ANALYSIS OF TRADITIONAL CHINESE MEDICINE INJECTIONS USED IN THE TREATMENT OF RESPIRATORY SYSTEM-RELATED DISEASES BASED ON THE CHINESE MARKET

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ABSTRACT

Traditional Chinese medicine (TCM) injections (TCMIs) comprise TCM formulations with vital functions in the treatment of cancer, cardiovascular diseases, respiratory system-related diseases (RSRDs) and so on. This article analyzes TCMIs used in the treatment of RSRDs in the Chinese market with special emphasis on the Xiyanping, Tanreqing, Xuebijing, Yanhuning, Reduning, Chuankezhi, Chuanhuning, and Shuanghuanglian (Chinese names of these TCMIs) injections, which present excellent market performances. Analysis of the clinical applications, herbal and chemical compositions, and pharmacological activities of these TCMIs were also conducted. TCMIs have vital functions in the treatment of RSRDs. This article aims to explore the market prospects and development of TCMIs used to treat RSRDs.

KEYWORDS: Traditional Chinese medicine injections (TCMIs), Respiratory system related-diseases (RSRDs), Qingre, adverse reactions, Chinese market

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INTRODUCTION

Many respiratory system-related diseases (RSRDs), such as asthma, chronic obstructive pulmonary disease and pneumonia are common diseases. According to a data from the World Health Organization (WHO), at least 3000 million people have died because of chronic respiratory diseases and more than 90% of the patients with such diseases come from low- or middle-income countries (WHO, 2012a). Lower respiratory tract infections are ranked third in the ten global death reasons and the first in low-income countries. Almost 14 million children below five years old are killed every year by pneumonia, a classic lower respiratory tract infection (WHO, 2012b).

According to data from the 2010 Chinese health statistical yearbook, the morbidity of RSRDs in China is about 6.94%, totaling over 80 million people, and RSRDs rank as the fourth leading cause of death in urban and rural areas (Ministry of Health of the People’s Republic of China, 2010).

Besides chemical drugs used for standard treatment of RSRDs, traditional Chinese medicine (TCM) use is increasing in China because of its excellent clinical effects (Wang et al., 2006). TCMs have important functions in preventing serious infections, such as SARS and H1N1, as they have multiple functions, which include relieving cough, diminishing inflammation, eliminating phlegm, and relieving asthma (Chang et al., 2011a).

TCM injections (TCMIs) are sterile formulations (emulsion, powder, or thick liquid) prepared for injecting into the body and are made after extraction and purification (National Pharmacopoeia Committee, 2005). TCMIs are becoming increasingly valued in China due to their positive clinical effects (Yao, 2007). This article aims to explore the market prospects and development of TCMIs used to treat RSRDs.

MATERIAL AND METHODS

Data sources

Data on the sales of TCMIs in the whole Chinese market were obtained from the Chinese Clinical Medicine Terminal Competition Pattern Database of the State Food and Drug Administration (SFDA), Southern Medicine Economic Research Institute (SMERI), (China Medicine Economic Information Network, 2012), which is calculated by the TCM purchasing practices of 150 sample hospitals from nine cities (i.e., Beijing, Guangzhou, Nanjing, Chongqing, Chengdu, Xian, Haerbin, Shenyang, and Zhengzhou) in China. Thirteen large categories and 75 small categories of drugs are listed based on the WHO therapeutic classification, Anatomical Therapeutic Chemical Code, and national essential drugs list classification for TCM. Data on clinical applications, herbal and chemical compositions and pharmacological activities were searched from China National Knowledge Infrastructure (CNKI) database and/or Pubmed database.

Data analysis

The annual sales and sales growth rate of TCMIs were analyzed: For market share calculations, the formula \( S_N / S_{total} \times 100\% \) was used; for sales growth rate, the formula \( (S_N - S_{N-1}) / S_N \times 100\% \) was used, where \( S_N \) is the sales of one injection at the year N and \( S_{total} \) are the total sales of the drugs, including the injections.

The top eight selling TCMIs used in the treatment of RSRDs in the Chinese market were chosen for analysis. The names of these injections were used as key words to search for...
their clinical applications, herbal and chemical compositions, and pharmacological activities in the CNKI database. The chemical names of the injections were further used as key words to perform searches in Pubmed database. All of the studies included in this work were published from 1994 to 2012.

RESULTS

TCM for RSRDs treatment in the Chinese market

The sales of chemical drugs and TCMs accounted for 82.6% and 17.4% of all drugs sales in 2010, respectively, based on the data from SFDA SMERI (China Medicine Economic Information Network, 2012). The sales of chemical drugs and TCMs for the treatment of RSRDs accounted for 54.5% and 45.5% of all sales, respectively, in 2010 (excluding systemic anti-infective drugs, which are mostly treated by antibiotics in China), indicating the importance of TCMs in treating RSRDs in China. The sales of TCMs for RSRDs increased from 2006 to 2011, with an average growth rate of 34% (Figure 1), the annual growth rates from 2007 to 2011 are 24%, 17%, 29%, 16% and 25% respectively.

Figure 1. The sales of TCM for the treatment of RSRDs from 2006 to 2011
TCMIs for RSRDs treatment in the Chinese market

At present, 1,269 TCMIs formulations are registered in SFDA, including 524 species (41.3%) for RSRDs treatment (China Medicine Economic Information Network, 2012). Among these injections, 365 species were listed in the National Health Insurance Directory and 135 species were listed in the national essential drugs list. These injections account for 70% and 26% of the total number of TCMIs used in the treatment of RSRDs, respectively.

The brand concentration of TCMIs for RSRDs treatment is high. In 2011, five species of injections were observed in the top ten sales of TCMs for RSRDs treatment and their sales accounted for 38% of the total sales of TCMs for RSRDs. Among these injections, the sales of three species added up to one billion (China Medicine Economic Information Network, 2012). The top five selling TCMIs for RSRDs treatment are Xiyangping, Tanreqing, Xuebijing, Yanhuning, and Reduning injections (Chinese names of some TCMIs) (see in Table 1). All of the injections maintained a positive growth trend, except for the Yanhuning injection, the growth rate of which declined by 1% (Figure 2). Xiyangping, Tanreqing, and Reduning injections are all listed in the national health insurance directory. The sales of Xiyangping injection increased to 0.32 billion yuan (RMB) in 2011, almost twice that of Bailing capsules, the best seller of other TCM formulations for RSRDs treatment (China Medicine Economic Information Network, 2012).

Figure 2. The change of TCMIs’ sales for the treatment of RSRDs from 2006 to 2011
Table 1. The rank of TCMIs’ sales for the treatment of RSRDs in 2011

<table>
<thead>
<tr>
<th>Rank</th>
<th>Injections</th>
<th>Chinese herbal medicine compositions</th>
<th>Main chemical compositions</th>
<th>Market share of RSRDs medicine</th>
<th>Sales (million, RMB)</th>
<th>Growth rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Xiyanping injection</td>
<td>Herba Andrographisis</td>
<td>Andrographolide, etc.</td>
<td>14.7%</td>
<td>323</td>
<td>73</td>
</tr>
<tr>
<td>2</td>
<td>Tanreqing injection</td>
<td>Radix Scutellariae, Bear bile powder, Goat horn, Flos Lonicerae Japonicae, Fructus Forsythiae</td>
<td>Baicalin, Chlorogenic acid, Ursodeoxycholic acid etc.</td>
<td>9.3%</td>
<td>204</td>
<td>22</td>
</tr>
<tr>
<td>3</td>
<td>Xuebijing injection</td>
<td>Flos Carthami, Radix Paeoniae Rubra, Rhizoma Chuanxiong, Radix Angelica Sinensis, Radix Salviae Miltiorrhiza</td>
<td>Danshensu, Safflower yellow pigment A, Tetramethylpyrazine, Ferulic acid, Paeoniflorin, Protocatechuic aldehyde etc.</td>
<td>6.5%</td>
<td>142</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>Yanhuning injection</td>
<td>Herba Andrographisis</td>
<td>Andrographolide, etc.</td>
<td>4.5%</td>
<td>98.2</td>
<td>-1</td>
</tr>
<tr>
<td>5</td>
<td>Reduning injection</td>
<td>Herba Artemisiae Annuae, Flos Lonicerae Japonicae, Fructus Gardeniae</td>
<td>Chlorogenicacid, Geniposide, Artemisinin etc.</td>
<td>2.2%</td>
<td>47.5</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>Chuankezhi injection</td>
<td>Herba Epimedi, Radix Morinda Officinalis</td>
<td>Epimedium polysaccharide, Icariin,Epimedium flavonoids etc.</td>
<td>0.4%</td>
<td>9.6</td>
<td>150</td>
</tr>
<tr>
<td>7</td>
<td>Chuanhuning injection</td>
<td>Herba Andrographisis</td>
<td>Andrographolide, etc.</td>
<td>0.4%</td>
<td>8.1</td>
<td>-32</td>
</tr>
<tr>
<td>8</td>
<td>Shuanghuanglian injection</td>
<td>Flos Lonicerae Japonicae, Radix Scutellariae, Fructus Forsythiae</td>
<td>Caffeic acid, Chlorogenic acid, Baicalin, Forsythin etc.</td>
<td>0.1%</td>
<td>2.6</td>
<td>-17</td>
</tr>
</tbody>
</table>
Clinical applications of TCMIs for RSRDs

Both Xiyanping and Reduning injections are used to treat infectious diseases and mainly focus on children (Liu et al., 2007; Zhang & Yang, 2012). These injections are also used to treat hand, foot, and mouth disease in babies, infantile diarrhoea, acute icteric model hepatitis, chronic prostatitis, and old herpes zoster, among others, in addition to the treatment of RSRDs (Liu et al., 2007; Zhang & Yang, 2012). Tanreqing, Yanhuning, and Chuankezhi injections are mostly used to treat bronchitis and various types of pneumonia (Feng, 2007; He, 2008; Liang, 2006). Besides treating bronchitis and the upper respiratory tract infections, both Chuanhuning and Shuanghuanglian injections are used to treat gastrointestinal tract inflammation, urinary tract infection, and myocarditis (Li, 2005; Liu & Xu, 2005). Xuebijing injection is significantly different from the aforementioned injections, as it is generally used for emergency and critical care, such as systemic inflammatory response syndrome caused by acute respiratory distress syndrome and sepsis (Zhang, 2008). Therefore, TCMIs have wide clinical applications and excellent performance in the market for RSRDs treatment.

Herbal compositions of TCMIs used for RSRDs treatment

Among the TCMIs mentioned in Table 1, most belong to the Qingre area (clearing heat) in TCM. For example, the major compositions of Xiyanping, Yanhuning, and Chuanhuning injections are herbs of Andrographis (Ma & Kuang, 2010; Zhong, Zeng, & Guo, 2010). Both Tanreqing and Shuanghuanglian injections contain Flos Lonicerae Japonicae, Radix Scutellariae and Fructus Forsythiae (Li & Li, 2011; Tu & Huang, 2008). Reduning injection contains Herba Artemisiae Annuae, Flos Lonicerae Japonicae and Fructus Gardeniae (Jiang, et al., 2008; Liang, Huang, & Cai, 2008). The main herbs that compose Xuebijing injection are Flos Carthami, Radix Paeonae Rubra, Rhizoma Chuanxiong, Radix Angelica Sinensis and Radix Salviae Miltiorrhizae, all of which have the effect of Huoxue (promoting blood circulation) (Chang et al., 2011b; Yu, 2011). The main herbs in Chuankezhi injection are Herba Epimedii and Radix Morinda Officinalis, which have the effect of Buyi (tonic) (Li et al., 2009). No herb belongs to the Huatan Zhike Pingchuan class (preventing phlegm from forming, stopping coughing and relieving asthma) of TCM, which is the most-represented TCM for RSRDs treatment among the top eight ranking injections. The absence of an herbal component is due to the dosage form, as syrup is the main form for the Huatan Zhike Pingchuan class of TCM.

Chemical compositions and pharmacological activities of TCMIs used for RSRDs treatment

We further analyzed the main chemical compositions and pharmacological activities of the top eight injections listed in Table 1. Three injections contained andrographolide or its derivatives. Andrographolide presents excellent antibacterial, antiviral, anti-inflammatory, and anticancer effects (Chen et al., 2009; Ji, 2011; Lim et al., 2012). Chlorogenic acid and baicalin have also emerged in numerous injections. Chlorogenic acid has anti-inflammatory, antioxidative, antibacterial, cardiovascular protective effects, and so on (Ji, 2011; Wang et al., 2011). Baicalin has antibacterial, antiviral, antioxidative, anti-inflammatory, sedation, and immune system regulation effects (Ji, 2011; Srinivas, 2010; Zhu et al., 2012). Several injections contain geniposide, danshensu, safflower...
yellow A, philyrin, and icariin, among others, all of which have numerous pharmacological activities (Ji, 2011).

**DISCUSSION**

Chemical drugs continue to enjoy several advantages in the Chinese market. However, the markets for TCM and chemical drugs are similar in RSRDs treatment if the influence of antibiotics is excluded. The TCM market in RSRDs treatment has continuously grown in recent years. If the Chinese government continues to enforce numerous policies to reduce antibiotic abuse, the advantages of TCM will significantly increase.

TCMIs can enter human tissues, blood, or organs directly, and can be absorbed faster than other forms of TCM. Thus, TCMIs overcome several disadvantages of TCM dosing, such as dose inaccuracy, slow effect and low bioavailability. Compared with anti-neoplastic TCMIs, which are mostly used for adjuvant therapy (Lai et al., 2012), TCMIs have more important functions in RSRDs treatment. From the herbal and chemical composition analysis, most TCMIs for RSRDs treatment have Qingre effects (clearing heat).

Classifying TCM against the standards of Western medicine is difficult due to the different theories behind Chinese and Western medicine. For example, Xuebijing injection is also used to treat cardiovascular diseases. Clinical applications of cross treatments could result in greater potential for TCMIs. With more and more TCMIs used in the treatment of RSRDs are into the national health insurance directory, along with the new medical reform policy is carried out constantly, the TCMIs market will continue to expand in China.

Although the TCMIs market for RSRDs treatment is increasing significantly, the entire market scale remains small. The market concentration is extremely high such that few products occupy most of the market. The increased market is mainly attributed to these products, which are almost exclusively manufactured or monopolized by a few companies. Thus, the medicine market and patients are cautious about the TCMIs used in RSRDs treatment. Besides, the credibility of TCMIs has decreased because numerous patients have reported adverse reactions (Liang & Shi, 2012; Ma & Kuang, 2010).

Chemical compositions, clinical applications, and individual differences are the three main reasons for the adverse reactions of TCMIs. TCMIs have several features, such as complex compositions, herb quality unsteadiness, and residual impurity, and these factors are the main sources of adverse events (Ma & Kuang, 2010; Wu et al., 2012). Irrational clinical applications also result in adverse reactions (Ma & Kuang, 2010; Wu et al., 2012). For such adverse events, legal and administrative regulations should be enhanced. The SFDA carried out a series of specialized policies for the quality of TCMIs and safety evaluation from 2007 to 2009. These policies have increased the threshold of TCMIs research and development and advanced efforts for the safety evaluation of TCMIs. Identifying and controlling the effective and toxic compositions of the injections are necessary. Technological studies and clinical compatibility studies for TCMIs should be given more attention.

**CONCLUSION**

TCMIs have highly important functions in RSRDs treatment in China. From the market’s perspective, TCMIs for RSRDs treatment show a positive trend and great potential, with rapid
increasing sales and expanding market demand. In clinical view, TCMIs show the predominant and effective feature, by combining some advantages between TCM and Western medicine. Development of TCMIs is a complicated issue with traditional theory and advanced technology, so research and development institutes, manufacturers, hospitals, and regulation departments must cooperate with one another to establish a positive outlook for the development of TCMIs.

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