ISSN: 2472-3703 DOI: 10.6911/WSRJ.202306_9(6).0003

Based on Data Mining to Explore Medication Rules of TCM Enema Combined with Mesalazine In the Treatment of UC

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Abstract

Based on the data mining method, the administration rules of TCM enema combined with mesalazine in the treatment of ulcerative colitis (UC) in journal literature were analyzed, and the basis for screening the best enema treatment drugs was provided. Methods The literatures of clinical randomized trials of TCM enema combined with mesalazine in the treatment of UC published in recent 10 years were retrieved from China National Knowledge Network, Wanfang Data Knowledge Service platform, Wep database and China Biomedical database. The database was established and the data mining was conducted from the aspects of enema high-frequency drug frequency, drug flavor, drug efficacy, drug pair association and so on. 95 literatures were included, including 95 enema formulas. There were 102 commonly used drugs, and 22 drugs with frequency ≥10%. The top 10 drugs were Phellodendri Phellodendri, Rhizoma coptidis, Radix bulgosa, Radix sanguinae, Radix sophora flavescens, Radix scutellariae, Chekhoa, Radix notoginseng and licorice. Among the drugs involved, heat-clearing and moisture-drying drugs accounted for 29.41%, heat-clearing antidotes accounted for 16.18%, lungactivating and astringent intestinal drugs accounted for 7.60%, and astringent and hemostatic drugs accounted for 6.86%. The medicinal properties are mainly cold, warm and flat. The use of medicinal flavor is mainly bitter, sweet and astringent. By drug association analysis, it was concluded that common drug combinations were added or subtracted based on Radix Paektuonis decoction. Conclusion The results of medication law obtained from data mining showed that: clearing heat and drying dampness, astringence and hemostasis, cooling blood and invigorating muscle, at the same time taking into account the spleen and liver tonifying, cold and heat Qi and blood leveling, attacking evil and invigorating. Clinical prescription drugs are mainly based on Baitouong decoction, with the increase or decrease of the syndrome.

Keywords

Data mining; Ulcerative colitis; TCM enema; Medication rule.

1. INTRODUCTION

Ulcerative colitis is a complex chronic, idiopathic inflammatory disease of the colon[1], and its typical manifestations include bloody stools and diarrhea[2]. Most of the lesions start in the rectum and usually extend continuously proximally through part or the entire colon[3]. Abnormalities in organs such as joints, skin, liver, eyes, and the blood system may also occur in a variable proportion of patients. It is characterized by the recurrence and remission of mucosal inflammation. If effective treatment is not taken in time, it can lead to continuous intestinal damage, which puts patients at higher risks of hospitalization, surgery, and colorectal cancer,

ISSN: 2472-3703 DOI: 10.6911/WSRJ.202306_9(6).0003

and may even be life-threatening. For mild and moderate UC, 5-aminosalicylate (5-ASAs) is the first recommended treatment drug, but because of the recurrence of the disease, long-term use of western medicine has many side effects, easy to form dependence, the disease is easy to relapse after drug withdrawal, and the long-term efficacy of medication is also reduced. There are various treatments of traditional Chinese medicine for UC, including oral administration of traditional Chinese medicine, enema of traditional Chinese medicine, acupoint application, and acupuncture. In particular, traditional Chinese medicine enema can directly reach the site of the disease, and the effect is remarkable, which is one of the characteristics of traditional Chinese medicine in the treatment of UC. The European Consensus and the 2018 consensus of the Chinese Medical Association also clearly pointed out that the efficacy of conventional treatment combined with local administration such as enema is better, and rectal administration is the first-line therapy to maintain remission treatment[4]. Clinical studies have also confirmed that traditional Chinese medicine irrigation combined with mesalazine can enhance the clinical efficacy of mild and moderate UC[5-8]. At the same time, some studies have shown that the combination of the two has a certain clinical effect in the treatment of severe UC[9]. The effect of integrated traditional Chinese and western medicine treatment is remarkable, and traditional Chinese medicine treatment can make up for the deficiency of western medicine. However, due to the flexibility of enema prescription, it is difficult to grasp the rules of medication, which brings some difficulties to summarize the experience of medication. This article excavates the prescription rules of traditional Chinese medicine enema combined with mesalazine in the treatment of UC, so as to provide reference for clinical treatment.

2. DATA AND METHODS

2.1. Literature sources

Literature search was conducted in multiple Chinese databases, including China National Knowledge Infrastructure (CNKI), Wanfang Med Online, VIP and CBM. We searched PubMed, Embase, Cochrane Library and other English databases. According to different databases, we used appropriate search terms and logical combinations to collect literatures as comprehensively as possible. The clinical Randomized Controlled trials (RCT) of traditional Chinese medicine enema combined with mesalazine in the treatment of UC were searched.

2.2. Retrieval method

The Chinese database is under the following terms: ulcerative colitis, chronic non-specific ulcerative colitis, ulcer-ulcer, UC, TCM enema, Chinese herbal enema, herbal enema, Chinese medicine prescription, plant, Chinese medicine prescription, prescription, powder, decoction, drink, mesalazine, aminosalicylate, randomized controlled trial, "RCT" and "RCT" were used as the search terms. Colitis, Ulcerative, Idiopathic Proctocolitis, Ulcerative Colitis, Enema, Enemata, mesalazine, m Aminosalicylic Acid, 5 Aminosalicylic acid Acid, randomized controlled trial, RCT, etc. were used as the search terms, and the retrieval mode was professional search, subject words combined with free words.

2.3. Inclusion criteria of literature

1. Randomized Controlled trials (RCTS) published before January 2010 to January 2023;

2. The subjects were patients with definite diagnosis of UC;

3. The experimental group was treated with traditional Chinese medicine enema combined with mesalazine, while the control group was treated with western medicine alone. Traditional Chinese medicine enema must have a complete prescription and composition of traditional Chinese medicine, and have been verified by clinical trials to be effective;

4. Duplicate published papers, only those published in the former were selected.

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2.4. Document exclusion criteria

1. Duplicate publications with similar data;

2. Includes non-clinical research, such as animal model experiments, famous doctors' experience, data mining, review, meta-analysis, classical research, case reports, etc;

3. There is no clear TCM prescription or no specific TCM name in the literature;

4. There are acupuncture, auricular points, acupoint application, psychotherapy and other therapies; 5. The original text cannot be obtained.

2.5. Data entry and processing

After careful screening by two researchers independently, the final literature will be included, but in case of disagreement or uncertainty, a third party Sub-I will participate in the discussion, so that in case of any possible disagreement or uncertainty, a consensus conclusion will be reached. The title, author, publication date, TCM formula, literature type, and treatment regimen of the literature were entered into an Excel spreadsheet for statistical analysis.

2.6. Prescription data analysis

2.6.1 Statistical analysis of frequency

According to the Pharmacopoeia of the People's Republic of China[10] and the Chinese Materia Medica[11], the Chinese herbs included in the TCM prescriptions were unified and standardized, and the TCM names, properties, tastes, meridians and effects were treated, such as "Bletilla" - "Baihe", "processed licorice" - "licorice", etc. The data were also ranked from high to low according to the frequency of occurrence, and the results were derived.

2.6.2 Drug association rule analysis

Through IBM SPSS Modeler18.0 and Apriori algorithm, we established the data flow of "Excel→ type → network" and "Excel→ type →Apriori", and analyzed the association rules of all traditional Chinese medicine, and finally drew the correlation network diagram, so as to better understand the characteristics of traditional Chinese medicine prescription.

3. RESULT

3.1. Literature screening results and basic information

We imported all the literature retrieved into EndnoteX9, established a database, and used the method consistent with the study to screen according to inclusion and exclusion criteria. Finally, 95 literatures with a total of 95 prescriptions were included.

3.2. Analysis of frequency of prescription Chinese medicine

A total of 102 Chinese herbs were used in 95 prescriptions, with a total frequency of 816 times. Among them, Phellodendron amurense was used the most frequently, up to 63 times. The top 10 most frequently used drugs were Phellodendron Huangbai (63 times), Pulsatillae pulsatillae (62 times), Rhizoma coptidis (57 times), Rhizoma pallidus (56 times), Rhizoma cordifolia (43 times), Sophora flavescens (33 times), Scutellaria baicalensis (26 times), Chebula (24 times), Panax notoginseng (23 times), and Licorice (20 times). See Table 1.

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Table 1. Drug frequency distribution (>=20 times)

serial number	drug	frequency/next	frequency/%	serial number	drug	frequency/next	serial number
1	golden cypress	63	66.32	11	Angelica sinensis	19	20.00
2	the root of Chinese pulsatilla	62	65.26	12	patrinia	18	18.95
3	Coptis chinensis	57	60.00	13	the bark of ash	17	17.89
4	rhizoma bletillae	56	58.95	14	smoked plum	16	16.84
5	garden burnet	43	45.26	15	indigo naturalis	15	15.79
6	kuh-seng	33	34.74	16	gallnut	15	15.79
7	Scutellaria baicalensis	26	27.37	17	elecampane	14	14.74
8	myrobalan	24	25.26	18	white atractylodes rhizome	13	13.68
9	pseudo-ginseng	23	24.21	19	cicada slough	12	12.63
10	liquorice	20	21.05	20	earthworm	12	12.63

3.3. Analysis of drug use frequency and frequency

We classified the efficacy of 102 TCMS. The total frequency of efficacy categories was 816 times. Among all the drugs, the use frequency of heat-clearing and dampness drugs was the highest, reaching 240 times, accounting for 29.41%, followed by the use frequency of heat-clearing and antidote drugs was 132 times, accounting for 16.18%, ranking the second. Followed by astringent and astringent drugs, astringent and hemostatic drugs, accounting for 7.60% and 6.86%, respectively. According to Table 2 , it can be clearly seen that the Chinese medicine category > =10 the frequency and frequency distribution of each TCM category.

Table 2. Frequency analysis of various traditional Chinese medicines

Drug class	frequency/next	frequency/%	usage quantity	frequency/%	Chinese medicine (frequency)
Clearing heat and drying dampness medicine	240	29.41	7	6.86	Phellodendron phellodendron (63), Coptis coptidis (57), Sanguisorma sanguinalis (43), Sophora flavescens (33), Scutellaria scutellariae (26), Radix chinensis (17), Radix chinensis (1)
Antipyretic antidote	132	16.18	17	16.67	Rhizoma anthurium (62), Rhizoma septica (18), Rhizoma aestivum (15), Purslane (12), Dandelion (5), Honeysuckle (5), Japanese ampelopsis ampelopsis (2), Lobelia lobelia (2), Japanese Blood vine (2), Japanese Japanese Ampelopsis ampelopsis (2), Chinese andrographitis (1), Forsythia forsythia (1), Poria cocos (1), Houttuynia corydata (1), Purple flower Diadem (1), Lucidum corydata (1)
Collect lung astringent intestinal medicine	62	7.60	7	6.68	Chekhoa (24), Ume (16), Gallnut (15), red stone fat (4), pomegranate peel (1), Schisandra (1), poppy husk (1)
Astringent hemostatic	56	6.86	1	0.98	Bai Wo (56)
qi-tonifying drug	52	6.37	7	6.68	White Rhizoma atractylodes (13), Licorice (20), Radix Astragalus (8), Codonopsis codonopsis (4), Broxed

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					licorice (4), Chinese yam (2), Radix pseudostellariae (1)
hematinic	31	3.80	3	2.94	Angelica sinensis (19), Paeony (11), Ejiao (1)
Antistasis and hemostasis	29	3.55	4	3.92	Panax notoginseng (23), Madder (4), Puhuang (1), blood charcoal (1)
Clearing heat and cooling blood medicine	26	3.19	3	2.94	Purple grass (11), Red Peony Root (9), Moutan bark (6)
Radiate wind chill medicine	18	2.21	3	2.94	Parsnip (8), Schizonepeta (5), Angelica Dahurica (5)
Radiate wind and heat medicine	17	2.08	3	2.94	Cicada slough (12), Pueraria root (4), Bupleurum (1)

3.4. Analysis of the frequency and frequency of the use of medicinal properties

After statistics, we found that all the Chinese medicine properties in this study included cold, heat, warm, cool and flat, and the total frequency of use was 816 times. The most frequently used drugs were cold drugs (541 times), followed by warm drugs (155 times), flat drugs (102 times), cold drugs (12 times) and hot drugs (4 times). The frequency and frequency analysis of each drug are shown in Table 3 and.

Table 3. Analysis of the frequency of TCM properties

drug properties	frequency /next	frequency /%	count	frequency /%	Drug (frequency)
cold	541	66.30	47	46.08	Radix paeoniae (62), Radix Cypress (63), Coptis chinensis (57), Radix Sanguinae (56), Radix Sanguinae (43), Radix sophora flavescens (33), Radix scutellaria scutellaria (26), Radix decidua (18), Radix Qinpi (17), Radix Qingdai (15), Gallnut (15), decidua cicada (12), Purslane oleracea (12), Radix paeoniae alba (11), Comfrey comfrey (11), Radix paeoniae alba (9)), Dantiorrhiza (8), Moutan bark (6), honeysuckle (5), dandelion (5), alum (4), Madder (4), catechucha (4), platyclade leaves (3), rhubarb (3), sophora japonica (3), pearl (3), Japanese ampelopsis root (2), Sophora japonica (2), Schisandra chinensis (1), Prunus schisandra (1), Wort wort (1), Alisma herba (1), Houttuynia Cordata (1), gardenia (1), Borneol (1), fresh skin (1), Bupleurum (1), Psyllium plantageae (1), Andrographolium andrographiae (1), Toona bark (1), Forsythia (1), reed root (1), Oyster (1), Lucia lineri (1), Diploid Purple flower (1)
warm	392	48.04	25	24.51	Panax notoginseng (23), Angelica sinensis (19), Wumei (16), wood fragrance (14), White Rhizome (13), Parsnips (8), Astragalus membranaceus (8), frankincense (6),Atractylodes atractylodes (6), Angelica Dahuricae (5), Nepeta Chinensis (5), red stone fat (4), Rhizoma corydalis (4), areca nut (3), wormwood leaf (3), Cuttlebone (3),Red flower (3), Gladiolus calamus (3), Ligusticum Chuanxiong (2), Acacia saponalis (2), Formosum (1), patchouli (1), Tribulus tribulus (1), Fructus cnidii (1),Pomegranate peel (1)
flat	102	0.13	25	24.51	Chekhoa (24), Glycyrrhiza (20), Gentianum Pall (12), Hemianwort (11), Hemianwort (5), Codonopsis Codonopsis (4), Sundried glycyrrhiza (4), Lobelia chinensis (2), Myrrh (2), Hemianwort Chinensis (2), Chinese yam (2), Ambrosia chinensis (2), Platycodon platycodon (1), keel (1), calcite (1), Pubohuang (1), Eichan (1), Hemianzhi Lotus (1), Radix pseudostellariae (1), peach kernel (1), soil poria (1), corrugated seed (1), blood charcoal (1), poppy shell (1)
cool	12	1.47	2	1.96	Coix seed (8) and Pueraria root (4)
hot	4	0.49	3	2.94	Cinnamon (2) Aconite (1) Dried ginger (1)

ISSN: 2472-3703 DOI: 10.6911/WSRJ.202306_9(6).0003

3.5. Analysis of the use frequency and frequency of medicinal flavor

After statistics, we found that all the Chinese herbs in this study were sour, bitter, sweet, spicy, salty, light and astringent. The total drug frequency was 1340 times, and the bitter drug was the most frequently used, with a frequency of 581 times. Followed by sweet medicine, the frequency was 229 times; The frequency of astringency was 189 times. The frequency of spicy herbs was 163 times. The frequency of sour medicine was 117 times. The frequency of salty medicine was 51 times. The frequency of light medicine was 10 times. The frequency and frequency analysis of each drug are shown in Table 4 and.

Table 4. Analysis of the frequency of traditional Chinese medicine flavor

herbal medicines in a prescription	frequency/next	frequency/%	count	frequency/%	Drug (frequency)
bitter	581	43.36	54	52.94	Phellodendron officinalis (63), Radix Paeonis (62), Rhizoma coptidis (57), Rhizoma Officinalis (56), Sanguinae Sophora (33), Scutellaria baicalensis (26), Chekhoa Chebula (24), Panax notoginseng (23), Candidatum officinalis (18), Radix Qinpi (17), Radix Xylostella (14), Atractylostella Officinalis (13), Gentianae Officinalis (12), Radix Paeoniae Paeoniae (11), Radix cringeoniae Officinalis (11), Radix Paeoniae Radix (9) , Salviopsis miltiorrhiza (8), Moutan bark (6), atractylode (6), frankincense (6), dandelion (5), catechu (4), Rhizoma corydalus (4), Madder (4), areca leaf (3), platycodendron japonica (3), rhubarb (3), calamus japonica (3), mugwort leaf (3), Japanese ampelopsis root (2), Amopsis japonica (2), Myrrh (2), sophora japonica (2), Sophora japonica (2), Myrrh (2), and sophora japonica (2)), cortex dictamni, (1), creat (1), the bark of (1), forsythia, platycodon grandiflorum (1), li (1) (1), light peach kernel (1), blood residual char (1), herba leonuri (1), (1), herba violae gardenia (1) (1), synthetic borneol, radix bupleuri, (1), bergamot briers (1), (1), common cnidium fruit, (1), radix pseudostellariae (1), selfheal (1)
sweet	229	17.09	32	31.37	Bai He (56), Panax notoginseng (23), Licorice (20), Angelica sinensis (19), Bai Chu (13), cicada slough (12), Comfrey (11), Astragalus membranaceus (8), Coix seed (8), Parsnips (8), Dandelion (5), Honeysuckle (5), blood dried (5), red stone fat (4), Codonopsis codonopsis (4), Pueraria root (4), Broxibustion Licorice (4), pearl (3), Cinnamon (2),

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					Chinese yam (2), Fragrant Rhizome (2), ejiao (1), Plantain seed (1), keel (1), reed root (1), calamine (1), Puhuang (1), Radix pseudostellariae (1), soil poria (1), Aconite (1), peach kernel (1)
acerbity	189	14.10	16	15.69	Bulgur (56), Sanguisorba (43), Chekhoa (24) Chin bark (17), gallnut (15), Chekhoa herb (11), alum (4), catechu (4), red stone fat (4), Platycodendron leaf (3), Cuttlebone (3), toona bark (1), keel (1), pomegranate bark (1), schisandra (1), poppy shell (1)
pungent	163	12.16	38	37.25	Angelica sinensis (19), Rhizoma septicum (18), Black plum (16), Woodroot (14), Gentianae Gentiana (12), Parsnapsyrus (8), Atractylodes atractylodes (6), Moutan bark (6), frankincense (6), Angelica Angelica (5), Rhizoma Corydalis (5), Rhizoma Corydalis (4), Artemisia arginiae (3), areca nut (3), red flower (3), Calamus calamus (3), Lobelia lobelis (2), Ligusticum Chuanxiong (2), Radix japonicae (2), Myrrh (2), Cinnamon (2), Radix japonicae (2), Radix saponicae (2), Schistosomiaceae (1), Borneol (1), Radix bupleurum (1), Formosa Formosa (1), Radix aconis (1), Dried ginger (1), Pogostemon Cabernet (1), Tribulus tribulus (1), Fructus cnidii (1), Fructus axanthii (1), Houttuynia Cordata (1), Platycodon platycodon (1), Leonuri (1), Purple Flower Diodin (1)
acidity	117	8.73	11	10.78	Ulmus sanguinalis (43), Chekhoa (24), Gallnut (15), Purslane (12), Paeony (11), alum (4), red stone fat (4), pomegranate peel (1), Schisandra (1), poppy shell (1), Buddha's hand (1)
all	51	3.81	8	7.84	Qingdai (15), Earth Dragon (12), Commosia (11), Cuttlebone (3), Oyster (1), corrugated seed (1), Blood dried (5), pearl (3)
tasteless	10	0.75	3	2.94	Coix seed (8), Poria coix (1), Alisma alisma (1)

3.6. Analysis of frequency and frequency of drug normalization

According to the statistics of the meridians of 102 Chinese herbs in 95 prescriptions, it was found that all the meridians were involved in 12 meridians, with a total frequency of 2390 times. Among them, the top six meridians were the liver meridian of foot-jueyin, the stomach meridian of foot-yangming, the large intestine meridian of hand-yangming, the lung meridian of hand-taiyin, the spleen meridian of foot-taiyin and the heart meridian of hand-shaoyin. Among these meridians, the frequency attributed to the liver meridian of foot-jueyin was the most, reaching 484 times. Table 5 and show the frequency and frequency of the first six drugs in detail.

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Table 5. Frequency analysis of traditional Chinese medicine menstruation

channel tropism	frequency/ next	frequency/ %	count	frequency/ %	Drug (frequency)
Jueyin liver meridian of foot	484	20.25	60	58.82	Rhizoma coptidis (57), Baihe (56), Alum (4), Sanguisornis (43), Sophora flavescens (33), Panax notoginseng (23), Angelica sinensis (19), Septicaria Pall (18), Radix chinensis (17), Radix Qingdai (15), Gentiana Pall (12), Radix cicada slurane (12), Purslane (12), Subterranea (12), Comfrey (11), Sidergrass (11), Radix Paeoniae alba (11) , Red Peony Root (9), Parsnip (8), Salviana miltiorrhiza (8), frankincense (6), atractylodes atractylodes (6), Moutan bark (6), blood dried (5), dandelion (5), Schizonepeta Rhizoma (5), Rhizoma corydalis (4), Madder grass (4), wormwood leaf (3), safflower (3), rhubarb (3), pearl (3), platyclade leaf (3), sophora sophora (3), sophora sophora (2), Rhizoma sophora (2), and Sichuan Ligusticum (2), Myrrh (2), Radix sanguinae (2), Cinnamon (2), Radix saponalis (2), Radix bupleurum (1), Psyllium plantaglium (1), Buddha's hand (1), calamine (1), Toona bark (1), Oyster (1), Puhuang (1), Tribulus tribulus (1), purple flower diadem (1), Prunus prunus (1), Blood charcoal (1), Leonuri (1) (1), Ejiao (1), peach kernel (1), keel (1), Qianli Guang (1), Corrugated Zi (1)
stomach meridian of foot-yangming	371	15.52	32	31.37	Rhizoma coptidis (57), Bai He (56), Radix Radix Radix (62), Sophora sophora (33), Panax notoginseng (23), Glycyrrhiza (20), Septicorrhiza septicorrhiza (18), Radix Xylosa (14), Radix atractylodes (13), Gentiana Pall (12), Coix seed (8), atractylodes atractylodes (6), Dahuricae Dahuricae (5), dandelion (5), honeysuckle (4), Radix Licorice (4), Radix Puerariae Radix Root (4), rhubarb (3), calamus (3), areca nut (3), Ampelopsis ampelopsis (2), saponopsis japonica (1), Toona bark (1), dried ginger (1), patchouli patchouli (1), reed root (1), soil poria (1), Varango seed (1), blood charcoal (1), Buddha's hand (1)
Hand-Yangming	355	14.85	26	25.45	Rhizoma pulsatilla (62), Coptidis (57), Sanguinis (43), Sophora flavescens (33), Scutellaria baicalensis (26), Chekhoa bulgosa (24), Papyrus papyriformis (18), Radix chinensis (17), gallnut (15), Xylobalm (14), Purslane (12), Angelica angelica (5), alum alum (4), red rock fat (4), rhubarb (3), sophora sophora (3), areca nut (3), and Radix chinensis Grass (2), sophora sophora (2), Blood vine (2), Toona bark (1), Andrographis paniculata (1), pomegranate bark (1), peach kernel (1), Schisandra (1), poppy shell (1)
lung meridian	260	10.88	40	39.22	Baihe (56), Scutellaria baicalensis (26), Chebula Chebula (24), Licorice (20), Ume plum (16), Gallnut (15), Xylobalm (14), cicada slough (12), Astragalus Radix (8), Coix seed (8), Angelica Dahuricae (5), Honeysuckle (5), Schizonepeta Nepeta (5), Codonopsis codonopsis (4), catechu (4), pueraria root (4), Sundried licorice (4), alum (4), Leaves (3), Lobelia chinensis (2), Lobelia Chinensis (1), Chinese yam (2), Prunella chinensis (1), poppy husk (1), Houttuynia Corydata (1), eichen (1), Platycodon platycodon (1), Forsythia Fructus (1), Andrographitis chinensis (1), Radix pseudostellariae (1), Gardenia gardenia (1), Borneol (1), Bupleurum chinensis (1), Plantagenae chinensis (1) Seeds (1), Patchouli (1), Buddha's hand (1), Dried ginger (1)
spleen meridian	258	10.79	34	33.33	Rhizoma coptidis (57), Scutellaria scutellaria (26), Licorice (20), Angelica sinensis (19), Ume plum (16), White Rhizome (13), Ground dragon (12), White Peony Root (11), parsnax (8), Astragalus Radix (8), Coix seed (8), frankincense (6), atractylodes atractylodes (6), Codonopsis coix (4), Pueraria rhizome (4), sundried licorice (4), alum (4), Rhizoma corydalis (4), sea Cuttlebone (3), wormwood (3), platyclad (3), rhubarb (3), Chinese yam (2), Myrrh (2), incense (2), cinnamon (2), Radix pseudostellarae (1), fresh white skin (1), dried ginger (1), patchouli (1), borneol (1), Buddhist hand (1), calcaline (1), aconite (1)
heart meridian	220	9.2	31	30.39	Rhizoma coptidis (57), Sophora flavescens (33), Licorice (20), Angelica sinensis (19), Tsuruga (11), Combula (11), Radix sanguinae (8), Moutan bark (6), frankincense (6), Honeysuckle (5), Blooddried licorice (4), catechu (4), pearl (3), safflower (3), Rhizoma calamus (3), Ampelopsis ampelopsis (2) , Lobelia chinensis (2), Myrrh (2), cinnamon (2), Schistoderma chinensis (1), Aconite aconite (1), Borneol (1), Andrographis andrographiae (1), keel (1), peach kernel (1), Gardenia chinensis (1), purple flower Diadem (1), Forsythia forsythia (1), dried ginger (1)

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3.7. Results of drug association rule analysis

By using Modeler18.1 software and Apriori algorithm, we conducted association rule analysis for all involved drugs and set the parameters: support > =20%, confidence > =80%, the maximum number of antecedents is 3, and only the true value of the flag variable is included. Among these parameters, support indicates the probability that the preceding and posterior items occur together, and confidence indicates the probability that the posterior items occur when the preceding items occur. Finally, we obtained 21 drug combinations with a lift greater than 1. All are valid rules. Among them, the drug association rule with the highest support was Rhizoma coptidis, with a support rate of 45.26%, and the drug association rule with the highest confidence was Phellodendron coptidis + Rhizoma coptidis, with a confidence rate of 94.73%. According to the support degree, the order is from high to low, and the results are shown in Table 6. Among them, the drug association rule with the highest support was Rhizoma coptidis, with a support rate of 45.26%, and the drug association rule with the highest confidence was Phellodendron coptidis + Rhizoma coptidis, with a confidence rate of 94.73%. According to the support degree, the order is from high to low, and the results are shown in Table 6.

Table 6. Drug-association Rule Analysis

succedent	antecedent	Support percentage %	Confidence percentage %
rhizoma bletillae	garden burnet	45.26	83.72
golden cypress	garden burnet	45.26	83.73
golden cypress	Coptis chinensis and the root of Chinese pulsatilla	44.21	80.95
Coptis chinensis	the root of Chinese pulsatilla and golden cypress	43.16	82.93
golden cypress	garden burnet and rhizoma bletillae	37.89	80.56
rhizoma bletillae	garden burnet and golden cypress	37.89	80.56
golden cypress	rhizoma bletillae and Coptis chinensis	35.79	82.35
golden cypress	kuh-seng	34.74	84.85
the root of Chinese pulsatilla	garden burnet and Coptis chinensis	31.58	80
golden cypress	garden burnet and Coptis chinensis	31.58	86.67
goldthread	garden burnet and the root of Chinese pulsatilla	28.42	88.89
golden cypress	garden burnet and the root of Chinese pulsatilla	28.42	85.19
golden cypress	garden burnet and Coptis chinensis and the root of Chinese pulsatilla	25.26	83.33
rhizoma bletillae	pseudo-ginseng	24.21	86.96
golden cypress	kuh-seng and rhizoma bletillae	24.21	82.61
golden cypress	garden burnet and rhizoma bletillae and goldthread	24.21	82.61
goldthread	garden burnet and the root of Chinese pulsatilla and golden cypress	24.21	86.96
goldthread	garden burnet and rhizoma bletillae and the root of Chinese pulsatilla	21.05	85
golden cypress	garden burnet and rhizoma bletillae and the root of Chinese pulsatilla	21.05	80
golden cypress	Chinese angelica	20	84.21
golden cypress	kuh-seng and goldthread	20	94.74

ISSN: 2472-3703 DOI: 10.6911/WSRJ.202306_9(6).0003

3.8. Frequency of enema, course of treatment, clinical treatment efficiency

Among the 95 articles, a total of 87 articles described the frequency of enema, of which the highest frequency was twice a day, the lowest was once every other day, and the proportion of once a day was the highest, accounting for 88.51%. Most of them were enema at night before going to bed, accounting for 11.49%. The longest course of enema with traditional Chinese medicine was 6 months and the shortest was 7 days. 90 articles described the course of enema, among which the course of enema was less than 1 month, accounting for 77.78% of the total course of enema. The duration and frequency of enema treatment from high to low were 28 days 56.67%, 21 days 6.67%, 15 days 5.56%, 14 days 5.56%, 16 days 0.12%, 10-14 days 0.12%, 7 days 0.12%. The proportion of January < enema course ≤2 months was 18.89%, and the specific course time and frequency from high to low were 56 days 14.45%, 60 days 0.12%, 50-60 days 0.12%, 42 days 0.12%, 49 days 0.12%. The proportion of 2 months < enema course ≤3 months was 0.12%, and the specific course of treatment was 3 months. Only 2.23% of the patients were treated with enema for more than 3 months, and the specific treatment time was 6 months. There were 47 articles detailing the temperature of enema. According to statistics, 37℃ was the highest frequency, with a frequency of 17 times and a frequency of 36.17%. The results showed that the highest clinical effective rate was 100%, the lowest was 81.25%, and the proportion of clinical effective rate ≥90% was as high as 92.77%.

4. ANALYSIS AND DISCUSSION

4.1. Analysis of high frequency drug use

A total of 95 prescriptions were included in this study, and 102 kinds of drugs were counted. The total use frequency was 816 times, of which 10 Chinese herbs were used more than 20 times. The top 4 drugs were Huangbai, Pulsatilweng, Rhizoma coptidis and Baihe, and the frequency of these four drugs was more than 50%. Huangbai was the most frequently used drug in this data mining, and its frequency of medication was 66.32%. The frequency of Baitouweng, Rhizoma coptidis and Radix blephariae were 65.26%, 60.00% and 58.95%, respectively. It can be seen that these drugs have significant effect in the treatment of ulcerative colitis with traditional Chinese medicine enema. Huangbai, bitter, cold, function of heat drying damp, reducing fire detoxification, in addition to bone steaming. In Shennong's Classic of Materia Medica[12], Huangbai is called berimu, "the main five hides, heat in the intestines and stomach... Intestinal hemorrhoids, antidiarrheal..." . According to the results of modern medical research, berberine, the active ingredient in Phelloberia Huangbai, not only helps to improve the expression of tight junction proteins in the intestine and restore the mechanical defense function of the intestinal wall[13], but also effectively prevents the transport of κB, has a good anti-inflammatory effect[14], protects the intestinal mucosal barrier, and promotes the normal immune response of the body. Berberine can play a role in the prevention and treatment of intestinal infectious diseases caused by intestinal microecological imbalance by regulating the structure, species, abundance and production of active metabolites of intestinal microflora[15]. Rhizoma coptidis, bitter, cold, function of heat drying damp, reducing fire detoxification. Rhizoma coptidis is the product of severe bitter and cold, which can clear the dampness and heat of upper coke, middle coke and lower coke[16]. In ancient times, Rhizoma coptidis was used as the most for the treatment of dysentery, and it was the king for the treatment of dysentery. Shennong Bencao Jing (Shennong's Classic of Materia Medica) recorded that Huang Lian could "suffer from eye pain caused by hot air, SOB from canthus, and diarrhea caused by abdominal pain caused by enteropathy"[17]. Modern studies have shown that substances contained in Coptis rhizoma have broad-spectrum antibacterial[18] and reduce mucosal inflammation[19-20]. Baitouweng, with the effect of clearing heat and detoxication, cooling blood and stopping dysentery, is one of the most commonly used traditional Chinese medicine

ISSN: 2472-3703 DOI: 10.6911/WSRJ.202306_9(6).0003

in the treatment of UC. Studies have shown that Baitouweng has a variety of functions [21], including antibacterial, anti-inflammatory, anti-cancer, immune regulation, ulcer healing promotion, and inhibition of intestinal motility. Its taste is bitter, sweet and astringent, and its nature is slightly cold, which has good effects of hemostasis and swelling, muscle growth and sore-collecting. It is known as "the best surgical method for astringent and closing, stopping bleeding into the lung, growing muscle and treating sore-collecting"[22]. Modern pharmacological research[23] believes that leucorrhea has hemostasis, antibacterial, protection of tissue healing, and can also help the repair of intestinal mucosa, inhibit inflammatory response, and restore immune balance. Therefore, it is widely used in the treatment of various bleeding, burns and ulcer diseases, and can significantly improve the effect of hemostasis and coagulation.

4.2. Analysis of major drug classes

Through this data mining, it was found that the main categories of Chinese medicine enema in the treatment of UC were heat-clearing drugs, astringent drugs, hemostatic drugs, tonic drugs, and surface drugs. Among them, heat-clearing drugs accounted for 48.78%, mainly heat-clearing and dampness drugs, heat-clearing and detoxifying substances; Hemostatic drugs accounted for 10.41%, mainly astringent hemostatic drugs and blood-stasis and hemostatic drugs. Tonic deficiency drugs accounted for 10.17%, mainly for invigorating qi and blood, and astringent drugs accounted for Through this data mining, it was found that the main categories of Chinese medicine enema in the treatment of UC were heat-clearing drugs, astringent drugs, hemostatic drugs, tonic drugs, and surface drugs. Among them, heat-clearing drugs accounted for 48.78%, mainly heat-clearing and dampness drugs, heat-clearing and detoxifying substances; Hemostatic drugs accounted for 10.41%, mainly astringent hemostatic drugs and blood-stasis and hemostatic drugs. Tonic deficiency drugs accounted for 10.17%, mainly for invigorating qi and blood, and astringent drugs accounted for 7.60%, mainly for invigorating lung and astringent intestine. The surface medicine accounted for 4.29%, mainly dispersing wind-cold medicine and dispersing wind-heat medicine. The results showed that the treatment of UC with traditional Chinese medicine enema was mainly focused on clearing heat, stopping bleeding, removing blood stasis and tonifying deficiency. This is also in line with the basic pathogenesis of the disease, which is deficiency of qi and accumulation of dampness, heat, silt and poison. The occurrence of heat-clearing drugs accounts for about half of the whole medication, and UC is mainly caused by heat and dampness. As pointed out in the "Similar Syndrome Treatment and Reduction of * Dysentery" [24], "the disease is caused by the wet steaming and heat of the stomach, resulting in the condensation of qi and blood, the stagnation of dfecal residue, the absorption into the large and small intestine, the scraping of fat fluid, and the injection of purulent

blood". The pathogenic factors of dampness and heat impede the intestinal bowels, and the fire, poison and blood stasis fight each other, the intestinal conduction is disrupted, and the lipid collaterals are damaged. Therefore, in enema, commonly used Huangbai, scutellaria, Coptidis and other drugs to clear heat and detoxify, and combined with Baitouweng, Qin PI, patrinia paste and other drugs to cool blood and stop bleeding and eliminate carbuncle. The main symptoms of the disease are dysentery, red, white, pus and blood. In the course of the disease, heat breaks the blood and the turbidified poison is breached, so the spleen does not control the blood outside the vein, and the blood overflows outside the vein and causes bleeding. Or disease long spleen disease transmission kidney, kidney qi by pathogenic factors, the slippage can not help. Traditional Chinese medicine enema can directly reach the disease in time to stop bleeding, such as panax notoginseng, rubia, Typha and other drugs to stop blood stasis, bleeding without leaving stasis. Use white and astringent to stop bleeding and grow muscle. With chebula, black plum, gallnut and other drugs, lung astringent intestine, but should pay attention to chronic

ISSN: 2472-3703 DOI: 10.6911/WSRJ.202306_9(6).0003

long shigeru Ji clear heat attack too much, so as not to damage the qi, for acute violent shigeru ji too early firm astringent, so as not to close the door. Throughout the tonic deficiency medicine, most of the use of Atractylodes, licorice, Astragalus, Angelica, Radix paeoniae and other drugs, and their meridians are mostly spleen and stomach meridians. Spleen deficiency is the root of this disease. When qi is insufficient, pathogenic factors will invade, resulting in phlegm dampness, blood stasis and other pathological factors. When qi is sufficient, it can resist the invasion of external pathogens. In the process of treatment, the spleen and stomach, as the "acquired origin", are the main source of qi, blood, body fluid in the human body, which cannot be ignored to invigorate qi and invigorate the spleen. It has the reputation of "the first essential medicine for invigorating qi and invigorating spleen". It is recorded as the top quality in Shennong Bencao Jing (Shennong's Classic of Materia Medica), which has good functions of invigorating qi, invigorating spleen and promoting water. Angelica sinensis can replenish blood, its nature is sweet and warm, it is a necessary medicine for replenishingblood, and it can invigorate blood, its taste is spicy and warm, it enters the blood points, it can invigorate blood, make the stasis go, bleeding stop, new blood, and the blood circulation is constant. On the one hand, the wind is the long of all diseases, on the other hand, the lung and the large intestine are on the other hand. If the lung is not ventilated and cannot be channeled, water flowing into the large intestine can cause diarrhea. Solid in the drug added to the surface of drugs, such as wind lifting and can powder, can play the role of dispelling the wind, can cure all wind pathogens, Chengfeng drugs second to no one, so the "main wind" three words for the outline. Compatibility of white paeony, Atractylodes, Tangerine peel with abdominal pain and diarrhea.

4.3. Analysis of the medicinal properties, medicinal flavor and normalization

The results of this study show that in the clinical application of traditional Chinese medicine enema in the treatment of UC patients, most of the drug properties are mainly cold, warm and even, and the damp-heat connotation is the main pathogenesis of UC. Therefore, cold drugs are often used in the treatment, as proposed in Shennong Bencao Jing · Xulu [89], "to treat cold with hot drugs, to treat heat with cold drugs". Therefore, cold medicine should be used for heat syndrome and hot medicine for cold syndrome to achieve the best effect. On the one hand, the disease is often complicated by cold and heat, so cold and heat should be used together in the treatment. According to the emphasis of cold and heat, repuricing drugs or warming Yang dissipating cold drugs can be considered in the treatment. On the other hand, cold and hot drugs are used together, cold drugs can prevent warm drugs from being too dry, which consumes air and hurts body fluid, and warm drugs can prevent cold drugs from being cold and damaging the spleen and stomach, so as to achieve the effect of complementing each other. Therefore, warm drugs are often used. It is a kind of traditional Chinese medicine with no significant bias, which is characterized by mild medicinal properties, and does not show cold and heat. Its medicinal properties are mild, but its medicinal properties are not necessarily smooth. In the treatment of UC, the use of mild medicinal properties mostly manifests its effect of toning deficiency or reconcilating various herbs. For example, liquorice is mainly sweet and flat in its medicinal taste, which has many effects such as tonifying spleen and qi, clearing heat and detoxifying, expectorant and cough, alleviating pain, and reconciling all drugs. In terms of meridians, this study mainly attributed to liver meridians. Just as Zhang Jingyue said in the Jing Yue Quanshu · Xie xie [25], "Although wood can also reduce, the injury of earth can also... Whoever has catharsis in response to anger... Cover with liver wood soil, temper injury and ran ". Liver Wang by spleen soil, grams lack of spleen and stomach, liver and spleen discord, spleen loss and can also be used for diarrhea. The disease of the liver is known to transmit the liver to the spleen. The relationship between liver and spleen is close. For example, Professor Wang Xinxue's treatment of UC starts with liver treatment, regulates qi and blood, and takes into account the spleen, stomach, heart and kidney, with remarkable results [26]. With the deepening of modern

ISSN: 2472-3703 DOI: 10.6911/WSRJ.202306_9(6).0003

medical research, it has been found that the onset of UC is also closely related to psychological factors such as sensitivity, anxiety, depression and so on.

4.4. Drug association rule analysis

The results of drug association rule analysis showed that the drug association groups with high support were: B. platyphylla, B. platyphylla, B. platyphylla + Pulsatilla, A. platyphylla + P. phellodendri, B. platyphylla + P. platyphylla, and B. platyphylla + P. platyphylla. According to the association rules, the relationship between heat-clearing drugs and hemostatic drugs is strong, indicating that the treatment of UC with traditional Chinese medicine enema is mainly to clear heat, dry dampness, stop bleeding and generate muscle. And it is mainly Baitouweng decoction from the point of view of these association rules. Baitouweng decoction has the effect of clearing heat and detoxifying, cooling blood and stopping dysentery. Baitouweng Decoction (Baitouweng Decoction) is the main medicine, and Qinpi is the main medicine, supplemented with Rhizoma coptidis and Phellodendri phellodendri. Baitouweng Decoction (Baitouweng Decoction) is considered by later doctors as the basic prescription for the treatment of damp-heat deficiency. Shang han Lun (Treatise on Febrile Diseases) said, "Those who are hot and cold are dominated by Baitouweng soup." "Those who are thirsty for water are dominated by Baitouweng soup." Therefore, we can refer to Baitouweng decoction as the basic prescription in clinical practice. In addition, this association rule also shows that Huangbai-Sanguisorba + Baiji, Huangbai-Sophora flavescens +, Huangbai-Angelica +, reflects the clinical treatment principle of TCM enema for UC, which is both clearing and tonifying, and regulating qi and blood.

In conclusion, in this study, in the treatment of UC with traditional Chinese medicine enema combined with mesalazine, the traditional Chinese medicine enema was used once a day, the enema time was less than 1 month, and the enema temperature was 37℃. The frequentlyused drugs were Phellodendron angustifolia, Pulsatilla baitouweng, Rhizoma coptidis, and Rhizoma pallidus. Most of the drugs were cold, warm and mild. The main medicinal flavor was bitter and sweet. The main meridians are liver meridians. The strong drug association rule is the main drug composition of Baitouweng decoction. It embodies the syndrome differentiation and treatment thought of clearing heat and drying dampness, converging and stopping bleeding, cooling blood and growing muscle in the treatment of UC. At the same time, it takes into consideration the tonifying spleen and soothing liver, leveling cold and heat qi and blood, attacking pathogens and strengthening health. In clinical prescription, Baitouweng decoction is the basic prescription, and it is added or subtracted according to the syndrome.

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