The correlation between gatifloxacin’s acute adverse reaction and intravenous drip velocity

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ABSTRACT

الأهداف: التحقق من العلاقة بين الرد فعل سلبي (AAR) والسرعة بالتقطير (جاتيفلوساسين) في الوريد.

الطرق: اشتملت هذه الدراسة على المرضى الذين تلقوا الحقن (0.2 جرم/100 مل) في مركز الطوارئ، مستشفى جونان، جامعة وهان، الصين خلال الفترة من يناير حتى أغسطس 2012 وتم تقسيم المرضى عشوائياً إلى 3 مجموعات وفقًا لسرعات التقطير المختلفة: مجموعة A (نالت 10 قطرات في الدقيقة الواحدة)، مجموعة B (نالت 20 قطرات في الدقيقة الواحدة) و مجموعة C (نالت 30 قطرات في الدقيقة الواحدة). وفي الأخير تم تسجيل و ذكر البيانات الديموغرافية من المرضى.

النتائج: رد فعل سلبي (AAR) من الجهاز الهضمي والجهاز العصبي و استقلال الجلوكوز ليس له ارتباط كبير مع سرعة التقطير في الوريد (جاتيفلوساسين).

خاتمة: من الجلد والجهاز الهضمي والجهاز العصبي الورائي يمكن ان تكون أعراضها مناسبة مع الوريد (جاتيفلوساسين) (0.2 جرم/100 مل) الذي هو أقل من 10 قطرات في الدقيقة الواحدة.

Objectives: To investigate the correlation between acute adverse reaction (AAR) and intravenous drip velocity of gatifloxacin.

Methods: Patients who had received intravenous gatifloxacin (0.2g/100ml) infusion in the Emergency Center, Zhongnan Hospital, Wuhan University, Wuhan, China from January to August 2012 were enrolled in this study. Patients were randomly divided into 3 groups according to different drip velocities: Group A: velocity ≤10 drops per minute; Group B: <10 velocity ≤20 drops per minute; Group C: <20 velocity ≤30 drops per minute. The AAR and demographic data of patients were documented.

Results: Acute adverse reaction of the skin and digestive system were significantly positively related to intravenous drip velocity. The AAR of the cardiovascular system significantly increased when the intravenous drip velocity was beyond 20 drops per minute. The AAR of nervous system and abnormal glycometabolism has no significant correlation with intravenous drip velocity of gatifloxacin.

Conclusion: Acute adverse reactions of skin, digestive system, and cardiovascular system would decrease with an appropriate velocity of intravenous gatifloxacin (0.2g/100ml) less than 10 drops per minute.


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injection was safe and well tolerated, the acute adverse reaction (AAR) reports increased with its wide application.\(^2\) Reactions of the gastrointestinal tract, the central nervous system (CNS) and the skin are the most often observed adverse effects.\(^3\) Over the years, several structure-activity and side-effect relationships have been developed, in an effort to improve overall antimicrobial efficacy while reducing undesirable adverse effects. However, the role of drip velocity has not been investigated. The objective of our study was to evaluate the possible correlation between the incidence of gatifloxacin’s AAR and its intravenous drip velocity.

**Methods.** From January to August in 2012, 1868 patients (18-60 years old) who had received intravenous gatifloxacin (0.2g/100ml) injections in the Emergency Centre, Zhongnan Hospital, Wuhan University, Wuhan, China were enrolled in this study. Patients with diabetes, chronic kidney disease and allergy reactions were excluded. The research committee of Zhongnan hospital affiliated to Wuhan University approved this observational study. The velocity of intravenous drip should be controlled at less than 30 drops per minute according to the instruction of gatifloxacin injection.

Patients were randomly divided into 3 groups according to different drop velocity: Group A: velocity ≤10 drops per minute; Group B: <10 velocity ≤20 drops per minute; and Group C: <20 velocity ≤30 drops per minute. The AAR and demographic data of patients were documented. If AAR occurred, the symptom of AAR should be documented, the patients who may have abnormal glucose metabolism should check the blood glucose and the patients who have cardiovascular adverse reactions should receive electrocardiogram test immediately.

**Statistical analysis.** We used the Statistical Package for Social Science Versus 13.0 (SPSS Inc., Chicago, IL., USA) software for statistical analysis. Chi-square test was used to compare the difference between groups. A \(p\)-value less than 0.05 was considered significant.

**Results.** There were 76 patients excluded due to diabetes, nephritis or the age above 60 years old. A total of 1792 patients were enrolled in this study: Group A (n=565), Group B (n=806), Group C (n=421) (male 1067 and female 725). The symptoms of patients with skin AAR were rash, itching and skin flushing, especially in infusion limb. The symptoms of patients with digestive system AAR were nausea, vomiting, abdominal pain and diarrhea. The symptoms of patients with cardiovascular system AAR were palpitations, chest tightness, arrhythmia and Q-T Interval prolongation. The symptoms of patients with abnormal glucose were hyperglycemia and hypoglycemia. The symptoms of patients with nervous system AAR were dizziness, headache, and hallucination. The number of patients with skin and digestive system AAR in Group C were significantly higher than that in the Groups A and B. Moreover, the number of patients in Group A who had skin and digestive system AAR was less than that in the Group B. The patients with cardiovascular system AAR in the Group C were significantly more than the Groups A and B. However, there were no differences between Groups A and B. The patients with abnormal glucose and nervous system AAR were similar among Groups A, B, and C. The total number of patients with AAR in Group C were significantly more than Groups A and B and Group A were lower than Group B (Table 1). There were no difference between male and female patients.

**Discussion.** With the ability of inhibiting bacterial DNA gyrase and topology isomerase, Gatifloxacin antibacterial activity can inhibit bacterial DNA replication, transcription and repair process. Gatifloxacin is widely used due to its high selectivity and sterilization.\(^4\) With the increasing ADR cases of injecting Gatifloxacin in clinical, especially AARs of intravenous gatifloxacin injection, the cases were widely reported around the world, which commonly presented in the skin, abnormal glucose metabolism, cardiovascular system, digestive system and the nervous system.\(^5\-7\) The mechanism of adverse reactions was numerous. Due to the high drug fat-soluble, it can easily pass through the blood-brain barrier. The combination of its metabolites and \(\gamma\)-amino-butyric acid may cause neurological symptoms.

**Table 1** - The result of acute adverse reaction (AAR) in the 3 groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total N=1792</th>
<th>Skin system</th>
<th>Digestive system</th>
<th>Cardiovascular system</th>
<th>Nervous system</th>
<th>Abnormal glucose</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>565</td>
<td>(4^c)</td>
<td>(4^c)</td>
<td>8</td>
<td>3</td>
<td>5</td>
<td>22(^c)</td>
</tr>
<tr>
<td>B</td>
<td>806</td>
<td>18(^a)</td>
<td>21(^a)</td>
<td>14(^a)</td>
<td>5</td>
<td>8</td>
<td>63(^a)</td>
</tr>
<tr>
<td>C</td>
<td>421</td>
<td>29</td>
<td>23</td>
<td>17</td>
<td>2</td>
<td>4</td>
<td>62</td>
</tr>
</tbody>
</table>

\(^a p<0.05\) versus group C, \(^b p<0.01\) versus group C, \(^c p<0.05\) versus group B
Meanwhile, the drug is excreted primarily through the kidney. So the older and renal dysfunction patients prone to adverse reactions. It is reported that gatifloxacin can also inhibit pancreatic β-cell ATP-sensitive K+ channel to promote the release of insulin, causing abnormal glucose metabolism. With their unstable glucose metabolism, diabetes patients are more prone to glucose metabolism disorders. Because gatifloxacin’s poor water-soluble, intravenous formulations regularly used excipients such as hydrochloric acid, sodium di-hydrogen phosphate, lactic acid to dissolve the drug, these excipients may also produce adverse reactions. Clinical observation showed that slowing down intravenous drip speed might reduce adverse reactions. The results of this study also showed that skin and acute digestive system adverse reactions have a significant correlation with the drip speed. The slower drip speed reduced the incidence of AARs. When the drip speed is more than 20 drops per minute, AARs of cardiovascular system increased significantly. There was no significant correlation between the drip speed and the incidence of nervous system adverse effects and glucose metabolism disorders. Moreover, there was no significant difference between male and female with incidence of AAR. Overall, AAR had a significant correlation with intravenous drip speed. Therefore, appropriate velocity of intravenous drip can reduce the incidence of the AAR of gatifloxacin, especially in skin, digestive system and cardiovascular system. However, AARs of nervous system and glycometabolism do not have remarkable relativity with intravenous drip velocity.

Study limitations. Some patients were injected other drugs at the same time, other drugs may affect the incidence of AAR and some patients change the drip speed by themselves. All these factors will affect the results of the study; thus, only patients who received intravenous injections of gatifloxacin and who use the infusion pump to inject were included in the study.

In conclusion, acute adverse skin reaction, digestive system, and cardiovascular system would decrease by an appropriate velocity of intravenous gatifloxacin (0.2g/100ml) less than 10 drops per minute.

References


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**Case Reports**

Case reports will only be considered for unusual topics that add something new to the literature. All Case Reports should include at least one figure. Written informed consent for publication must accompany any photograph in which the subject can be identified. Figures should be submitted with a 300 dpi resolution when submitting electronically or printed on high-contrast glossy paper when submitting print copies. The abstract should be unstructured, and the introductory section should always include the objective and reason why the author is presenting this particular case. References should be up to date, preferably not exceeding 15.