Review Article

Comparative Analysis of ADR on China’s National Essential Medicines List (2015 Edition) and WHO Model List of Essential Medicines (19th Edition)

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Objective. To explore the safety of the essential medicines recorded in China’s list through the comparison of the list of essential medicines of China and the World Health Organization (WHO), as well as the analysis of the basic situation and characteristics of adverse drug reactions (ADRs) on the two essential medicines recorded in China’s and WHO lists in order to provide a reference for the improvement of China’s list.

Methods. A retrospective descriptive study was conducted, based on the database in Jiangsu Province ADR Monitoring Center from 2013 to 2015. A total of 266869 cases reports were collected within this period, comparing the differences between the two essential medicines recorded in China’s and WHO lists, considering number of ADRs, type of report, and modes of administration. Compare the differences between the two groups of drugs in the presence of new, severe, and new severe adverse events using chi square test.

Results. Comparing the two essential medicines list, they have the same 117 species. When comparing ADRs in the two groups, most are antimicrobial, electrolytes, and acid-base balance drugs, regulate water, and are higher in China. In addition, with respect to the number of ADR types in the two groups, there is statistical significance ($p<0.001$) (total number is 68603 and 47515, new types are 12601 and 7262, the severe are 2714 and 7566, and the new severe are 820 and 716).

Conclusion. Compared to the WHO list of essential drugs, China’s list is still to be improved.

1. Introduction

Essential medicines satisfy people’s desire for health; they are selected through cost-effectiveness comparison and according to the current situation, effectiveness, and safety of public health [1, 2]. The establishment of essential medicines list of China has been based on the directory of WHO [3, 4].

Although many reports which used the ADR database to advance the safety of drugs have been published [5, 6], there are also authors who based on the small sample of ADR of individual breeds analyzed essential medicines list of China [7]. These earlier findings lead us to other imperative, comprehensive, and updated questions. The goal of this study was to characterize the differences between the two essential medicines recorded in China’s national essential medicines list (2015) [8] and WHO model list of essential medicines (19th edition) [9], considering classification, number of ADRs, type of report, and the way of administration during the period 2013-2015. The data comes from National Center for ADR Monitoring of Jiangsu Province.

2. Materials and Methods

China’s national essential medicines list (2015 edition) and WHO model list of essential medicines (19th edition) were obtained from the ministry of health website. Using the database of Jiangsu Province ADR Monitoring Center from 2013 to 2015 to perform a retrospective study, we analyze the differences between the two essential medicines recorded in China’s and WHO lists with ADR by the number, type of report, and the way of administration. Analyzes employed descriptive statistics and chi square test.
Table 1: The occurrence of ADR with medicines recorded in China's and WHO list.

| Drug classification          | WHO model list | China's list | The same number | WHO essential medicines | China essential medicines |
|------------------------------|----------------|--------------|------------------|-------------------------|--------------------------|
|                              | ADR cases      | Composition% | ADR cases        | Composition%            |                          |
| Anti-infective               | 76             | 55           | 27               | 18128                   | 37.52                    |
| Anthelminthics               | 31             | 9            | 7                | 495                     | 1.02                     |
| anaesthetics                 | 13             | 4            | 2                | 455                     | 0.94                     |
| Medicines for pain and palliative care | 34             | 18           | 4                | 4089                    | 7.65                     |
| The nervous system           | 9              | 18           | 7                | 959                     | 1.99                     |
| Medicines used in mood disorders | 14             | 6            | 3                | 2768                    | 5.73                     |
| Cardiovascular               | 21             | 31           | 13               | 1958                    | 4.05                     |
| Respiratory medicines        | 5              | 8            | 1                | 229                     | 0.47                     |
| Gastrointestinal medicines   | 10             | 29           | 4                | 1673                    | 3.46                     |
| Urinary medicines            | 5              | 7            | 3                | 971                     | 2.01                     |
| Medicines affecting the blood | 22             | 16           | 4                | 657                     | 1.36                     |
| Endocrine medicines          | 23             | 21           | 4                | 1398                    | 3.10                     |
| Antiallergic medicines       | 5              | 5            | 1                | 983                     | 2.04                     |
| Immune system medicines      | 4              | 2            | 1                | 61                      | 0.13                     |
| Vitamins, minerals           | 12             | 15           | 2                | 110                     | 0.23                     |
| Adjust water, electrolyte and acid base balance | 9            | 9           | 6                | 11266                   | 23.87                    |
| Antidotes                    | 15             | 6            | 3                | 203                     | 0.48                     |
| Biological products          | 8              | 4            | 2                | 28                      | 0.06                     |
| Diagnostic agents            | 7              | 2            | 1                | 326                     | 0.68                     |
| Dermatological medicines     | 16             | 12           | 9                | 730                     | 1.51                     |
| Ophthalmic medicines         | 13             | 13           | 9                | 142                     | 0.29                     |
| Ear and nose medicines       | 4              | 3            | 0                | 68                      | 0.14                     |
| obstetrics and gynecology medicine | 4              | 7            | 3                | 515                     | 1.07                     |
| Family planning medicines    | 13             | 1            | 1                | 98                      | 0.20                     |

Note: Repeat medication for one

3. Results

3.1. Comparison of the Occurrence of ADR with Medicines Recorded in China’s and WHO Lists. There are 373 essential medicines recorded in WHO and 301 in China. The same species are 117. A total of 266869 cases of ADR were discharged within this period, with 76282 cases occurring in essential medicines recorded in China and 48310 cases in WHO. Among them, the most ADR are all anti-infective adjust water, electrolyte, and acid-base balance medicines. The second are respiratory medicines, medicines for pain and palliative care, and gastrointestinal medicines. The number of ADRs of these medicines in China’s list is significantly higher than that in WHO (Table 1).

3.2. Comparison of the Type of ADR. It is presents the characteristics of the type of ADR discharged in the two essential medicines list (Table 2). Comparing the China’s essential medicines list with number of ADRs with WHO, they have higher new and new severe adverse events (12601
Table 2: Comparison the type of the ADR.

| Total  | New   | Sever  | New severe |
|--------|-------|--------|------------|
| China  | WHO   | China  | WHO        | China  | WHO   | China  | WHO   |
| 2013   | 23234 | 13705  | 4449       | 2253   | 932   | 2199   | 256   |
| 2014   | 21618 | 14882  | 4134       | 2280   | 877   | 2827   | 272   |
| 2015   | 23751 | 18928  | 4018       | 2729   | 905   | 2540   | 292   |
| Total  | 68603 | 47515  | 12601      | 7262   | 2714  | 7566   | 820   |

Note: using chi-square test to compare the differences between the two groups of drugs in the presence of new, severe, and new severe adverse events; statistically significant (p < 0.05). New: the adverse reactions are not specified in the drug specification. Severe: reaction to one of the following, damage caused by taking a drug: (1) death; (2) carcinogenic, teratogenic, or birth defects; (3) dangerous to life and can cause permanent or significant disability; (4) permanent damage to organ function; and (5) being hospitalized or staying in hospital for too long. New severe: the adverse reactions are severe and not specified in the drug specification.

Figure 1: Administration route.

and 820) and lower number of severe adverse events (2714). When comparing the type of new, new severe, and severe adverse events, all results are statistically significant (p < 0.01).

3.3. Comparison of the Modes of Administration of ADR. It is illustrate that oral, intravenous drip, external use, local, Yin/intestinal administration, and inhalation are the main modes of administration for adverse reactions to essential medicines recorded in China and WHO list (Figure 1). Also it was found that oral and intravenous drip modes of administration have the highest proportion, 47.0% and 51.8% in essential medicines list of China and 34.2% and 64.3% in WHO essential medicines list. The other modes of administration have a lower ratio.

4. Discussion

In recent years, the ADR reporting systems have been providing a basis for drug safety evaluation. There are authors who showed the necessity and feasibility of using big data to study the research on active monitoring of drugs [10, 11]. According to the China Food and Drug Administration (CFDA) “annual report on national drug adverse reaction monitoring” (2015), 1398,000 ADR reports have been reported in nationwide. However, nearly 90,000 reports have been reported annually in Jiangsu Province, accounting for 6.4 percent of the national sample size. It can reflect the overall situation of the national ADR.

Therefore, exploring the safety of the drugs recorded in China’s essential medicines list based on a large sample is necessary. The results showed that the number of ADRs in China’s list was much higher than that of the WHO.

It is necessary to discuss the safety of the drugs recorded in China’s essential medicines list based on the large sample data. The results showed that the number of ADRs in China’s list was much higher than that of the WHO. Among them, anti-infective medicine and regulating water, electrolyte, and acid-base balance drugs have the most ADR (Table 1) and China was also higher than WHO. This is closely related to its usage amount, but we should pay more attention to irrational drug-induced ADR. The use of anti-infective drugs without indications, long course of treatment, and unreasonable preventive are very universal in clinical practice [12].

In administration, our study shows that oral and intravenous drips have the highest proportion, in the two essential medicines lists. The other modes of administration have a lower ratio. The reason may be due to injection and injection of sterile powder compared with other medication, endotoxin, pH, osmotic pressure, and particles and other internal factors are more likely to lead to ADR in injection [14]. Oral administration is relative to a large number of applications [15].

Therefore, we should pay close attention to the patient’s complaints and first-line clinical feedback of adverse
reactions. For the revision of China’s essential medicines list, an updated drug manual provides the most stringent basis [16].

Conflicts of Interest

The authors declare no conflicts of interest.

Authors’ Contributions

Hongdou Chen participated in the design of the study. Fangfang Zheng was involved in writing of the paper and statistical analysis. Lu Ye and Yanfang Chen performed the statistical analysis. Huanhuan Wu helped to draft the manuscript. Fangfang Zheng and Hongdou Chen have contributed equally to this work.

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