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Chaotic characteristics analysis of inpatient intravenous medication time series by the 0-1 test

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ABSTRACT

Medication safety concerns the wellbeing of patients. Ambroxol hydrochloride, as a commonly used medicine for respiratory diseases, is investigated in this paper. 0-1 test method is adopted to analyze chaotic characteristics of inpatient intravenous medication time series whose data is collected from a hospital in the second half year of 2013. By comparing the correlation coefficients and regression method, we can learn the results that the average value of K-c of time series is close to 1, and the P-Q diagram presents a Brownian motion. Finally, Poincare section and the largest Lyapunov exponent are used to verify the accuracy of the 0-1test. Analysis results show that the medication time series in treatment of respiratory diseases is chaotic and not periodic with the development of time. It enjoys an important guiding significance for further studies of rational medication and trends analysis of respiratory diseases.

KEYWORDS

Medication time series; Chaos; 0-1 test; Lyapunov exponent; Poincare section.

INTRODUCTION

Medication safety is directly related to health outcomes and patient safety, medication regularity of the patient has been investigated as one of the key quality management of pharmaceutical care in hospitals.

Currently research is mainly confined to unsynchronization of theory and practice, the lack of quantitative research methods and the corresponding theoretical support, only local problems are solved, but the PIVAS is the most important part of protecting patient safety, and its heavy workload, many circulation, demand changes quickly of patients and health care workers, easily medical disputes, especially the overall business efficiency cannot meet the low error rate under high standards. The study about drug laws maintain regular and irregular systems, rules systems are generally linear or cyclical variation between several drugs, obviously irregular system with nonlinear characteristics, and it often contains some certainty law. Therefore, characteristics analysis of inpatient intravenous drug use time series becomes necessary.

Chaos is a common phenomenon in nature. With the development of computer technology its theory has been rapid development, and have been widely applications in the military, economic, transportation, electronics, biomedical and other fields, which greatly promoted the development of these disciplines. Chaotic theory and method are applied to a variety of medical time series, such as analysis of ECG HRV disease. At present, domestic and foreign medical nonlinear characteristics of time series analysis are as following: Wang et al[1-2] analyzed the chaos characteristic of time series of the healthy and morbid fetal heart rate by using surrogates data. The result indicated that the healthy signals have the non- linear chaos characteristic; while the morbid signals do not have the chaos characteristic. Han et al[3] studied the neural coding of the electrical signal by the Lyapunov exponent, correlation dimension and power spectrum. It is also shown that under the effect of the acupuncture, the electrical signals of dorsal spinal nerve root based on acupuncture at Zusanli point has distinguished chaotic features. In [4], the original EEG signals were de-noise processed, and chaos time series analysis was carried out to calculate the correlation dimension using G-P method and the largest Lyapunov exponent using small data set method. The result shows that the largest Lyapunov exponent of all the EEG signals is greater than zero, which indicates that the EEG signal may be chaotic. The ECoG time series of anaesthetized SD rat before and after epileptic seizure are exactly analyzed[5]. The computational results show that there are distinct differences in the largest Lyapunov exponents and the approximate entropies before and after epileptic onset, which can provide with some clues for understanding the mechanism of epilepsy and predicting epileptic seizure and curing epileptic patients. In[6], Effect of nortriptyline and paroxetine on measures of chaos of heart rate time series in patients with panic disorder were analyzed by the largest Lyapunov exponents. Mekler et al.[7-13] used correlation dimension, attractor, and the largest Lyapunov exponents to investigate the chaotic characteristics of human electroencephalogram (EEG). It makes it possible to evaluate variability of human brain functioning. Zhu et al.[14] proposes a fast weighted horizontal visibility graph constructing algorithm (FWHVA) to identify seizure from EEG signals. Vesna[15] investigated nonlinear and linear characteristics of heart period variability with aging in supine and standing posture. Wysocki et al.[16] shows that the noise titration approach evidences a chaotic dimension to the behavior of ventilatory flow over time in normal humans during tidal breathing. Ren[17] used the time series analysis method to study the DNA sequences of the influenza virus from 1913 to 2010. Effect of chaotic and periodic sympathetic nerve stimulation on DRG neurons was compared[18]. The singularity of chaotic signals is studied by using the maximum Lyapunov exponent[19]. A cerebral vascular hemodynamic chaotic characteristic was investigated by time series analysis[20]. Jiao et al[21] introduced the basic concepts and research methods of chaos and fractals, and it was used in ECG study. Hospital inpatient time law was explored by spectral analysis[22]. Li et al[23] establish a trend model of time series on drug consumption of the hospital by means of time series decomposition forecasting base on the drug consumption related data which is cumulated in the hospital information system (HIS). Results indicate much better prediction.

In summary, the study abroad for a chaotic medical time-series analysis, mainly related to the phase space reconstruction method, maximum Lyapunov exponent method, power spectrum method. Recently, a new test has been proposed to detect the presence of low-dimensional chaos in time series[24]. Unlike the classic method of calculating MLE, The method does not need the underlying equations, the reconstruction of the phase space, or the dimension of the actual system. The test has been applied successfully on theoretical time series, both with and without noise, from various dynamical systems, as well as on experimental data[25]. It is, furthermore, relatively easy to implement. The test only gives two possible results: 0 for a non-chaotic system, and 1 otherwise.

Therefore, based on hospital information systems (HIS) and inherent correlation and regularity of medication time series, we introduced 0-1test method to investigate the chaotic characteristics of inpatient intravenous drug use time series. The results will provide the necessary data base and decision-making for inpatient medication safety.

MEDICATION DATA ACQUISITION

Respiratory disease is a commonly and frequently encountered disease, which results from pathologic changes in trachea, bronchus, lung and thoracic cavity. Symptoms of patients with respiratory disease are cough, chest pain and affected breathing. More severe symptoms are labored breathing, oxygen lack and even death. It ranks third in urban areas with high death rate and tops in rural areas. What's more, factors like air pollution, smoking, and ageing of population lead to higher disease incidence and death rate throughout the world.

From this perspective, case study of respiratory diseases is conducted in this paper. Vein medication database in the second half year of 2013 is obtained from HIS system in some hospital. A commonly used medicine is determined from analyzing

the data. The rules of this medicine, Ambroxol Hydrochloride (Yunnan, 2ml: 15mg*1), are shown in Figure 1. It is for acute or chronic respiratory diseases featured as the dysfunction of sputum secretion. For instance, the expectorant treatment of chronic bronchitis, asthmatoid bronchitis and bronchial asthma; pretest probability treatment of post operation pulmonary complications; treatment of respiratory distress syndrome of premature infant and newborns.

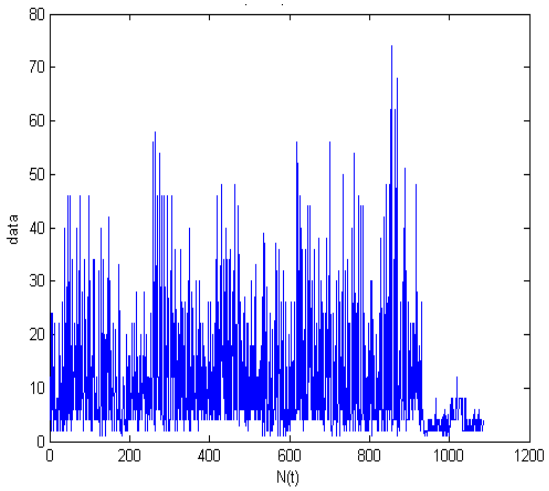

Figure 1 : Time Series plot of Ambroxol Hydrochloride

THE 0-1 TEST FOR CHAOS

Principles of 0-1 test are as follows.

Consider an obtainable set $\phi(j)$, $j = 1, ..., N$,

For $c \in (0, \pi)$, we calculate its transformed variables

$$p_c(n) = \sum_{j=1}^{n} \phi(j) \cos jc, \qquad q_c(n) = \sum_{j=1}^{n} \phi(j) \sin jc \tag{1}$$

$n = 1, 2, ..., N$.

To determine the increase of p_c and q_c, mean square displacement (MSD) is taken into consideration, which is defined by

$$M_c(n) = \lim_{N \to \infty} \frac{1}{N} \sum_{j=1}^{N} [(p_c(j+n) - p_c(j))^2 + (q_c(j+n) - q_c(j))^2] \tag{2}$$

It requires $n << N$. In practice, better outcome occurs when $n_{cut} = N/10$. This method is based on the premise $M_c(n)$ acts as the growth rate of n-related function. Next, the rising growth rate of $K - c$ is estimated.

In this paper, correlation coefficient is introduced to determine $K - c$. By calculating vectors $\xi = (1, 2, 3, ..., n_{cut})$ and $\Delta = (M_c(1), M_c(2), M_c(3), ..., M_c(n_{cut}))$, and the extent of vector x, y, we define the covariance and variance as:

$$\operatorname{cov}(x, y) = \frac{1}{q} \sum_{j=1}^{q} (x(j) - \bar{x})(y(j) - \bar{y}) \tag{3}$$

In the equation (2.3), $\bar{x} = \frac{1}{q} \sum_{j=1}^{q} x(j)$

$\operatorname{var}(x) = \operatorname{cov}(x, x)$, correlation coefficient is defined as

$$K - c = corr(\xi, \Delta) = \frac{\mathrm{cov}(\xi, \Delta)}{\sqrt{\mathrm{var}(\xi)\,\mathrm{var}(\Delta)}} \in [-1,1] \quad \textbf{(4)}$$

When the value of $K-c$ is close to 0, it is a regular dynamic system; when the value of $K-c$ is close to 1, it is a chaotic dynamic system.

RESULTS AND DISCUSSION

Chaotic characteristics of drug-use time series of common respiratory diseases are analyzed in this paper. $K-c$ is calculated by correlation coefficients, shown in Figure 2 (left). Figure 2 (left) indicates that the value of $K-c$ is around 1. The outcome after enlargement shows as well the value of $K-c$ is around 1. According to 0-1 test, medication amount of Ambroxol Hydrochloride in treatment of respiratory diseases in the second half year of 2013 changes in a chaotic and non-periodic manner with the change of time, which further indicates the trend of treating patients with respiratory diseases in this hospital. It is random rather than periodic. Figure 2 (right) presents regression method determining the value of $K-c$. Similarly, the value of $K-c$ is around 1 and close to 1, which reflects this system is chaotic.

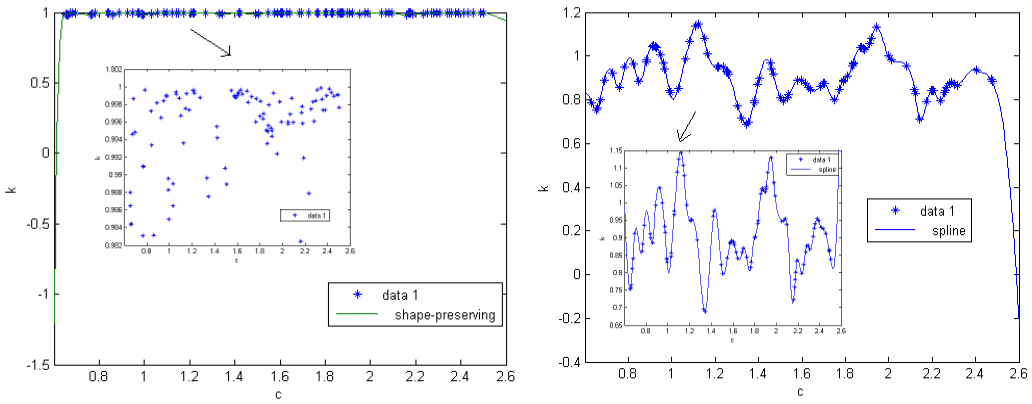

Figure 2 : Comparison between correlation coefficient and regression method

Figure 3 is a p-q diagram based on 0-1 test. It is noticed that it presents a Brownian motion, which verifies the correctness of this calculation. To determine the dynamic system chaotic depends on verification of several approaches. Next, Poincare surface of section and the largest Lyapunov exponent are adopted.

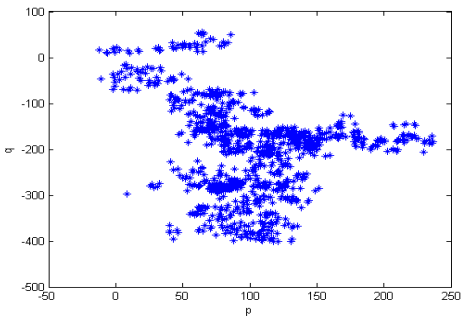

Figure 3 : P-Q diagram of Ambroxol Hydrochloride time series

Principles of Poincare section are as follows. When the system takes a periodic motion, there are n dots on the surface of Poincare section (called periodic n movement); when the system takes a quasi-periodic motion, there is a closed curve on the surface of Poincare section; when the system takes a non-periodic and chaotic motion, there are dense dots with fractural structure on the surface of Poincare section. Therefore, Poincare section can be used to determine a system is chaotic or not. As in figure 4, Ambroxol Hydrochloride series presents dense dots with fractural structure on the surface of Poincare section, and after enlargement, similar phenomenon occurs, thus, this time series is chaotic.

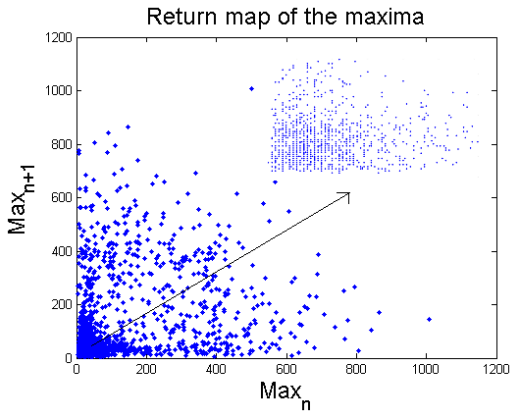

Figure 4 : Poincare section of Ambroxol Hydrochloride series

When Lyapunov exponent is greater than 0, adjacent tracks separate as time evolves. After a relative long time, it becomes more sensitive to the original conditions, and its movement takes a chaotic trend. When Lyapunov exponent is smaller than 0, adjacent tracks draw close with time evolving. Its phase volume narrows and the movement become stable. It is unsensitive about the original conditions. When Lyapunov exponent is 0, adjacent tracks keep parallel with the development of time, which indicates that the system is in critical state. Figure 5 shows the determination of a system embedding dimension. The embedding dimension of this system is 3. Figure 6 is Lyapunov Exponent graph. Rosenstein method is used to acquire the nonlinear time series, LLE=0.0036, greater than 0, the system is chaotic. Main advantages of calculating the largest Lyapunov Exponent using Rosenstein method lie in the robustness in dimension reconstruction, time delay and noise level. It gets the largest Lyapunov Exponent more accurate than by other approaches.

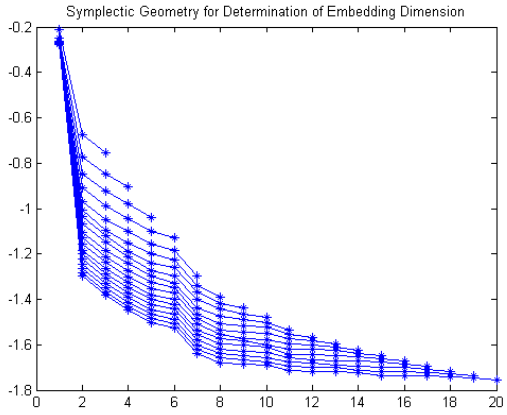

Figure 5 : Determination of embedding dimension

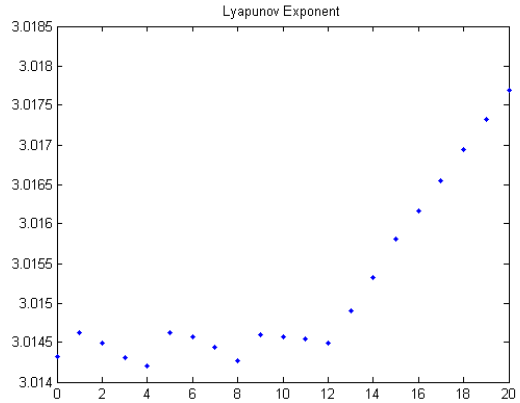

Figure 6 : Lyapunov Exponent

CONCLUSIONS

This paper proposes to adopt 0-1 test method to conduct a chaotic-characteristic analysis of medication time series of Ambroxol Hydrochloride in treating patients with respiratory diseases in the second half of 2013. Compared with other approaches, it is easy to carry out and avoids using basic functions, phase space reconstruction and embedding dimension. It can obtain the chaotic state with real-time medication time series. Results show that the medication time series of Ambroxol Hydrochloride changes in a non-periodic manner. Based on 0-1 test, K-c calculations with correlation coefficients and regression method are conducted respectively. The calculation outcomes are close to 1 and the simultaneous p-q diagram presents a Brownian motion, which reflects this system is chaotic. Finally, Poincare section and the largest Lyapunov exponent are used to verify the accuracy of 0-1 test. There are clustered dense areas on the surface of Poincare section. It is self-similar in part and whole. The largest Lyapunov Exponent using Rosenstein method is 0.0036, which demonstrates that the system is chaotic. It also indicates that the medication time series of this hospital in treating patients with respiratory diseases is chaotic. It is of great significance to further explore the rational medication time and its changing trend.

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