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ORIGINAL RESEARCH

Compatibility and Stability of Ten Commonly Used Clinical Drugs in Pediatric Electrolyte Supplements Injection

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Objective: Pediatric electrolyte supplements injection is mainly used to supplement heat and body fluid, and commonly used in pediatrics. Its compatibility and stability with common clinical drugs such as antibiotics was rarely reported to ensure the children's safety and the rational use of drugs. The aim of the present study was to investigate physical and chemical stability of pediatric electrolyte supplements injection mixed with ten commonly used clinical drugs.

Methods: According to clinical drug concentration, we mix the pediatric electrolyte supplements injection mixed with ten drugs. The compatible solutions were withdrawn at certain time intervals (0, 0.5, 1, 2, 4, 6 hours) after mixing and tested by description, insoluble particles detection, pH determination and high performance liquid chromatography (HPLC) assay of active ingredient as measures of physicochemical compatibility.

Results: No obvious appearance changes were observed when mixing. Furthermore, over the 6 hours post-preparation period the pH values were within the requirements of each drug quality standard and the number of insoluble particles (≥10 and ≥25μm) met requirements of Chinese Pharmacopeia (Edition 2020) except for mezlocillin sodium for injection. The percentages of the initial concentrations maintained at a minimum of 97% in the mixtures within 6 hours.

Conclusions: Nine commonly used clinical drugs remained stable in the pediatric electrolyte supplements injection for 6 hours at 25°C and avoiding from light. Mezlocillin sodium for injection was not recommended to be combined with electrolyte supplement injection for children because its insoluble particles exceed the standard.

Keywords: compatibility, stability, pediatric electrolyte supplements injection

Introduction

The purpose of liquid therapy is to maintain the stability of body fluid interval capacity, osmotic concentration and composition. It is an important and commonly used means of clinical rescue and treatment. In pediatric practice, medications are administered intravenously for faster action, liquid therapy or due to patient's inability to swallow oral medication. However, the combination of drug and menstruum has the potential for physical and chemical reactions based on pharmaceutical formulation principles. The intravenous injections which directly entering the patient circulation may lead to morbidity or mortality.[1] In order to ensure the safety, effectiveness and timeliness of intravenous medication, we should not only focus on the quality of drugs, but also strictly ensure the compatibility of drug and menstruum. Whether the solvent can be selected correctly is very important for drug stability and treatment. If the obvious appearance change is easy to be found during drug mixing, it will stop the injection immediately without damage. The slightly appearance change is easy to be ignored.[2]

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Pediatric electrolyte supplements injection is compound preparation, which contains 37.5g glucose and 2.25g sodium chloride in 1000 mL. It is mainly used to supplement heat and body fluid, and commonly used in pediatrics in various hospitals. It is unknown for the compatibility and stability of some unstable and commonly used drugs in pediatric electrolyte supplements injection. As has been noted, cephalosporins are antibiotics with high efficiency, low side effects and wide clinical application. The structure contains unstable β- Lactam ring which is easy to hydrolyze in the presence of water. And acid, alkali and temperature rise can promote hydrolysis.[2] Therefore, most of the cephalosporin injections are made in powder injection, which can be stored for a long time. It can be dissolved by injection solvent before clinical application. The study on the stability of vidarabine monophosphate in pediatric electrolyte supplements injection had been investigated,[3] but the stability of mezlocillin sodium for injection, cefoperazone sodium and sulbactam sodium for injection, ceftazidime for injection, cefradine for injection, ceftriaxone sodium for injection, ambroxol hydrochloride for injection, cefazolin sodium for injection, cefathiamidine for injection, cefmetazole sodium for injection, cefoxitin sodium for injection with pediatric electrolyte supplements injection had not been reported.

Reasonable compatibility promotes clinical rational drug use. It is not only related to the safety and effectiveness of clinical medication, but also about medication economic loss, health damage and even life loss. The objective of this study was to assess the compatibility and stability of ten drugs (mezlocillin sodium for injection, cefoperazone sodium and sulbactam sodium for injection, ceftazidime for injection, cefradine for injection, ceftriaxone sodium for injection, ambroxol hydrochloride for injection, cefazolin sodium for injection, cefathiamidine for injection, cefmetazole sodium for injection, cefoxitin sodium for injection) in pediatric electrolyte supplements injection stored for 6 hours at 25°C avoiding from light. It may provide a scientific basis for clinical application of these combinations.

Methods

Materials and Reagents

Mezlocillin, cefoperazone, sulbactam, ceftazidime, Cefradine, ceftriaxone sodium, ambroxol hydrochloride, cefazolin, cefathiamidine, cefmetazole, cefoxitin reference standards were purchased from China Institute for Food and Drug Control (Beijing, China). Pediatric electrolyte supplements injection (100mL) was obtained from Jiangsu Hengrui Pharmaceutical Co., Ltd. (Jiangsu, China). Mezlocillin sodium for injection (2.0g) was purchased from Sichuan pharmaceutical preparation Co., Ltd. (Chengdu, China). Cefoperazone sodium sulbactam sodium for injection (1.0g), ceftazidime for injection (1.0g) and ceftriaxone sodium for injection (0.5g) were purchased from Qilu Pharmaceutical Co., Ltd. (Jinan, China). Cefradine for injection (0.5g) and cefazolin sodium for injection were obtained from Shandong Lukang Pharmaceutical Co., Ltd. (Jining, China). Ambroxol hydrochloride for injection (15mg) was supplied by Shandong Yuxin Pharmaceutical Co., Ltd. (Linyi, China). Cefathiamidine for injection (0.5g) was obtained from Guangzhou Baiyun Pharmaceutical Group Co., Ltd. (Guangzhou, China). Cefmetazole sodium for injection (1.0g) was purchased from Sichuan Hexin Pharmaceutical Co., Ltd. (Chengdu, China). Cefoxitin sodium for injection (1.0g) was supplied by Sinopharm (Shenzhen) Pharmaceutical Co., Ltd. (Shenzhen, China). Methanol and acetonitrile were chromatographic purity and other chemicals used were of analytical grade, and totally purchased from Chengdu Hengxin Chemical Reagent Co., Ltd (Chengdu, China).

Instrumentation

Insoluble particles of each sample were detected by Particle analyzer (GWF-DS1, Tianjin Tianhe Analytical Instrument Co., Ltd.). The pH values of samples were measured with pH metre (Phs-3C+, Chengdu Century ark Technology Co., Ltd). The content of each sample was analyzed by high-performance liquid chromatography (1200, Agilent, USA). Ultrapure water was acquired by equipment (SSY-GDE-500L, Sichuan Shuisiyuan Environmental Technology Co., Ltd.)

Insoluble Particles Detection and pH Measure

Pediatric electrolyte supplements injection was used to mix with ten drugs according to the clinical drug concentration. The compatible solutions were analyzed at certain time intervals (0, 0.5, 1, 2, 4, 6 hours) after mixing, and stored avoiding from light at room temperature. Tests were according to the insoluble particle test method (general rule 0903,

Part IV of Chinese Pharmacopoeia (2020 Edition)),[4] and PH value determination method (general rule 0631, Part IV of Chinese Pharmacopoeia (2020 Edition)).[5]

Chromatographic Conditions

The amount of active components were determined by HPLC using a Shimadzu C18 column (250mm×4.6mm, 5μm). The column was maintained at a temperature of 35°C, and at a flow rate of 1.0 mL/min while ceftazidime was 1.5 mL/min. For mezlocillin, the mobile phase was composed of phosphate buffer (potassium dihydrogen phosphate 4.9g and potassium dihydrogen phosphate 0.45g, dissolved with water to 1000mL) and acetonitrile in the ratio of 80:20 (v/v), and injection volume was 20μL, and the selected detection wavelength was 210nm. For cefoperazone and sulbactam, the mobile phase was composed of 0.005mol/L tetrabutylammonium hydroxide solution (add 1800mL of water to 6.6mL of 40% tetrabutylammonium hydroxide solution, adjust pH value to 4.0 with 1mol/L phosphoric acid, and then dilute to 2000mL) and acetonitrile in the ratio of 75:25 (v/v), and injection volume was 10μL, and the selected detection wavelength was 220nm. For ceftazidime, the mobile phase was composed of acetonitrile, pH 7.0 phosphate buffer (42.59g of anhydrous disodium hydrogen phosphate and 27.22g of potassium dihydrogen phosphate, diluted to 1000mL with water) and water in the ratio of 40:200:1760 (v/v/v), and injection volume was 20μL, and the selected detection wavelength was 254nm. For cefazolin, the mobile phase was composed of disodium hydrogen phosphate – citric acid solution (1.33g anhydrous disodium hydrogen phosphate and 1.12g citric acid, diluted to 1000mL with water) and acetonitrile in the ratio of 88:12 (v/v), and injection volume was 10 μL, and the selected detection wavelength was 254 nm. For ceftriaxone, the mobile phase was composed of 0.02 mol/L octylamine solution and acetonitrile in the ratio of 73:27 (v/v, pH 6.5), and injection volume was 20μL, and the selected detection wavelength was 254nm. For ambroxol hydrochloride, the mobile phase was composed of 0.01mol/l diammonium hydrogen phosphate solution (pH 7.0) and acetonitrile in the ratio of 50:50 (v/v), and injection volume was 20 μL, and the selected detection wavelength was 248 nm. For cefathiamidine, the mobile phase was composed of phosphate buffer (2.76 g of anhydrous disodium hydrogen phosphate and 1.29 g of citric acid, diluted to 1000mL with water) and acetonitrile in the ratio of 80:20 (v/v), and injection volume was 10μL, and the selected detection wavelength was 254nm. For cefradine, the mobile phase was composed of 0.027mol/ L disodium hydrogen phosphate solution containing 0.027 mol/L sodium octane sulfonate (pH 8.0) and methanol in the ratio of 75:25 (v/v), and injection volume was 10 μL, and the selected detection wavelength was 206 nm. For cefmetazole, the mobile phase was composed of ammonium dihydrogen phosphate solution (5.75 g of ammonium dihydrogen phosphate, add 730 mL of water to dissolve it, add 10% tetrabutyl ammonium hydroxide solution 19.2 mL), tetrahydrofuran and methanol in the ratio of 730:12.5:300 (v/v/v, pH 4.5), and injection volume was 20 μL, and the selected detection wavelength was 254 nm. For cefoxitin, the mobile phase was composed of water, acetonitrile and glacial acetic acid in the ratio of 81:19:1 (v/v/v), and injection volume was 10 μL, and the selected detection wavelength was 254 nm.

Method Validation

The validation of method was performed in terms of specificity, linearity, accuracy, intraday and interday precision.

According to the corresponding content determination methods, the reference solution and pediatric electrolyte supplements injection were determined to investigate whether the blank sample solution interferes with the chromatographic peaks of the main drug components and whether the separation between main drug components and adjacent impurities meets the requirements.

Calibration curves were constructed from a linear plot of peak area versus concentration of the reference standards for mezlocillin (0.02713–0.5426 mg/mL), cefoperazone (0.04823–0.9646 mg/mL), sulbactam (0.04646–0.9292 mg/mL), ceftazidime (0.02485–0.4970mg/mL), cefazolin (0.01997–0.3994 mg/mL), ceftriaxone (0.03737–0.7474mg/mL), ambroxol hydrochloride (0.006186–0.1237 mg/mL), cefathiamidine (0.02157–0.4313 mg/mL), cefradine (0.02684–0.5369 mg/mL), cefmetazole (0.02170–0.4340 mg/mL), and cefoxitin (0.02906–0.5812 mg/mL).

According to the corresponding content determination methods, quality control samples were analyzed in sextuplicate (n = 6). They were calculated based on drug recovery for the accuracy, and calculated as coefficient of relative standard deviation (RSD %) for intraday/interday precisions.

Stability of Compatible Solutions

The reference control and compatible solutions were prepared at the following final concentrations: mezlocillin 0.15 mg/mL, cefoperazone 0.5 mg/mL, sulbactam 0.5 mg/mL, ceftazidime 0.15 mg/mL, cefazolin 0.1 mg/mL, ceftriaxone 0.22 mg/mL, ambroxol hydrochloride 30 μg/mL, cefathiamidine 0.1 mg/mL, cefradine 0.3 mg/mL, cefmetazole 0.1 mg/mL, cefoxitin 0.3 mg/mL. The compatible solutions were analyzed at certain time intervals (0, 0.5, 1, 2, 4, 6 hours) after mixing, and stored avoiding from light at room temperature.

Analysis of the Data

The initial concentration of compatible solutions was defined as 100%, and the subsequent samples' concentration was expressed as percentage of the initial concentration. It was considered to be stable if they retained 95% of the initial concentrations.

Results

Description

Within 6 hours, the properties of compatible liquids for ten drugs did not change significantly. Visual examination indicated that they were clear and transparent liquids, without color change, precipitation, crystallization and gas production.

Insoluble Particles Detection

For 10 kinds of compatible solutions, the number of insoluble particles at 0, 0.5, 1, 2, 4 and 6 h after mixing are shown in Table 1. According to the criteria of insoluble particles set by Chinese Pharmacopeia (Edition 2020), intravenous injection with a marked amount of 100mL contains the number of particles that are equal to or greater than 10 μm not exceed 25, and equal to or greater than 25 μm not exceed 3. In this experiment, the number of particles in the compatibility solution of mezlocillin sodium for injection and pediatric electrolyte supplements injection exceeded the standard requirements, and the other solutions met the standard requirements.

pH Measure

The pH values of prepared compatible solutions at 0, 0.5, 1, 2, 4 and 6 h after mixing are shown in Table 2. The pH of cefoperazone sodium for injection, sulbactam sodium, ceftriaxone for injection, ceftazidime for injection, ambroxol hydrochloride for injection, cefradine for injection, mezlocillin sodium for injection and cefmetazole sodium for injection did not change significantly after compatibility with pediatric electrolyte supplements injection. The pH value increased when cefazolin sodium for injection was compatible with pediatric electrolyte supplements injection, and decreased when cefathiamidine for injection was compatible with pediatric electrolyte supplements injection. According to the pharmaceutics, range of pH for injections is 4–9. The pH values of compatible solutions for ten drugs are within the allowable range, and the pH values of compatible solutions are within the requirements of each drug quality standard within 6 hours after compatibility.

Validation of HPLC Method

The HPLC methods of ten drugs were validated that the pediatric electrolyte supplements injection did not interfere with the chromatographic peak of the active drug, and the separation between the main drug and adjacent impurities met the requirements (shown in Supplementary Figure 1). Five-point standard curves were constructed for all ten drugs at varying concentrations and showed a good linear between the peak area vs the concentration with a correlation coefficient for all ten curves better than 0.9999 (shown in Table 3). The intraday variations (n = 6), interday variations (n=12), and accuracy in mezlocillin, cefoperazone, sulbactam, ceftazidime, cefazolin, ceftriaxone, ambroxol hydrochloride, cefathiamidine, cefradine, cefmetazole, cefoxitin were shown in Table 3. The results showed that the proposed HPLC methods are simple, accurate and precise, which are useful for the determination of ten drugs in pediatric electrolyte supplements injection.

Table 1 The Number of Insoluble Particles in Pediatric Electrolyte Supplements Injection After Compatibility with 10 Drugs

Compatible Drugs	Size	0h	0.5h	1h	2h	4h	6h
Mezlocillin sodium for injection	≥10μm	29.5	32.2	27.9	25.7	62.8	45.4
	≥25μm	0.4	1	0.1	0.7	1.1	0.5
Cefoperazone sodium and sulbactam sodium for injection	≥10μm	18	6.9	4.1	5.6	19.8	5.5
	≥25μm	0.5	0.5	0.3	0.7	0.7	0.5
Ceftazidime for injection	≥10μm	1.8	4.5	12.8	5.9	3.2	8.9
	≥25μm	0.2	0.4	0.8	0.9	0.1	0.1
Cefradine for injection	≥10μm	6.1	4.4	3.1	1.7	2.7	1.5
	≥25μm	0.2	0.2	0.1	0.1	0.3	0.1
Ceftriaxone sodium For injection	≥10μm	3.3	17.1	16.7	1.8	3.7	5
	≥25μm	0.2	0.7	0	0.1	0.3	0.1
Ambroxol hydrochloride for injection	≥10μm	31.1	17.5	6.8	7.6	13.3	3.9
	≥25μm	0.2	0.2	0.2	0.8	0.7	0.1
Cefazolin sodium for injection	≥10μm	7.4	17.3	1.1	4.6	5.1	14.1
	≥25μm	0.2	0.5	0.1	0.1	0.1	0.3
Cefathiamidine for injection	≥10μm	5.1	2.2	1.9	2	6.1	3.4
	≥25μm	0.1	0	0.1	0.3	0.1	0
Cefmetazole sodium for injection	≥10μm	1.3	1.5	1.5	2.2	2.7	2.2
	≥25μm	0	0.1	0.1	0.6	0.5	0.3
Cefoxitin sodium for injection	≥10μm	2.6	8.9	7.4	4.7	3.4	2.7
	≥25μm	0.1	0.5	0.7	0.5	0.3	0.3

Table 2 pH Values of Pediatric Electrolyte Supplements Injection Mixed with 10 Drugs

Compatible Drugs	0h	0.5h	1h	2h	4h	6h
Mezlocillin sodium for injection	5.69	5.65	5.64	5.58	5.50	5.46
Cefoperazone sodium and sulbactam sodium for injection	4.83	4.84	4.83	4.83	4.83	4.83
Ceftazidime for injection	6.81	6.81	6.92	6.81	6.84	6.90
Cefradine for injection	8.57	8.55	8.53	8.53	8.45	8.46
Ceftriaxone sodium for injection	6.50	6.49	6.49	6.52	6.50	6.52
Ambroxol hydrochloride for injection	4.49	4.45	4.47	4.44	4.47	4.47
Cefazolin sodium for injection	4.77	4.80	4.85	4.97	5.15	5.29
Cefathiamidine for injection	4.77	4.64	4.56	4.47	4.33	4.30
Cefmetazole sodium for injection	4.44	4.39	4.39	4.37	4.31	4.29
Cefoxitin sodium for injection	5.40	5.51	5.60	5.80	6.01	6.26

The concentration of each drug in the compatible solutions was expressed as the percentage of initial concentration. As shown in Table 4, they retained >97% of their initial concentrations in the compatible solutions without precipitating degradation when stored avoiding from light at room temperature.

Discussion

Some commonly used drugs in clinic, such as antibiotics, are often produced as powder injections because of their poor stability in solution. They need to be compatible with the corresponding solvent. However, unreasonable compatibility will reduce the curative effect and increase the adverse reactions. Therefore, we investigated compatibility and stability of ten commonly used clinical drugs in pediatric electrolyte supplements injection which was a rare suitable and commonly used crystal solution for children.[6]

More than 90% of drugs are organic, weak electrolytes, especially those compounded, manufactured, or reconstituted as injections in predominantly ionized or salt form.[7] Consequently, acid–base reactions are the most common causes of drug incompatibility. Some injections have a basic pH (>7) or high pKa and will theoretically cause precipitation when in low pH solutions such as 5% glucose (pH 4–4.5). It is well known that they are very prone to precipitation during dilution if the pH is allowed to drift too low.[8] The inappropriate pH of solutions will accelerate drug decomposition or precipitate.[9] Therefore, it can be used as a necessary reference to predict the compatibility change. In our study, the pH values of compatible solutions are within the requirements of each drug quality standard within 6h after compatibility.

Insoluble particles widely exist in infusion products and are important factor leading to adverse reactions/events of intravenous administration. They can cause phlebitis, vascular embolism and pyrogen reaction, etc.[10] The Pharmacopoeia

Table 3 Validation of HPLC Method for Determination of Ten Drugs

Drug	Linearity	Measurement Range	Accuracy, %	Precision RSD,%	
				Intraday	Interday
Mezlocillin	Y=65169x+56.025 (R^2=0.9999)	0.02713–0.5426mg/mL	99.57	0.06%	0.17%
Cefoperazone	Y=20061x+43.763 (R^2=0.9999)	0.04823–0.9646mg/mL	98.20	0.18	0.68
Sulbactam	Y = 6042.6x-8.5088 (R^2=0.9999)	0.04646–0.9292mg/mL	98.46	0.28	0.69
Ceftazidime	Y=33163x+1.9096 (R^2=0.9999)	0.02485–0.4970mg/mL	99.74	0.32	0.34
Cefradine	Y=22719x+30.406 (R^2=0.9999)	0.02684–0.5369 mg/mL	100.37	0.71	0.78
Ceftriaxone	Y=66553x-103.58 (R^2=0.9999)	0.03737–0.7474mg/mL	98.35	0.12	0.10
Ambroxol hydrochloride	Y=25714x-0.5696 (R^2=0.9999)	0.006186–0.1237mg/mL	99.33	0.07	0.20
Cefazolin	Y=12357x-4.4348 (R^2=0.9999)	0.01997–0.3994mg/mL	99.51	0.12	0.24
Cefathiamidine	Y=12457x+5.8678 (R^2=0.9999)	0.02157–0.4313 mg/mL	99.24	0.27	0.27
Cefmetazole	Y=20495x+0.2917 R2=0.9999	0.02170–0.4340 mg/mL	99.34	0.12	0.20
Cefoxitin	Y=14885x+8.6736 (R^2=0.9999)	0.02906–0.5812 mg/mL	99.63	1.88	1.54

Table 4 Stability of 10 Drugs in Pediatric Electrolyte Supplements Injection

Compatible Drugs		% Initial Concentration Remaining				
		0.5h	1h	2h	4h	6h
Mezlocillin sodium for injection		99.82%	99.77%	99.81%	99.91%	99.05%
Cefoperazone sodium and sulbactam sodium for injection	Cefoperazone	99.85%	99.80%	100.00%	99.89%	99.59%
	Sulbactam	100.54%	100.58%	100.06%	100.28%	99.79%
Ceftazidime for injection		99.34%	98.51%	98.99%	98.10%	97.40%
Cefradine for injection		99.19%	99.80%	99.40%	99.99%	99.16%
Ceftriaxone sodium for injection		99.90%	99.90%	99.80%	99.71%	99.80%
Ambroxol hydrochloride for injection		98.62%	99.80%	99.40%	99.99%	99.16%
Cefazolin sodium for injection		100.07%	99.5%	99.94%	100.18%	100.16%
Cefathiamidine for injection		99.42%	99.39%	98.54%	98.56%	97.84%
Cefmetazole sodium for injection		99.21%	99.00%	99.18%	98.70%	98.46%
Cefoxitin sodium for injection		99.46%	99.66%	99.52%	99.31%	98.24%

of China, United States, Japan, United Kingdom and Europe have stipulated the detection and limiting standards for insoluble particles in injections. Except for mezlocillin sodium for injection, they meted the standards of Chinese Pharmacopoeia when the other nine drugs were compatible with pediatric electrolyte supplements injection. Because the amount of insoluble particles exceeds the standard, it is not recommended to combine mezlocillin sodium for injection with pediatric electrolyte supplements injection to avoid adverse drug reactions. Excessive insoluble particle could be explained by the following: the higher concentration of mezlocillin used in this study compared with other researches; dust particles produced during the preparation of mixture; incomplete dissolution of powder.[11] The number of insoluble particles of ambroxol hydrochloride in pediatric electrolyte supplements injection was more than 25 at 0 hours. However, the number of insoluble particles at other time intervals (0.5, 1, 2, 4 and 6 h) was all not exceed 25. Since the injection solutions were not used at 0 hour after mixing in practice, and excessive insoluble particle could be explained by the incomplete dissolution of powder at 0 hour after mixing.[11] Therefore, ambroxol hydrochloride and pediatric electrolyte supplements injection were compatible.

We detect the content stability of 10 drugs in children's electrolyte supplement injection within 6h by HPLC. The method is more accurate than UV spectrophotometry.[2] There was no interference with the quantification of each drug and the combination of drugs. The determination results are not disturbed by other components. The results showed the percentages of ten drugs remaining in the drug admixtures were all higher than 97% within 6 hours. However, a limitation of this study is that it did not investigate the stability of related substances for ten drugs. Studies have shown that many drugs, such as cefmetazole sodium for injection, are prone to degradation after compatibility with children's electrolyte supplement injection, which may reduce the content of the preparation and increase the related substances during storage, thus affecting the efficacy and increasing the incidence of adverse reactions.[12] Therefore, in order to ensure the safety of clinical use, It should be used as soon as possible after compatibility. Furthermore, it was reported that higher drug concentrations have been associated with greater incompatibility than lower drug concentrations.[13] Therefore, the compatibility and stability of ten commonly used clinical drugs in pediatric electrolyte supplements injection may be verified by multiple concentrations to provide more reliable decision basis for advisable utilization of drugs.

Conclusion

The clinical implications of our results are that nine diluted infusion solution containing, cefoperazone sodium and sulbactam sodium, ceftazidime, cefradine, ceftriaxone sodium, ambroxol hydrochloride, cefazolin sodium, cefathiamidine, cefmetazole sodium, cefoxitin sodium in pediatric electrolyte supplements injection may be pre-prepared and used up to at least 6hours at 25°C and protected from light. Admixture containing mezlocillin sodium in pediatric electrolyte supplements injection was not recommended for application. Considering the satisfactory stability results in the current study for these 10 chemicals, it can be concluded that the nine admixture can be safe for up to 6 h, and there are potential risks in the combined solution of mezlocillin sodium.

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Disclosure

The authors report no conflicts of interest in this work.

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