Real-World Prescribing Pattern of Asthma Management in China: A Retrospective, Descriptive Analysis

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Research Article

Keywords: Asthma exacerbation, Inhaled corticosteroids, Traditional Chinese medicine, Pulmonary diseases

Posted Date: January 10th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1158031/v2>

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Abstract

Background

Asthma is a chronic inflammatory disorder of the airway that requires long-term medication management.

Objective

To describe the real-world prescribing patterns for asthma management in the Chinese population.

Methods

A retrospective analysis of 8,732 patients from January 2011 to September 2019 in 10 hospitals was conducted. Prescribing patterns of short-acting beta-agonists (SABA), long-acting beta-agonists (LABA), inhaled corticosteroids (ICS), intravenous corticosteroids, antihistamines, leukotriene receptor antagonists (LTRA), theophylline, antibiotics, and Chinese patent medicines were included in the analysis. Chi-square and logistic regression were calculated. P value of <0.05 was considered as statistical significance.

Results

ICS/LABA were prescribed for 2,940 (33.67%) patients with stable asthma and 141 (31.4%) patients with asthma exacerbations. LTRA was prescribed in 2,006 (22.97%) patients with stable asthma, and 86 (19.15%) patients with asthma exacerbations. Systemic antibiotics (46.12%), systemic corticosteroids (57.91%), and theophylline (51.45%) were frequently prescribed during exacerbations. A total of 5,766 patients (64.95%) were managed with traditional Chinese medication (TCM); 3237 patients (36.47%) received western medicine. Patients using ICS/LABA ($P=0.019$) and SABA ($P=0.008$) had a significantly lower rate of asthma exacerbations.

Conclusions

This study provides valuable insight into clinical practices of asthma management in China. Poor adherence to clinical reports was identified. Efforts are required to improve the quality of asthma care.

Background

Asthma is a chronic inflammatory disease of the airway presented with episodes of wheezing, shortness of breath, chest tightness[1–3]. Over 300 million people suffer from asthma worldwide, causing about 461,000 deaths per year[4, 5]. A recent epidemiology study pointed out that about 45.7 million people in China have asthma, 28.8% of which were physician diagnosed[6]. Asthma poses a significant burden on the lives of patients and healthcare systems. An analysis of the UK national databases revealed that asthma resulted in 93,000 hospitalizations and 1,800 intensive-care unit visits[7]. The average asthma cost, varied from country to country, is \$USD 1,900 to \$USD3,100. The cost is much higher in patients with severe, uncontrolled asthmas, or asthma exacerbations[8, 9].

Asthma exacerbations are commonly triggered by viral/bacterial infections, allergen exposure, and tobacco smoke[10]. It is presented as episodes of progressive increase in signs and symptoms, often leading to emergency department (ED) visits and hospital admissions. Therefore, proper asthma management and optimizing asthma medications are essential to alleviate the disease burden and economic burden on asthma patients. Inhale corticosteroids (ICS) remain the cornerstone of asthma treatment due to their efficacy in lowering risks of airway inflammations, exacerbations, and decline in lung function[11, 12]. The 2021 Global Initiative for Asthma (GINA) Report recommends ICS-formoterol as the preferred therapy in adult patients with mild asthma while using short-acting beta-agonist (SABA) alone is considered as an alternative[13]. Maintenance long-acting beta-agonists (LABA) are considered as part of the preferred therapy to whose asthma cannot be controlled with as-needed ICS/LABA[13, 14].

Several studies regarding the real-world pharmacological management of asthma mainly focused on the effectiveness of different types of inhalers, the risk of exacerbations in asthma of different severities, the choices of medications when initiating asthma treatment, and patient adherence to asthma medications[15–18]. Few research described the different prescribing patterns for asthma between traditional Chinese medication TCM and western medicine, well and poorly controlled asthma, as well as changes in the number of medications prescribed over the past decade. Whether these factors are associated with the risk of acute asthma exacerbations is still unclear.

This study used longitudinal data of an asthma cohort from 10 hospitals in Jinan, China. The primary objective was to describe the real-world prescribing patterns for asthma management.

Methods

Study Design

This was a retrospective, descriptive analysis of patients over the age of 18 with at least one diagnosis of asthma from January 2011 to September 2019 in 10 hospitals. Patients were excluded if they had missing data for age or had surgical interventions during the same office visit. Data were extracted through a review of medical encounters documented in the Jinan Health Medical Big Data Platform, administered by Shandong Health Medical Big Data Co., Ltd.

Clinical data and definitions

Medications considered as parts of asthma regimens were short-acting beta-agonists (SABA), long-acting beta-agonists (LABA), inhaled corticosteroids (ICS), intravenous corticosteroids, antihistamines, leukotriene receptor antagonists (LTRA), theophylline, antibiotics, and Chinese patent medicines. Treatments using TCM were defined as any visit with prescription of Chinese medicine or proprietary Chinese medicine preparations to traditional Chinese medicine hospitals, department of TCM in tertiary hospitals, and/or department of TCM and integrative medicine in medical institutions. All other office visits were considered as western medicine treatments.

Primary Endpoint

The primary endpoint of the study is the proportion of different classes of asthma prescriptions. differences between western and Chinese medicine, stable asthma and acute asthma exacerbations, and yearly changes of asthma prescriptions were analyzed.

Statistical analysis

The counts and proportion of prescriptions in different aspects were calculated. The statistical analysis was conducted with R software, version 3.3.3 (R Foundation for Statistical Computing).

Results

Medication use during the study period

During the study period, 14,264 patients with asthma were identified, of which 8,789 patients had prescription-filling records. A total of 8,732 patients had prescriptions for stable asthma; 499 patients had prescriptions for acute asthma exacerbations. Classes of medications prescribed are presented in Table 1. A total of 1,192 ICS prescriptions were documented in 698 (7.99%) patients with stable asthma and 160 prescriptions in 105 patients had asthma exacerbations. ICS/LABA was prescribed for 2,940 (33.67%) patients with stable asthma and 141 (31.4%) patients with asthma exacerbations, respectively. LTRA was prescribed in 2,006 (22.97%) patients with stable asthma and 86 (19.15%) patients with asthma exacerbations. Chinese herbal medicines or Chinese patent medicines were used in over 40% of patients with stable asthma and over 30% of patients with asthma exacerbations. Systemic antibiotics (57.91%), systemic corticosteroids (46.1%), and theophylline (51.45%) were three of the top medications prescribed during acute asthma exacerbations.

Table 1
Medication use in all patients with asthma

	Stable Asthma		Acute Asthma Exacerbations	
	No. of patients	No. of prescriptions	No. of patients	No. of prescriptions
Patient Numbers	8,732	23,617 ^a	449	981
Total ICS Prescriptions	698(7.99)	1,192	105(23.39%)	160
ICS combination therapy ^a	19(0.22%)	22	32(7.13%)	33
ICS monotherapy	681(7.8%)	1170	78(17.37%)	127
ICS/LABA	2,940(33.67%)	5,955	141(31.4%)	174
LAMA	83(0.95%)	138	8(1.78%)	11
LABA	8(0.09%)	8	3(0.67%)	3
SABA	703(8.05%)	1,338	95(21.26%)	153
SAMA	45(0.52%)	106	5(1.11%)	6
SAMA+SABA	41(0.47%)	54	21(4.68%)	27
Theophylline IR	236(2.7%)	386	231(51.45%)	636
Theophylline SR	16(0.18%)	37	3(0.67%)	3
Theophylline IV	0(0%)	0	228(50.78%)	631
LTRA	2,006(22.97%)	4,080	86(19.15%)	104
Systemic corticosteroids (IV or PO)	120(1.37%)	256	207(46.1%)	473
Oral corticosteroids	120(1.37%)	256	16(3.56%)	19
Intravenous corticosteroids	0(0%)	0	202(44.99%)	465
Ambroxol+SABA	16(0.18%)	17	2(0.45%)	2
Antihistamines	711(8.14%)	878	33(7.35%)	39
Anti-IgE	0(0%)	0	0(0%)	0
Mast cell stablizers	326(3.73%)	409	24(5.35%)	26
Inhaled corticosteroids nasal spray	349(4%)	430	5(1.11%)	5
Antitussive	68(0.78%)	83	11(2.45%)	13
Systemic antibiotics	1,230(14.09%)	2,133	260(57.91%)	660
Local antibiotics	160(1.83%)	198	56(12.47%)	61
Immune modulator (Thymopolypeptide/Interferon)	25(0.29%)	46	15(3.34%)	18
Chinese herbal medicine	4,228(48.42%)	10,407	163(36.3%)	214
Chinese patent medicine	4738(54.26%)	10,340	176(39.2%)	223
ICS: Inhaled corticosteroids; LABA: Long-acting beta-agonists; LAMA: Long-acting muscarinic antagonists; ICS/LABA: An ICS and LABA combination inhaler; SABA: Short-acting beta-agonists; SAMA: Short-acting muscarinic antagonists; IR: Immediate release; SR: Sustained-release; IV: Intravenous; PO: Oral				
a. ICS combination therapy: A regimen that contains ICS and LABA, or ICS and LAMA.				

Patients receiving TCM and western medicine for asthma management

Of the identified asthma patients, 8,877 patients received TCM, of which 6 (0.07%) had physician office visits that did not specify the department they visited; 3,237 patients were managed by western medicine (Table 2). Prescription filling records were found in 3,212 patients, out of which 3,160 took medications for stable asthma. A total of 282 patients took medications for acute asthma exacerbations.

ICSLABA was prescribed in 1,365 (43.2%) patients with stable asthma and 75 (26.6%) patients with asthma exacerbations, respectively. LTRA was used in 900 (28.48%) patients with stable asthma and 51 (18.09%) patients with acute asthma exacerbations (Table 3).

Table 2
Patients receiving TCM and Western Medicine

	Total	TCM	Western Medicine	N/A
Number of Patients	8877	5766(64.95%)	3237(36.47%)	6(0.07%)
Number of Office Visits	26027	17429(66.97%)	8589(33%)	9(0.03%)

Table 3
Medication use in asthma patients treated with western medicine

	Stable Asthma		Acute Asthma Exacerbations	
	No. of patients	No. of prescriptions	No. of patients	No. of prescriptions
Patient Numbers	3,160	7,552 ^a	282	734
Total ICS Prescriptions	453(14.34%)	719	66(23.4%)	112
ICS combination therapy ^a	18(0.57%)	21	13(4.61%)	13
ICS monotherapy	437(13.83%)	698	56(19.86%)	99
ICS/LABA	1,365(43.2%)	2,626	75(26.6%)	97
LAMA	72(2.28%)	121	6(2.13%)	9
LABA	8(0.25%)	8	3(1.06%)	3
SABA	473(14.97%)	946	65(23.05%)	112
SAMA	31(0.98%)	88	3(1.06%)	3
SAMA+SABA	40(1.27%)	53	21(7.45%)	27
Theophylline IR	117(3.7%)	174	152(53.9%)	513
Theophylline SR	16(0.51%)	37	3(1.06%)	3
Theophylline IV	0(0%)	0	150(53.19%)	510
LTRA	900(28.48%)	1,829	51(18.09%)	61
Systemic corticosteroids (IV or PO)	55(1.74%)	114	135(47.87%)	368
Oral corticosteroids	55(1.74%)	114	8(2.84%)	10
Intravenous corticosteroids	0(0%)	0	134(47.52%)	365
Ambroxol+SABA	7(0.22%)	7	2(0.71%)	2
Antihistamines	445(14.08%)	557	20(7.09%)	23
Anti-IgE	0(0%)	0	0(0%)	0
Mast cell stabilizers	51(1.61%)	89	8(2.84%)	10
Inhaled corticosteroids nasal spray	219(6.93%)	256	4(1.42%)	4
Antitussives	49(1.55%)	62	10(3.55%)	12
Systemic antibiotics	646(20.44%)	998	161(57.09%)	517
Local antibiotics	97(3.07%)	124	21(7.45%)	24
Immune modulator (Thymopolypeptide/Interferon)	10(0.32%)	19	6(2.13%)	8
Chinese herbal medicine	402(12.72%)	938	78(27.66%)	111
Chinese patent medicine	1,171(37.06%)	2,281	81(28.72%)	112
ICS: Inhaled corticosteroids; LABA: Long-acting beta-agonists; LAMA: Long-acting muscarinic antagonists; ICS/LABA: An ICS and LABA combination inhaler; SABA: Short-acting beta-agonists; SAMA: Short-acting muscarinic antagonists; IR: Immediate release; SR: Sustained-release; IV: Intravenous; PO: Oral				
a. ICS combination therapy: A regimen that contains ICS and LABA, or ICS and LAMA.				

Prescription counts and numbers of asthma exacerbations

A gradual increase in total prescription counts was identified during the study period. Thirteen prescriptions were recorded from 2011 to 2012, including 2 (15.38%) ICS/LABA, 7 (53.85%) SABA, and 11 (84.62%) Chinese patent medicine prescriptions. During 2018 and 2019, a

total of 1,481 prescriptions were documented, including 23 (1.55%) ICS, 663 (44.77%) ICS/LABA, 384 (25.93%) LTRA, 137 (9.25%) SABA, and 353 (23.84%) Chinese patent medicine prescriptions (Table 3). The increase in ICS/LABA and LTRA use were similar. A decrease in prescriptions counts was found in SABA and Chinese patent medicine. From 2011 to 2012, 21 (1.9%) asthma exacerbations and 14 (3.56%) patients experienced exacerbations were identified. From 2018 to 2019, 155 (4.55%) asthma exacerbations and 59 (3.61%) patients had exacerbations were diagnosed (Table 4).

Table 4
Prescription counts in patients receiving western medicine for asthma management

Year	Total	ICS monotherapy	ICS/LABA	LTRA	SABA	Systemic antibiotics	Local antibiotics	Chinese patent medicine
2011-2012	13	0(0%)	2(15.38%)	0(0%)	7(53.85%)	2(15.38%)	0(0%)	11(84.62%)
2012-2013	42	0(0%)	5(11.9%)	1(2.38%)	3(7.14%)	4(9.52%)	0(0%)	16(38.1%)
2013-2014	614	5(0.81%)	91(14.82%)	97(15.8%)	136(22.15%)	201(32.74%)	11(1.79%)	196(31.92%)
2014-2015	1,268	15(1.18%)	321(25.32%)	283(22.32%)	174(13.72%)	189(14.91%)	15(1.18%)	415(32.73%)
2015-2016	1,519	19(1.25%)	503(33.11%)	349(22.98%)	194(12.77%)	271(17.84%)	22(1.45%)	470(30.94%)
2016-2017	1,673	21(1.26%)	544(32.52%)	399(23.85%)	195(11.66%)	275(16.44%)	32(1.91%)	484(28.93%)
2017-2018	1,676	29(1.73%)	594(35.44%)	377(22.49%)	212(12.65%)	342(20.41%)	39(2.33%)	448(26.73%)
2018-2019	1,481	23(1.55%)	663(44.77%)	384(25.93%)	137(9.25%)	231(15.6%)	29(1.96%)	353(23.84%)
∑	8,286	112(1.35%)	2,723(32.86%)	1,890(22.81%)	1,058(12.77%)	1,515(18.28%)	148(1.79%)	2,393(28.88%)

Table 5
Number of asthma exacerbations and number of patients with asthma exacerbations

Year	Number of asthma exacerbations (%)	Number of patients with asthma exacerbations (%)
2011-2012	21 (1.9%)	14(3.56%)
2012-2013	32 (1.98%)	20(3.97%)
2013-2014	146 (6.16%)	40(6.79%)
2014-2015	132 (3.29%)	70(5.93%)
2015-2016	167 (3.71%)	83(5.98%)
2016-2017	182 (3.44%)	99(6.49%)
2017-2018	199 (5.34%)	88(5.29%)
2018-2019	155 (4.55%)	59(3.61%)
Total	1034	473

Discussion

There is a sharp increase in asthma prevalence since the 1960s, especially in developed countries[4]. It was proposed that decreased exposure to house dust, mites, fungi, and other unhygienic environments in the developed country contributes to the increasing number of asthma patients[19]. As expected, our study highlights the increase in total prescription counts per year and the number of patients with asthma exacerbations. However, the rise in physician-identified patients and the implementation of electronic medical records can also contribute to the increase in our findings.

In this retrospective, real-world analysis, we demonstrated the prevalence of different medications used for asthma management in China. ICS is part of the first-line therapy in asthma, regardless of disease severity. It is delivered directly into the lungs, thus, limiting the systemic adverse effects of corticosteroids[20]. The underuse of ICS may be due to poor adherence, intolerable side effects, contraindications, and concerns for increased risk of pneumonia, especially in patients with mild or moderate asthma. Over half of the cohort uses ICS for stable asthma. ICS-containing medications were prescribed to 44.66% of patients with stable asthma, similar to ICS uses in the U.K. and the U.S, both over 40%[21, 22], and much higher than those in Japan and Korea, which were around 10% [23]. This proportion is also higher than 10.2% reported by Huang, et al in patients with physician-diagnosed asthma[6]. The conflicting results of ICS use may be due to the changes in the guidelines, the perceptions of long-term steroid use, and the transformation of hand-written medical records to electronic data.

According to the GINA report, ICS/LABA is recommended in almost all adult asthma patients. Regular use of ICS and LABA allows a lower dose of ICS, improves symptom management, and reduces the risk of exacerbations[24]. In addition, the combination is more effective than ICS+LTRA[25]. In our study, ICS/LABA was the most frequently prescribed medication (33.67%) to patients with stable asthma, much lower than 90.2% of patients in the INITIAL study[26]. There was a significantly decreased risk of exacerbations ($P < 0.05$) in patients using ICS+LTRA. Our finding is consistent with earlier studies regarding the benefits of ICS/LABA[24, 27-29].

LTRA improves asthma control and reduces the frequency of asthma exacerbations, but is less effective than ICS[30]. Therefore, LTRA is listed by the guidelines as an alternative add-on in patients with moderate or severe asthma. LTRA is the second most prescribed medication in our cohort (22.97%). However, LTRA did not show significant benefit in preventing exacerbations in this study.

In our cohort, over 60% of patients received TCM management. Though the exact mechanisms of TCM are still unclear, it has shown some effects in anti-inflammation, airway relaxation, and reducing airway hypersensitivity[31]. TCM, used as adjuvant therapy, can reduce asthma symptoms, enhance patients' lung function, and improve the quality of life, but the treatment effects were limited and may not reduce the risk of exacerbations[31, 32]. Our study showed a continuous decrease in TCM use over the years while increasing use of western medicine, which may be explained by the implementation of the guidelines or the limited efficacy of TCM in patients with moderate to severe asthma.

The GINA report recommends using SABA, oxygen, intravenous corticosteroids, and ICS for managing exacerbations. Other studies showed that 87% to 92.24% of patients with asthma exacerbation received ICS or ICS/LABA or ICS/LABA[33, 34]. In the current study, systemic antibiotics (57.91%), systemic corticosteroids (46.1%), and theophylline (51.45%) were frequently prescribed to patients with asthma exacerbations. The rate (51.45%) of theophylline use during acute exacerbations of asthma, which is comparable to theophylline application in the UK[35]. Theophylline reduces days of hospitalizations but is not as effective as SABA in improving lung functions in acute settings[36]. In addition, theophylline requires frequent blood concentration monitoring to avoid toxicity. It is no longer recommended due to its poor efficacy and safety profile.

Strengths and Limitations

To our knowledge, this is the largest retrospective observational cohort study evaluating real-world prescribing patterns of asthma medications in China. It is also the first one that includes both western medicine and TCM for asthma management, and changes in asthma medication use over time. The study has several limitations. First, the data extraction was based on the medical encounters recorded in the data platform. Office visits and prescriptions that were in paper-based records were not included which might account for the lower proportion of patients receiving each medication. Changes in medications in patients did not experience exacerbations, and medication adherence was also not analyzed in the study. Due to the nature of retrospective observational design, the strength and frequency of medication were decided by physicians. In addition, it is unclear why each medication was prescribed. Lastly, the specific TCM prescribed was not included in the study, thus the effect of TCM in addition to western medicine on asthma management cannot be determined.

Conclusions

Our study suggests that more asthma patients in China were managed with TCM than western medicine. In those managed with western medicine, there are gaps between practical medication management and guideline recommendations, partly due to the study design and physicians' perspectives of asthma management. The study provided valuable insight into clinical practices of asthma management in China. Whether TCM reduced the rate of asthma exacerbation requires further investigation. National and regional efforts are necessary to improve the medication selections for patients with asthma.

Abbreviations

GINA
Global Initiative for Asthma
ICS
Inhaled corticosteroids
ICS/LABA
An ICS and LABA combination inhaler
IR
Immediate release
IV
Intravenous
LABA
Long-acting beta agonists
LAMA
Long-acting muscarinic antagonists
PO
OralSABA:Short-acting beta agonists
SAMA
Short-acting muscarinic antagonists
SR
Sustained-release
TCM
Tradition Chinese medicine

Declarations

Ethics approval and consent to participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Committee on Ethics of Jinan Central Hospital affiliated to Shandong First Medical University, Shandong (No. JCH2020-136-01). Patient consents were waived due to retrospective study design.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests that could have influenced the present study.

Funding

This work was supported by Shandong Provincial Natural Science Foundation (ZR2020QH003, ZR2020MH005, ZR2021ZD35), Jinan Science and Technology Plan (202019064), Shandong Provincial Medical and Health Science and Technology Development Plan Project(2019WS475), and Shandong Provincial Postdoctoral Innovation Project(202003008).

Authors' contributions

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(II) Administrative support: Jian Sun

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(V) Data analysis and interpretation: Jian Sun

(VI) Manuscript writing: All authors

(VII) Final approval of manuscript: All authors

Acknowledgements

We are particularly indebted to Jinan Health Medical Big Data Platform, administered by Shandong Health Medical Big Data Co., Ltd.

Footnotes

Trialregistration:ChineseClinicalTrialRegistry,ChiCTR2100053610,Registered21November2021<http://www.chictr.org.cn/showproj.aspx?proj=66131>

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