THE EFFECT OF THREE METHODS ON DISSOLVING PIPERACILLIN SODIUM AND TAZOBACTAM SODIUM FOR INFECTION

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ABSTRACT

Objective: *This article compares the effects of three different methods on dissolving piperacillin sodium and tazobactam sodium for infection to improve nursing efficiency.*

Methods: *According to the random number table method, 120 bottles of piperacillin sodium and tazobactam sodium of the same manufacturer, batch number, and specification were divided into control group 1, control group 2, an experimental group, with 40 bottles in each group.The control group 1 shook the medicine evenly by the method of holding the "bottleneck"; The control group 2 shook the medicine evenly by the method of holding the "bottleneck and bottle";The experimental group shook the medicine evenly by the method of holding the "bottleneck and bottle" combing with knocking between corks,after shaking the vial twice up and down. The dissolution time and dissolution adequacy of the three groups of powder drugs are observed and compared.*

Results: *The experimental group was better than the other two groups in terms of drug dissolution time and dissolution adequacy, and the difference between the three groups was statistically significant (P<0.05).*

Conclusion: *After shaking the vial twice up and down, the method of holding the "bottleneck and bottle" combing with knocking between corks can not only shorten the dissolution time of the powder and improve the efficiency of nurses, but also make the medicine fully dissolved and ensure the accurate dosage of the medicine.*

Keywords: *Piperacillin sodium and tazobactam sodium, the method of holding bottle, dissolution.*

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Introduction

In order to comply with the development of clinical pharmacy and ensure the safety of intravenous infusion, many comprehensive tertiary hospitals at home and abroad have set up intravenous drug allocation centers[1-2] (Pharmacy Intravenous Admixture Services, PIVAS) in recent years. The center centrally configures and manages most of the intravenous medications in the hospital, which effectively relieves the pressure of medication allocation in various clinical departments. Piperacillin sodium and tazobactam sodium has a wide range of clinical applications and is a relatively insoluble antibiotic. PIVAS also undertakes the preparation of this drug. However, few PIVAS in domestic hospitals implement the 24-hour operation mode[3-4]. During the non-centralized dispensing period of PIVAS, the few and urgent medications of piperacillin sodium and tazobactam sodium prescribed by clinicians are still carried out by clinical nurses in the ward treatment room without oscillators, water incubators and other dissolution aids. Manual configuration leads to time-consuming,

labor-consuming and low dispensing efficiency for nurses. And a study[5] shows that the incidence of joint muscle strain among nurses who have been engaged in drug configuration for a long time is as high as about 70%. Based on this, this study used three methods to compare the effects of dissolving piperacillin sodium and tazobactam sodium, in order to find a way for clinical nurses to formulate the drug faster and better by hand.

Materials and methods

Materials

The experiment was carried out in the PIVAS of our hospital, and 120 bottles of piperacillin sodium and tazobactam sodium of the same manufacturer, batch number, and specification used for clinical treatment in this center in November 2021 were selected. Materials include: 120 bottles of piperacillin sodium and tazobactam sodium (trade name Ruiyang Yongkang, Shandong Ruiyang Pharmaceutical Co., Ltd., batch number H20073602, 2.25g/bottle), and 10 mL of 0.9% sodium chloride solution (China Otsuka Pharmaceutical Co., Ltd., batch number 0I88A2), 30mL syringe produced by Shandong Weigao Group, electronic timer and 5 times magnifying glass.

Methods

According to the random number table method, 120 bottles of piperacillin sodium and tazobactam sodium were divided into control group 1, control group 2, an experimental group, with 40 bottles in each group. The three groups of drug configuration were all completed at the same room temperature (18~26°C, 35~75%) and the same biological safety cabinet in the configuration center.

Two nurses were responsible, one was responsible for dissolving the medicine, and the other one was responsible for recording the time and checking the dissolution effect.

After wearing sterile gloves, the operator first uncovered the outer cap of the piperacillin sodium and tazobactam sodium, and then placed it upright in the biological safety cabinet. The operator disinfected the cork of the vial with 75% ethanol, and injected 10mL of 0.9% sodium chloride solution into the bottle through the cork. The operator drew back 15mL of air through the syringe and then pulled out the needle. Finally, the operator used three different methods to shake the medicine, without touching the mouth of the bottle during the shaking process. The specific method is as follows.

Control group 1

The operator held the "bottleneck" , and shook the bottle back and forth at an angle of 180° to shake the medicine with a frequency of 60 times/min. The dissolution of the drug was observed by a 5x magnifying glass every 10 seconds. Shaking technique was shown in Figure 1.

Figure 1: Shaking technique of control group 1.

Control group 2

The operator held the "bottleneck and bottle body" at the same time, and shook the bottle back and forth at an angle of 180° to shake the medicine at a frequency of 60 times/min.

The dissolution of the drug was observed by a 5x magnifying glass every 10 seconds. Shaking technique was shown in Figure 2.

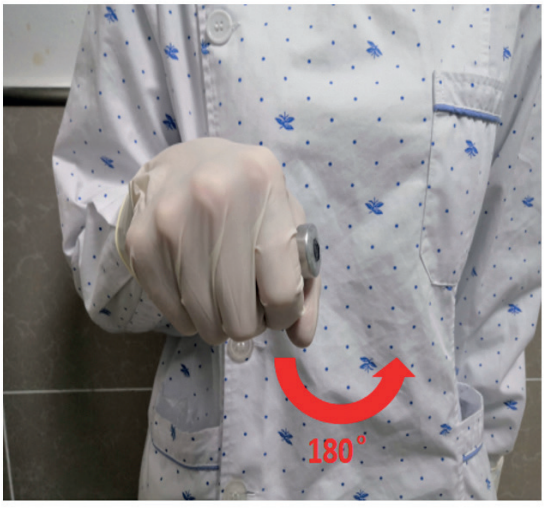

Figure 2: Shaking technique of control group 2 .

Experimental group

The operator held a bottle of medicine in each hand, and shook the vial up and down twice before injecting 0.9% sodium chloride solution and evacuating the air. Then both hands held the bottleneck and bottle body of the medicine bottle at the same time and used the force of the wrist to tap the cork of the vial each other at a frequency of 60 times/min. The bottle body was rotated every 5 seconds.Pay attention to the moderate knocking force, so as not to cause the vial to rupture.

The dissolution of the drug was observed by a 5x magnifying glass every 10 seconds.Shaking technique was shown in Figure 3.

Figure 3: Shaking technique of experimental group.

Observation indicators

The dissolution time and dissolution adequacy of the three groups of drugs were observed and compared. An electronic timer was used to record the dissolution time of each bottle of medicine; 5 times magnifying glass was used to observe the dissolution effect of the medicine.

Evaluation criteria for the complete dissolution of the drug: the liquid in the vial is clear and transparent, without particles, flocs, and wall-mounted powder[6].

Statistical methods

Statistical analysis was performed using SPSS22.0 software. The measurement data (dissolution time) used analysis of variance, and the count data (dissolution adequacy) used the χ^2 test. P<0.05 was considered as the difference was statistically significant.

Results

Comparison of dissolution time of the three groups of drugs

The experimental group drug was better than the control group 1 and the control group 2 in terms of dissolution time,and the difference is statistically significant (P<0.05), see Table 1.

Groups	Cases	Dissolution time(s)
Control group 1	40	221.53±10.48
Control group 2	40	150.70±8.82 [1)]
Experimental group	40	31.9±10.13 [1) 2)]
F		3795.774
P		<0.001

Table 1: Comparison of dissolution time of the three groups of drugs.

[1)]Compared with the control group 1, the difference is statistically significant(P<0.05). [2)]Compared with the control group 2, the difference is statistically significant(P<0.05).

Comparison of dissolution adequacy of the three groups of drugs

The overall comparison of the dissolution adequacy of the three groups of drugs was statistically significant (P<0.05), see Table 2.

Groups	Cases	Dissolution adequacy(n,%)	Non-dissolution adequacy(n,%)
Control group 1	40	5 (12.50)	35 (87.50)
Control group 2	40	25 (62.5)	15 (37.50)
Experimental group	40	40 (100.00)	0 (0.00)
χ^2		63.429	
P		<0.001	

Table 2: Comparison of dissolution adequacy of the three groups of drugs.

Pairwise comparison of the adequacy of dissolution of the three groups of drugs

Through pairwise comparisons between the three groups, the experimental group drug is significantly better than the control group 1 and the control group 2 in terms of dissolution adequacy, and the difference is statistically significant (P<0.0125), see Table 3.

Comparison groups	Dissolution adequacy	Non-dissolution adequacy	Total	χ^2	*P*
Experimental group	40	0	40	62.22	<0.00313
Control group 1	5	35	40		
Total	45	35	80		
Experimental group	40	0	40	18.46	<0.00313
Control group 2	25	15	40		
Total	65	15	80		
Control group 1	5	35	40	21.33	<0.00313
Control group 2	25	15	40		
Total	30	50	80		

Table 3: Pairwise comparison of the adequacy of dissolution of the three groups of drugs.

Discussion

Properly shaking the powder before adding the medicine can speed up the dissolution of the medicine

Piperacillin sodium tazobactam sodium is a compound preparation made of piperacillin sodium and tazobactam sodium in a specific ratio. It is a white or off-white powder or loose lumps containing sodium, which is extremely hygroscopic.

The reasons why the drug is difficult to dissolve include:

• During the storage of the drug, the powder will accumulate at the bottom or bottleneck of the bottle for a long time. When it comes into contact with the injected solvent, it will easily condense and form a protective layer on the surface. The interaction between them is blocked, so it is difficult to break up by the impact of saline injection, which affects the dissolution time and dissolution adequacy of the drug[7].

• Although the compatibility of piperacillin sodium and tazobactam sodium and the solvent 0.9% sodium chloride solution is highly stable, both contain sodium ions. After compatibility, the same ion effect is likely to affect the dissociation[8-9].

• It can be known from the dissolution principle of Noyes-Whitney equation[10]: the larger the contact area between the solvent and the drug particles, the faster the drug dissolution rate. The experimental group in this study shakes the vial up and down twice before infusing saline. The purpose is to loosen the agglomerated powder drugs appropriately and increase the contact area between the medicine particles and the solvent. This measure can effectively increase the dissolution rate of the drug and shorten the dissolution time of the drug.

Negative pressure can speed up the dissolution of the drug

The dissolution process of the powder drug after adding the solvent generally requires three steps[11]: gas desorption on the drug surface, hydration, and movement and diffusion into the liquid.When 10mL of 0.9% sodium chloride solution is injected into the vial and 15mL of air is evacuated, this operation can make the vial under negative pressure.

The air between the drug molecules is released due to the negative pressure, so that the gas adsorbed on the surface of the powder drug is quickly desorption; negative pressure can also reduce the cohesion between drug molecules, increase the contact area between the solvent and the drug, increase the affinity with water molecules, and promote hydration; in addition,the negative pressure accelerates the movement speed of the medicine into the liquid through the effect of the pressure difference, thereby accelerating the dissolution of the medicine.

Appropriate temperature can speed up the dissolution of the drug

The solubility of a drug refers to the maximum amount of a drug that can be dissolved in a certain amount of solvent at a certain temperature. Temperature is one of the main factors affecting the solubility of drugs. Elevated temperature will accelerate the dissolution of the drug, but too high a temperature will cause the drug to decompose and denature, and even affect the stability of the drug. Studies have shown[7] that dissolving powdered drugs with 37°C saline or heating the infusion bag in a 37°C water bath will quickly dissolve the drug particles, and the solution will remain clear at the end of the infusion.

Because the water temperature is close to the temperature of the human body, it will not affect the physical and chemical properties of the drug, and there are no adverse reactions in clinical observation. In this study, the experimental group used both hands to hold the "bottleneck and bottle body" and rotate the bottle body once every 5 seconds. In this way, the temperature of the nurse's palm can be evenly transferred to the bottle, and the dissolution of the medicine can be accelerated.

Knocking the corks on each other can speed up the dissolution of the drug

Piperacillin sodium and tazobactam sodium are white or almost white loose lumps or powders. During storage, its powder often gathers at the bottom or bottleneck of the bottle.

When it comes in contact with the solvent, it is easy to condense into a white powder block, which hinders the dissolution of the drug. In this study, the experimental group used the wrist force to gently tap the cork of the vial at a frequency of 60 times/min after holding the "bottleneck and bottle body" with both hands at the same time. By knocking each other[12], the white powder clumps attached to the bottom of the bottle and the periphery of the bottle cap are dispersed and quickly fall off, so that the powder medicine and the solvent are

fully mixed, thereby the dissolution time of the medicine is greatly shortened. Piperacillin sodium and tazobactam sodium are effective against a variety of gram-positive bacteria, gram-negative bacteria and β-lactamase-producing bacteria. It has the dual properties of broad antibacterial spectrum and inhibition of β-lactamase[13]. It is widely used in patients with severe infections. The average annual dosage in our hospital is about 12,000, and there is a trend of increasing year by year. It is an antibacterial drug that is difficult to be dissolved according to conventional methods.

The results of this study show that the dissolution time and dissolution adequacy of the drug in the experimental group are better than those in the control group 1 and control group 2 (both $P<0.05$). In this study, dissolving the drug according to the method of the experimental group was not only simple, quick and easy to learn, but also improved the nurse's dispensing efficiency and reduced drug waste. In the same way, this method can also be used to configure other insoluble antibiotics, which is worthy of clinical promotion.

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