifepristone has the same effect as taking 12.5 mg/d of low-dose mifepristone, which can both reduce the level of female progesterone, promote the obvious reduction of fibroids and uterine volume, reduce the amount of vaginal bleeding, and improve
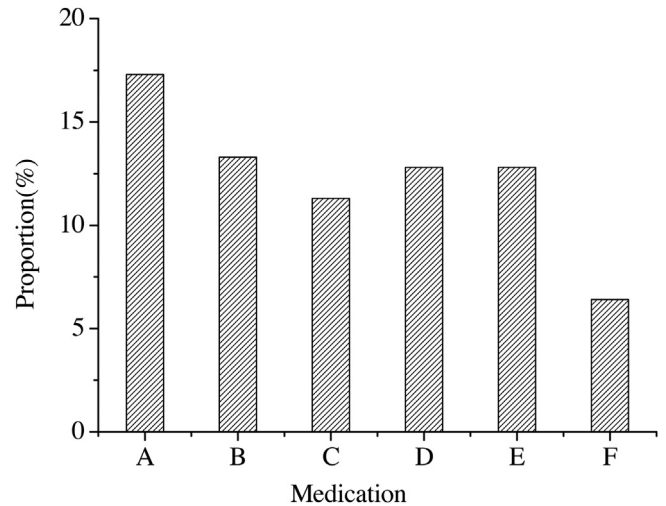
the hemoglobin content. However, low-dose mifepristone is safer and reduces complications such as nausea, hot flashes, night sweats and vaginal dryness.

Analysis of adverse drug reactions

In the analysis of the overall medication, the overall statistical analysis of the probability of adverse reactions appearing in the literature was performed. Based on the data mining algorithm, the five main adverse drug reactions were summarized as liver damage, gastrointestinal reaction, vertigo and endometrial thickening. Adverse fanmusic occurred in 9 cases (17.3%) of leuprorelin, 8 cases (13.3%) of danazol, 5 cases (11.3%) of progesterone, and 10 cases (12.8%) of mifepristone. In addition, there were 6 cases (12.8%) of mifepristone combined with danazol, and 3 cases (6.4%) of mifepristone combined with guizhifuling capsule and Gong Liu Xiao Jiao Nang, which were represented by A–F respectively, as shown in Table 1 and Fig. 3.

Conclusion

Uterine fibroid is a kind of benign tumor commonly observed in female reproductive organs, which is caused by hyperplasia of uterine smooth muscle and connective tissue, also known as uterine leiomyoma. It is one of the more common benign tumors in the human body. Most patients have no obvious clinical symptoms in the early stage of the disease. The rest of the patients are mainly manifested as menstrual changes, such as prolonged menstruation, menstrual volume, leucorrhea abnormalities, and most patients can appear anemia symptoms.

At present, the pathogenesis of uterine fibroids is still unclear, and the treatment methods are varied. With the development of the society, the improvement of people's living standard and

the enhancement of their self-awareness, more and more people hope to avoid surgical treatment, so drug treatment has gradually become an indispensable way. At present, there are many drugs for the treatment of uterine fibroids in the clinic, including gonadotropin-releasing hormone agonist, gestrinone, danazol, guizhifuling capsule, etc., but they still have some shortcomings compared with mifepristone. As a synthetic hormone, mifepristone has the effect of anti-progesterone and low anti-glucocorticoid, and has a strong affinity with the progesterone receptor. It can affect ovary ovulation, at the same time, it can interfere with the role of estrogen and progesterone receptor and vascular endothelial growth factor in fibroid tissue, so as to reduce the level of estrogen and progesterone in fibroid tissue, inhibit blood angiogenesis of fibroid, affect fibroid growth, and reduce the size of uterus.

With the advent of the big data era, big data research also gets more attention. In this study, data mining technology was used to analyze and excavate the prescriptions for the treatment of uterine fibroids in the literature of recent 15 years, the ideas and rules of medication for the treatment of uterine fibroids in the literature were preliminarily explored, and the drug frequency, drug combination, common drug pair and alternative new prescription for the treatment of uterine fibroids were analyzed. In addition, the regularity of medication in the treatment of uterine fibroids was analyzed to provide support and reference for clinical drug use. However, it only draws a conclusion through data mining. How to combine theory with practice still needs further verification of animal experiment, clinical trial and clinical application.

Funding

Conflict of interest

None declared.

Ethical approval

Not required.

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