

Cefepime Stability in IV Solutions and Admixtures

Cefepime is widely used in clinical practice, yet only limited data are available on its stability in a variety of IV fluids and containers at room temperature and at 5°C. The objective of our study was to investigate the stability of cefepime in IV solutions commonly used in clinical practice.

Solutions of cefepime (Maxipime, Bristol Myers-Squibb, Cairo, Egypt) at concentrations of 10 mg/mL and 20 mg/mL were prepared in each of the 10 IV solutions listed in Table 1. Each admixture was prepared in both glass (supplied by Bristol Myers-Squibb) and polyethylene containers (supplied by Misr Co., Cairo, Egypt). The solutions were stored at room temperature (25°C) for 8 h under normal fluorescent light or in a refrigerator (5°C) for 120 h in darkness. Samples were taken at 0, 2, 5, and 8 h from the solutions stored at room temperature. Samples were taken every 24 h for 5 days (120 h) from the solutions stored in the refrigerator. Each sample was visually examined for colour change and formation of precipitate; a pH

Table 1. IV Solutions Used for Testing the Stability of Cefepime

4.2% sodium bicarbonate
2.5% mannitol
5% mannitol
10% mannitol
10% fructose
Ringer's solution
0.18% sodium chloride in 5% dextrose
0.2% potassium chloride in 5% dextrose
10% dextran 40 in 5% dextrose
10% dextran 40 in 0.9% sodium chloride

meter (Griffin and George Ltd, London, England) was used to measure pH. The concentration of cefepime in each sample was determined by a spectrophotometric stability-indicating method.¹ The cefepime solutions were considered stable if more than 90% of the initial concentration was retained.²

Neither the concentration of the solution nor the type of container influenced stability. All cefepime solutions tested, other than those prepared in 4.2% sodium bicarbonate and 10% dextran 40 in 5% dextrose were stable for up to 120 h at 5°C and up to 8 h at room temperature under fluorescent light. Solutions of both concentrations prepared in 4.2% sodium bicarbonate were stable for up to 48 h at 5°C and up to 5 h at room temperature under fluorescent light. Solutions of both concentrations prepared in 10% dextran 40 in 5% dextrose were compatible for up to 96 h at 5°C and up to 8 h at room temperature under fluorescent light.

Incorporation of this information into the expiry dates used at individual institutions must be supported by sterility testing.

References

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Stability of Magnesium Sulfate 20% in Viaflex Bags

Magnesium sulfate is the drug of choice for treating eclamptic seizures and for seizure prophylaxis in women with severe pre-eclampsia.¹ Recommendations for IV administration specify a loading dose of 4 g, followed by continuous infusion of 1 g/h.² The new guidelines for hypertension in pregnancy from the British Columbia Reproductive Care Program specify that IV fluid administration should be restricted to 80 mL/h to minimize pulmonary edema.² To meet these fluid guidelines, the team at our hospital chose to maximize the magnesium sulfate concentration. Magnesium sulfate can be given peripherally at a maximum concentration of 20%, and solutions with this concentration are available commercially in vials.³ To

administer magnesium sulfate at our site, the vial contents had to be transferred to an empty Viaflex bag and administered with an infusion pump.

We conducted a small study to determine the stability of magnesium sulfate USP 20% (Sabex, Boucherville, Quebec; lot 131614, expiry April 2009) in 50-mL Viaflex bags (Baxter Intravia Containers, Deerfield, Illinois; lot UR299784). We tested the magnesium concentration on days 0 and 30 for a bag stored at room temperature (21.5°C to 22°C) and on days 0, 30, 60, and 90 for a bag stored in the refrigerator (4°C to 6°C). The samples were diluted with sterile saline 1:1000 to meet the analytical range of the assay used (magnesium assay, part no. 445360, and UniCel DxC 600i Synchron Access clinical system, both from Beckman Coulter, Fullerton, California). This method has a coefficient of variation of 1.6% at a target mean concentration



of 0.81 mmol/L. The dilution provided an approximate magnesium concentration of 0.8 mmol/L. The analysis was performed in duplicate, and the results are reported as means.

The solution in the bags remained clear and colourless throughout the study period. The magnesium concentration for the bag stored at room temperature was 0.8 mmol/L on day 0 and 0.79 mmol/L on day 30. The concentration for the refrigerated bag was 0.85 mmol/L on day 0, 0.82 mmol/L on day 30, 0.83 mmol/L on day 60, and 0.74 mmol/L on day 90; the duplicate results were identical for each study day. Therefore, after transfer to Vialflex bags, the magnesium sulfate solutions appeared to maintain at least 95% of the initial magnesium concentration for up to 30 days at room temperature and up to 60 days in the refrigerator.

Medication errors involving magnesium sulfate are relatively common. Simpson and Knox⁴ reported 52 cases of magnesium sulfate overdose in obstetric patients; of these, 7 women died or remained in a persistent vegetative state. Patient safety could be promoted by having pharmacy prepare magnesium sulfate solutions for IV administration. This would eliminate preparation on the ward by nursing staff, which would allow vials of concentrated magnesium sulfate to be removed from ward stock. Because the maximum concentration would become the standard concentration, there would be no need for further dilutions, which would allow for standard dosing and pump settings. Finally, use of small-volume parenterals eliminates the need for 1000-mL IV bags, which Simpson and Knox⁴ identified as a common factor in the lethal overdoses.

The major limitation of the assay used in our study was its inability to discriminate between free magnesium and magnesium bound to substances that might have leached from the bag surface.⁵

In conclusion, magnesium sulfate USP 20% transferred from vials to Vialflex bags appeared to retain more than 95% of its initial magnesium concentration for up to 30 days at room temperature and up to 60 days in the refrigerator.

References

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