

# 2019 冠状病毒病(COVID-19)基于推荐诊疗方案的中医用药特点分析

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**[摘要]** **目的:**分析国家卫生健康委员会(卫健委)、国家中医药管理局(中管局)及各省市自治区卫健委、中管局通过公开渠道发布的2019冠状病毒病(COVID-19)治疗方案中中医药处方用药特点。**方法:**收集自我国COVID-19疫情发生以来至2020年2月19日国家及各省市自治区卫健委、中管局通过公开渠道发布的COVID-19推荐诊疗方案中中医药相关内容,并进行所有数据的频数分析、关联分析和聚类分析。**结果:**共收集国家诊疗方案4个,各省市自治区防治方案34个,样本578条,得到有名称的传统方剂84首,中成药60种,涉及单味药230味。高频用药有甘草、黄芩、杏仁、石膏等,常见方剂有麻杏石甘汤、银翘散、宣白承气汤等,常用中成药有安宫牛黄丸、血必净注射液、连花清瘟胶囊等,高频药对有“麻黄,杏仁”“连翘,甘草”等,挖掘出核心药物组合2个,新处方1个。**结论:**COVID-19卫分证以银翘散、藿朴夏苓汤为基础方,气分证可以麻杏石甘汤、凉膈散、清瘟败毒饮、达原饮等为基础方。用药特点以宣肺清热、解毒祛浊为主,体现中医治疫解毒透邪的处方思路。



**[关键词]** 2019冠状病毒病;严重急性呼吸综合征冠状病毒2;新型冠状病毒肺炎;中医药治疗;数据挖掘;频数分析;关联分析;聚类分析

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## Analysis of medication characteristics of traditional Chinese medicine in treating COVID-19 based on data mining

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**[Abstract] Objective:** To analysis the medication characteristics of the prescriptions issued via open channel by the National and Provincial Health Committee and the State Administration of Traditional Chinese Medicine in treating coronavirus disease 2019 (COVID-19). **Methods:** We collected the data of traditional Chinese medicine related to treatment plans published by the National and Provincial Health Committee and the State Administration of Traditional Chinese Medicine from the start of COVID-19 outbreak to February 19, 2020. The frequency analysis, cluster analysis and association analysis were performed. **Results:** The study collected 4 national and 34 regional prevention and treatment plans, 578 items, 84 traditional Chinese formulations, 60 Chinese patent medicines, and 230 Chinese herbs. The high frequently used herbs were *Liquorice*, *Scutellariabaicalensis*, *Semen armeniacaeamarae*, and *Gypsum*. The commonly used traditional formulations included *Maxing Shigan* decoction, *Yin Qiao* powder, and *Xuanbai Chengqi* decoction. The Chinese patent drugs included *Angong Niuhuang* pill, *Xuebijing* injection, and *Lianhua Qingwen* capsule. The most common paired medications were *Ephedra* and *Semen armeniacaeamarae*, *Fructusforsythiae* and *Liquorice*. Two core combinations and one novel formula were discovered in the study. **Conclusions:** *Yin Qiao* powder and *Huopo Xialing* decoction are the basic formulations for *Weifen* syndrome of COVID-19. In addition, *Maxing Shigan* decoction, *Liang Ge* powder, *Qingwen Baidu* decoction and *Da Yuan* decoction are the basic formulations for *Qifen* syndrome of COVID-19. The main medication characteristics are clearing heat, entilating lung, removing toxicity and removing turbidity. It shows that removing toxicity and eliminating evil are the prescription thought in treating epidemic disease of traditional Chinese medicine.

**[Key words]** Coronavirus disease 2019; Severe acute respiratory syndrome coronavirus 2; Novel coronavirus pneumonia; Traditional Chinese medicine treatment; Data mining; Frequency analysis; Association analysis; Cluster analysis

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自我国 2019 冠状病毒病 (coronavirus disease 2019, COVID-19) 疫情发生以来, 国家及各省、自治区、直辖市卫生健康委员会 (卫健委) 和中医药管理局 (中管局) 先后印发了 COVID-19 诊治的国家方案<sup>[1-4]</sup> 和地区方案<sup>[5-38]</sup>。COVID-19 是一种新发传染病, 在尚无疫苗和抗病毒特效药的情况下, 临床强调支持治疗、对症治疗、抗病毒治疗、中医药等综合运用, 充分发挥中国医药卫生领域的本土优势。中医重视整体观念和个性化治疗, 越来越多的省市定点医院运用中医药治疗取得了良好的疗效。夏文广等<sup>[39-40]</sup> 采用中西医结合方案治疗 COVID-19 患者, 结果普通型患者改善症状, 缩短病程, 加快痊愈; 重型、危重型患者肺部渗出减少, 炎症反应得到控制, 防止了病情恶化; 恢复期患者清除余邪, 扶助正气, 促进康复进程。为明

晰中医药治疗本病的用药特点和组方规律, 本研究收集目前公布的国家和省、自治区、直辖市推荐诊疗方案中关于中医治疗部分的用药资料, 进行频数分析、关联分析及聚类分析, 以期为进一步临床研究和科研设计提供借鉴。

## 1 资料与方法

### 1.1 数据来源及检索方法

收集自疫情发生以来至 2020 年 2 月 19 日互联网上发布的新闻通告, 国家卫健委或中管局发布的不同版本诊疗方案, 各省、自治区、直辖市卫健委或中管局发布的不同版本防治方案, 以及尽可能全面的各省市官方渠道获取的中医药治疗方药。

### 1.2 纳入和排除标准

纳入标准: ①由国家或各省、自治区、直辖市

卫健委或中管局颁布的国家方案和地区方案(因武汉为疫情最严重地区,故包括武汉方案);②中医药治疗方案。排除标准:①中医药预防方案;②其他未涉及中医药的防控、防护指南或建议。

### 1.3 数据录入

由两名研究人员负责资料的检索和收集,一人将搜集好的具有明确方剂名称的传统方剂和中成药相关资料录入 Microsoft Excel 2018,一人将搜集好的所有方案中的方药录入中医传承辅助平台软件(V2.5);两名研究人员将录入后的数据分别进行一致性检验和修正,以确保数据的准确性,一人将检验后的数据校正 V2.5 基本参数并导出。

### 1.4 方药规范

依据 2015 版《中国药典》对中药名称进行标准化,如双花规范为金银花、山栀子规范为栀子;依据“中国医药信息在线查询平台”对中成药进行标准化拆分录入药物,或相关中药提取物以相对应的中药进行规范,如喜炎平注射液规范为穿心莲。

### 1.5 数据分析

采用 Microsoft Excel 2018 及 V2.5 系统的“医案统计”功能,对所收录传统方剂、中成药和单味药频次进行描述性统计分析;运用 V2.5“数据分析”模块的“方剂分析”功能,对录入数据进行关联规则、聚类分析等可视化统计分析。

## 2 结果

本研究共收集国家卫健委和中管局印发的国家方案(试行第三至六版)4 个,各省市自治区(广东、贵州、河北、黑龙江、吉林、辽宁、山西、四川、云南、浙江、甘肃、海南、湖南、江苏、江西、山东、陕西、北京市、上海市、天津市、西藏自治区、新疆维吾尔自治区、内蒙古自治区、广西壮族自治区、宁夏回族自治区)卫健委或中管局印发的地区方案等共计 25 个省、直辖市和自治区方案 33 个<sup>[1-37]</sup>,加湖北省武汉市方案 1 个<sup>[38]</sup>,共计 38 个方案。共录入数据 578 条,涉及单味药 230 味,有具体名称传统方剂 84 首,中成药 60 种。

### 2.1 描述性统计分析

**2.1.1 高频单味药** 共收集单味药 230 味,频次区间(1,216)。将出现频次至少 80 次者作为高频药,得到高频单味药共 18 味,其中甘草、黄芩、

杏仁、石膏、连翘、麻黄、金银花及藿香出现频次高达 100 次以上,见表 1。

**2.1.2 高频方剂** 共录入传统方剂 84 首,频次区间(1,29)。将出现频次至少 5 次者作为高频方剂,得到高频方剂共 20 首,见表 2。

表 1 治疗 2019 冠状病毒病中医药方案中的高频单味药 (频次≥80)

Table 1 High frequency Chinese herbal medicine for COVID-19 treatment in programs (frequency ≥80)

单味药	频 次	单味药	频 次
甘草	216	茯苓	95
黄芩	188	半夏	92
杏仁	169	大黄	89
石膏	165	白术	88
连翘	153	栀子	88
麻黄	142	水牛角	86
金银花	134	厚朴	85
藿香	115	人参	82
桔梗	98	陈皮	80

表 2 治疗 2019 冠状病毒病中医药方案中的高频方剂 (频次≥5)

Table 2 High frequency Chinese medicine formulations for COVID-19 treatment in programs (frequency ≥5)

方 剂	频 次	方 剂	频 次
麻杏石甘汤	29	清瘟败毒饮	8
银翘散	28	参附汤	7
宣白承气汤	20	三仁汤	7
升降散	19	小柴胡汤	6
麻杏苡甘汤	18	甘露消毒丹	6
达原饮	18	竹叶石膏汤	6
黄连解毒汤	16	二陈汤	5
四逆加人参汤	16	王氏清暑益气汤	5
藿朴夏苓汤	16	白虎汤	5
解毒活血汤	15	荆防败毒散	5

**2.1.3 高频中成药** 共录入中成药 60 种,频次区间(1,37)。将出现频次至少 5 次者作为高频中成药,得到高频中成药 16 种,见表 3。

### 2.2 可视化统计分析结果

**2.2.1 基于关联规则分析得到的药物组合** 基于 Apriori 算法,运用中医药数据挖掘系统中的关联规则挖掘药物间高频药物组合,使用支持度和置信度两个属性来判别 2 个变量之间的规律性。其中,支持度(AB)指药物组合在处方中出现的频次,置信度(B|A)为当 A 药物出现时 B 药物出现

**表3** 治疗 2019 冠状病毒病中医药方案中的高频中成药(频次≥5)

**Table 3** High frequency Chinese patent preparations for COVID-19 treatment in programs (frequency ≥5)

中成药	频 次	中成药	频 次
安宫牛黄丸	37	清开灵胶囊/注射液	14
血必净注射液	30	金花清感颗粒	14
连花清瘟胶囊/颗粒	26	疏风解毒胶囊/颗粒	11
紫雪丹/散	23	防风通圣丸/颗粒	11
藿香正气水/散/胶囊/口服液	21	喜炎平注射液	10
苏合香丸	19	痰热清注射液	8
参附注射液	18	热毒宁注射液	7
生脉饮/注射液	16	至宝丹	5

的概率。根据样本数量,设支持度个数为 70,置信度为 0.8,共获得关联数据 24 条,涉及中药 12 味,其中涉及麻黄、杏仁、连翘、甘草、石膏等用药组合频次在 100 次以上,此条件下生成的关联药物组合见表 4。

**表4** 治疗 2019 冠状病毒病中医药方案中的关联药物组合(支持度 = 70,置信度 = 0.8)

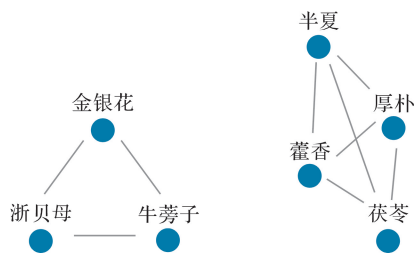
**Table 4** Frequency of herbal combination for COVID-19 treatment in programs (support degree = 70 and confidence coefficient = 0.8)

关联药物组合	频 次	关联药物组合	频 次
麻黄,杏仁	124	黄芩,甘草	81
连翘,甘草	110	连翘,麻黄	78
甘草,杏仁	109	连翘,杏仁	78
石膏,麻黄	106	石膏,甘草,杏仁	77
甘草,麻黄	105	石膏,连翘	76
石膏,杏仁	104	甘草,桔梗	76
石膏,甘草	102	半夏,茯苓	75
石膏,麻黄,杏仁	96	石膏,大黄	74
甘草,麻黄,杏仁	94	石膏,甘草,麻黄,杏仁	74
黄芩,连翘	87	黄芩,栀子	73
金银花,连翘	86	黄芩,杏仁	71
石膏,甘草,麻黄	84	黄芩,金银花	71

**2.2.2 基于聚类分析得到的核心组方**

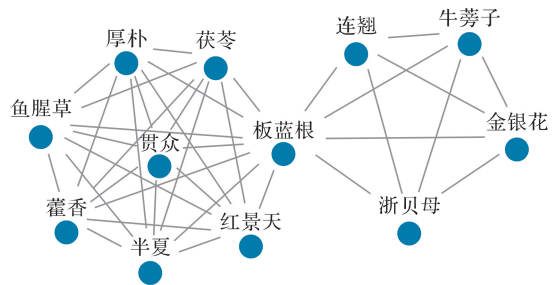
基于熵聚类和改进的互信息法,运用中医药数据挖掘系统中的聚类分析收集药物分类。使用相关度和惩罚度两个属性来判别 2 个变量之间的规律性。其中,相关度指药物之间存在的正相关,即临床意义。惩罚度指药物之间的负相关,即临床禁忌。设相关度为 5,惩罚度为 2,进行熵聚类,共有 21 条数据,得到核心组合 2 个,即浙贝母、牛蒡子、金

银花和半夏、厚朴、藿香、茯苓(图 1);新方 1 个,由板蓝根、厚朴、半夏、浙贝母、鱼腥草、藿香、连翘、红景天、金银花、贯众、牛蒡子、茯苓组成(图 2)。



**图1** 治疗 2019 冠状病毒病中药方案中的核心药物组合展示图

**Figure 1** Core herbal combinations for COVID-19 treatment in programs



**图2** 治疗 2019 冠状病毒病中药方案中的新方网络图

**Figure 2** Novel formulations for COVID-19 treatment in programs

**3 讨论**

从临床表现看,COVID-19 可归属中医疫病范畴。明代吴又可可在《温疫论·自序》中指出:“夫温疫之为病,非风、非寒、非暑、非湿,乃天地间别有一种异气所感。”中国中医科学院广安门医院全小林院士根据武汉实地考察结果,指出本病为“寒湿疫”,认为寒湿之邪袭表、阻肺、碍脾,产生一系列临床征象,但寒湿易郁而入里化热、化燥、伤阴、致瘀,甚至闭脱,形成以“湿、热、毒、瘀”为主的病机特点<sup>[41]</sup>。由于患者的发病时间、所处地域及自身体质不同,临床可表现为寒湿疫、湿热疫等。本研究所收集国家和各地区方案,虽未达成一致,但基本不离中医瘟疫的病因病机主线。本研究通过尽可能全面地检索已经公开的方案,运用中国中医科学院中药研究所研制的 V2.5 软件进行数据挖掘,对中医药治疗 COVID-19 的用药特点、处方规律进行统计分析。



本研究通过描述性统计分析,得到单味药 230 味,出现频次不少于 80 次共 18 味。这些高频药物适应证符合中医瘟疫的病机演变。多数 COVID-19 患者初期具有畏寒发热、肌肉酸痛等表证,应用麻黄、金银花、连翘、藿香、桔梗、甘草等辛宣透表;继而邪热壅肺,肺气郁闭,应用诸如黄芩、麻黄、杏仁、石膏、大黄、水牛角、栀子等清宣肺热,下泄痰毒。证属湿浊留滞者,取茯苓、半夏、厚朴、陈皮等理气化湿祛浊。体质较弱,元气偏亏或恢复期脾胃虚弱,用人参、白术等健脾益气,培土生金。从这些高频药物看,基本包括中医治疫名方银翘散、麻杏石甘汤、清瘟败毒饮、藿朴夏苓汤等的药物组成。这些用药也体现出中医治疫因势利导、扶正解毒、驱邪外出的治疗原则,具体如金银花、连翘辛凉解表,大黄、栀子泻下通肠,藿香、茯苓化湿利尿,石膏、黄芩、水牛角清热泄毒,人参、白术扶正抗邪,麻黄、杏仁、桔梗、半夏宣肺导痰,陈皮、厚朴理气化浊,而甘草既能清热解毒,又能健脾护胃,具有调和作用。如此使人体表里上下的疫毒之邪由窍道而出。

本研究获得 84 首具有明确名称的传统方剂,出现频次不少于 5 次共 20 首。其中高频方剂,尤其是频次不少于 18 次的麻杏石甘汤、银翘散、宣白承气汤、升降散、麻杏苡甘汤以及达原饮被多个方案所推荐<sup>[1]</sup>。银翘散为吴鞠通《温病条辨·上焦篇》辛凉平剂,卫分证常用方。COVID-19 以发热为主症,在初期的轻症阶段运用此方,切中机要。麻杏石甘汤在《伤寒论》和《温病条辨》皆有提及,用于肺气分实热证,临床已证实其对于各种肺炎的确切效果<sup>[42]</sup>。麻黄与石膏合用,寒温兼施,一清肺热,一宣肺气,加杏仁止咳,甘草调和诸药。干咳、喘鸣亦为 COVID-19 主要表现,在卫气同病、由表入里的阶段运用此方宣肺止咳。宣白承气汤乃吴鞠通肺热移肠代表方剂,因肺与大肠相表里,若肺气分证未愈,则下移大肠,肺肠同病,用此方治疗 COVID-19 兼便秘者最为适宜。升降散是杨栗山《伤寒瘟疫条辨》主治温病表里三焦大热代表方,若上述肺、肠气分实热未解,波及三焦,此方升清降浊,升降相因。麻杏苡甘汤为张仲景《金匮要略》治疗风湿在表方,散寒解表,健脾除湿,针对寒湿型 COVID-19 患者比较贴合。达原饮作为吴又可《温疫论》中用于瘟疫或疟疾邪伏膜原证牵头方,祛湿清热。有学者研究发现,达

原饮中的活性化合物能通过与血管紧张素转换酶 2 (ACE2) 结合作用于 PTGS2、HSP90AA1、ESR1 等靶点调节多条信号通路,从而可能对疾病有治疗作用<sup>[43]</sup>。

本研究得到中成药 60 种,出现频次不少于 5 次共 16 种,如用于观察期乏力伴肠胃不适的藿香正气水/散/胶囊/口服液,乏力伴发热的连花清瘟胶囊/颗粒、金花清感颗粒、疏风解毒胶囊/颗粒或防风通圣丸/颗粒。用于危重型(内闭外脱证)的凉开三宝、苏合香丸以开窍醒神;参附注射液、生脉注射液益气补虚,回阳通脉,用于脓毒症休克等抢救。喜炎平注射液和血必净注射液为多个方案推荐的中期疫毒闭肺中成药,清热解毒与活血化瘀并用。清开灵注射液、痰热清注射液和热毒宁注射液皆为临床清热解毒制剂,运用于多种临床急危重症的治疗<sup>[44]</sup>。

本研究通过可视化统计分析,在支持度为 70、置信度为 0.8 的前提下,得到关联数据 24 条,涉及中药 12 味,包含多个经典方剂核心药物及药对。如频次  $\geq 105$  次的前 5 组,大致为麻杏石甘汤组合;其余如连翘、甘草、黄芩、桔梗、栀子皆为凉膈散重要组成药物,用于邪盛胸膈的气分证。其中连翘、栀子、黄芩清肺治上,清泄膈热;大黄泻热治下,以泻代清;甘草调和诸药,清热解毒。现代药理研究表明,此方能够调控肺组织 NF- $\kappa$ B,改善 Th1/Th2 比值,通过多个基因和通路发挥抗炎和免疫调节功能<sup>[45]</sup>。金银花和连翘为银翘散关键药对,甘草、半夏与茯苓是二陈汤重要药物,金银花、栀子、热毒宁注射液的主要组成等。而石膏、甘草、连翘、黄芩、栀子、桔梗等为清瘟败毒饮重要药物,用于气血两燔,全面清解不同阶段的热毒,具有解热、抗炎、抗菌、抗病毒及免疫调节作用,常用于多种感染性疾病<sup>[46]</sup>。

在相关度为 5,惩罚度为 2 条件下的聚类结果得到 2 个核心组合和 1 个新方。两个核心组合:①浙贝母、牛蒡子、金银花为中成药金花清感颗粒核心药物,疏风宣肺,清热化痰,已广泛用于流感的治疗;②半夏、厚朴、藿香、茯苓用药蕴含藿香正气散、藿朴夏苓汤和雷氏芳香化浊法等,理气机,化湿浊,符合 COVID-19 患者湿浊疫病的病机特点。新方用药有板蓝根、厚朴、半夏、浙贝母、鱼腥草、藿香、连翘、红景天、金银花、贯众、牛蒡子、茯苓,实则集中清热解毒、宣肺化痰、理气祛浊的功

效,其组成与连花清瘟胶囊有相似之处。有学者运用连花清瘟胶囊治疗 COVID-19 疑似病例 63 例,结果显示疑似病例发热、咳嗽、乏力、气促等症状明显改善,且转化为重症患者的比例有所降低<sup>[47]</sup>。

通过相关诊疗方案的数据挖掘和综合分析,COVID-19 患者出现卫分证可以银翘散、藿朴夏苓汤为基础方;出现气分证,可以麻杏石甘汤、凉膈散、清瘟败毒饮、达原饮等为基础方。用药以宣肺清热、解毒祛浊为主,体现中医治疫因势利导,透邪外出的处方思路,印证了吴又可所谓“以驱邪为第一要义”的治疗温疫之旨。中医学在介入此次 COVID-19 疫情过程中,其安全性和有效性日益凸显,充分显示了中西医结合治疗的优越性。未来应更多开展关于上述方药的相关基础和临床研究,着眼不同分期、不同证型,进行有针对性的辨证论治,以期对临床有所借鉴,对今后中医治疫提供更多启迪。

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