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Annual Review

Y-Site Compatibility of Medications with Parenteral Nutrition

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The most discussed change in parenteral nutrition compatibility within the last two years was with ceftriaxone. In the summer of 2007, Roche Laboratories updated their prescribing information for Rocephin® (ceftriaxone sodium) to include a contraindication for the co-administration of ceftriaxone with calcium-containing intravenous solutions in neonates due to reported fatal cases of pulmonary and renal precipitates in this patient population.[1] The additional warnings to avoid a potential interaction are the most controversial. It is now recommended that ceftriaxone and calcium-containing intravenous solutions, such as parenteral nutrition, not be administered within 48 hours of each other regardless of patient age or remote administration sites. Institutions have struggled with the theoretical expansion of this interaction to older children and adults. At this time, no published case reports could be found in the literature.

Obtaining and maintaining venous access in pediatric patients can be complicated. Many patients require multiple treatment modalities to be administered intravenously including medications, fluids, blood products and nutrition. Clinicians must optimize available access to ensure appropriate and timely administration of all products prior to establishing additional access. Separate administration of intravenous products, if feasible, is always preferred, however, many times simultaneous administration of medications and parenteral nutrition will be required making compatibility considerations essential. It is important to recognize that compatibility only reflects the physical interactions such as formation of a precipitate and does not necessarily address stability or pharmacologic activity of the products. Published data may report both compatibility and stability, however most evaluate visual compatibility alone. Currently there are multiple resources to use when answering the question of compatibility with parenteral nutrition. We strove to evaluate and present the available published data as a comprehensive and practical reference. Primary literature regarding y-site compatibility of medications with three different parenteral nutrition formulas, 3-in-1, 2-in-1 and lipids alone was reviewed. When conflicting results were encountered the clinical strength was considered. When published data was not accessible *Trissel's Handbook on Injectable Drugs*[2] was used.

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ABBREVIATIONS

C Compatibility has been demonstrated. When Y-site compatibility was not available, medications compatible in solution for 24 hours were assumed to be Y-site compatible. Medications compatible with 3-in-1 admixtures were assumed to be compatible with lipids alone.[2]
I Incompatibility has been demonstrated
— Compatibility data not available
C/I Conflicting compatibility has been demonstrated and strength of the evidence supports compatible
I/C Conflicting compatibility has been demonstrated and strength of the evidence supports incompatible

Medication	Admixture Type			Comments	References	
	2-in-1	lipids	3-in-1		C	I
Acetazolamide	I	—	—	White precipitate forms immediately		3
Acyclovir sodium	I	I	I	White precipitate forms immediately		3,4,5
Albumin	C	I	I	Although albumin appears visually compatible with 2:1 solutions, the potential of increased growth of fungi and bacteria warrants separate administration; visually apparent emulsion disruption	2,6	7
Aldesleukin	C	C	—		8	
Alprostadil	C	—	—		9	
Amikacin sulfate	C	C/I	C/I	Visual breaking of emulsion within 1 hour in select formulations	3,4,5,10,11,12	13
Aminophylline	C/I	C	C		4,5,14,15,16	3
Amphotericin B	I	I	I	Yellow precipitate forms immediately		4,5
Ampicillin sodium	C/I	C	C		4,5,17	3,10,12, 18
Ampicillin sodium - Sulbactam sodium	C	C	C		4,5	
Argatroban	C	—	—		19	
Ascorbic acid	C	—	—		20	
Atracurium besylate	C	—	—		20	
Aztreonam	C	C	C		4,5	
Bumetanide	C	C	C		4,5	
Buprenorphine HCl	C	C	C		4,5	
Butorphanol tartrate	C	C	C		4,5	
Caffeine citrate	C	—	—		21	
Carboplatin	C	C	C		4,5	
Cefamandole nafate	C	C	C		10,12,17	

Cefazolin sodium	**C/I**	**C**	**C**	Incompatible at a dextrose concentration of 25%	4,5,10,17,21	4
Cefepime HCl	**C**	—	—		22	
Cefoperazone sodium	**C**	**C**	**C**		4,5,10	
Cefotaxime sodium	**C**	**C**	**C**		3,4,5,10	
Cefotetan disodium	**C**	**C**	**C**		4,5	
Cefoxitin sodium	**C**	**C**	**C**		4,5,10,17	
Ceftazidime sodium	**C**	**C**	**C**		3,4,5,23	
Ceftizoxime sodium	**C**	**C**	**C**		4,5	
Ceftriaxone sodium	**C/I**	**C**	**C/I**	Per manufacturing labeling, ceftriaxone should not be administered with calcium-containing IV solutions within 48 hours of each other	4,5,20	1
Cefuroxime sodium	**C**	**C**	**C**		4,5	
Cephalothin sodium	**C**	—	—		10,12,18	
Chloramphenicol sodium succinate	**C**	**C**	—		2,10	
Chlorpromazine HCl	**C**	**C**	**C**		4,5	
Cimetidine HCl	**C**	**C**	**C**		4,5,24	
Ciprofloxacin lactate	**I**	**C**	**C**	Amber discoloration in 1 to 4 hours	5	4
Cisplatin	**I**	**C**	**C**	Amber discoloration in 1 to 4 hours	5	4
Clindamycin phosphate	**C**	**C**	**C**		4,5,10,17	
Cyclophosphamide	**C**	**C**	**C**		4,5	
Cyclosporine	**C/I**	**C/I**	**C/I**	For 2:1, found to be compatible with Dextrose 5%/ Amino Acids 4.25%, but not compatible with Dextrose 25%/Amino Acid 3.5%	4,5,25	4,5
Cytarabine	**I**	**C**	**C**	Substantial loss of natural turbidity occurs immediately	5	4
Dexamethasone sodium phosphate	**C**	**C**	**C**		3,4,5	
Diazepam	**C**	—	—		20	
Digoxin	**C**	**C**	**C**		4,5,26	
Diphenhydramine HCl	**C**	**C**	**C**		4,5	
Dobutamine HCl	**C**	**C**	**C**		3,4,5,11	
Dopamine HCl	**C**	**C/I**	**C/I**		3,4,5,26	5
Doxorubicin HCl	**I**	**I**	**I**	Substantial loss of natural turbidity occurs immediately; emulsion disruption occurs immediately		4,5
Doxycycline hyclate	**C**	**I**	**I**	Emulsion disruption occurs immediately	4,10	5

Droperidol	**C**	**I**	**I**	Emulsion disruption occurs in 1 to 4 hours	4	5
Enalaprilat	**C**	**C**	**C**		4,5	
Epinephrine HCl	**C**	—	—		20	
Epoetin alfa	**C**	—	—		27	
Erythromycin lactobionate	**C**	**C**	**C**		10,17,20	
Famotidine	**C**	**C**	**C**		4,5,24,28, 29,30,31,32	
Fentanyl citrate	**C**	**C**	**C**		3,4,5,33	
Fluconazole	**C**	**C**	**C**		4,5,34	
Fluorouracil	**I**	**C/I**	**C/I**	Slight haze, small crystals and amber discoloration form in 1 to 4 hours; turbidity forms immediately; very small amount of white precipitate forms immediately in select 3:1 formulations	5	4,5
Folic acid	**C**	—	—		20,35,36,37	
Foscarnet	**C**	—	—		38	
Furosemide	**C/I**	**C**	**C**	Small amount of precipitate forms in 4 hours in select formulations	3,5,20,26	4
Gallium nitrate	**C**	**C**	**C**		4,5	
Ganciclovir sodium	**I/C**	**I**	**I**	Concentrations of ≥ 10mg/mL result in precipitation within 0 to 30 mins	39,40	4,5,39
Gentamicin sulfate	**C**	**C**	**C**		3,4,5,10,11, 12,13,17,18,20	
Granisetron HCl	**C**	**C**	**C**		4,5	
Haloperidol lactate	**C**	**I**	**I**	Emulsion disruption occurs immediately	4,20	5
Heparin sodium	**C**	**I**	**I**	Emulsion disruption occurs immediately with heparin 100 units/mL	4,20	5
Hydrochloric acid	**C**	—	—		41	
Hydrocortisone sodium / phosphate / succinate	**C**	**C**	**C**		4,5,20	
Hydromorphone HCl	**C**	**I/C**	**I/C**	Emulsion disruption occurs immediately in select formulations	4,5	5
Hydroxyzine HCl	**C**	**C**	**C**		4,5	
Ibuprofen lysine	**I**	—	—			42
Idarubicin HCl	**C**	—	—		43	
Ifosfamide	**C**	**C**	**C**		4,5	
Imipenem-Cilastatin sodium	**C**	**C**	**C**		4,5	

Immune Globulin	—/C	—	—	Only supportive of Gammagard® 2.5%; not recommended to infuse with other drugs or solutions	44	
Indomethacin sodium trihydrate	I	—	—			45
Insulin, regular human	C	C	C		4,5,20	
Iron dextran	C/I	—	I/C	For 2:1, found to be compatible in solution at amino acid concentrations of 2% or greater	46,47,48	47,49
Isoproterenol HCl	C	C	C	For 2:1, compatible with dextrose 25%/amino acids 4.25% (electrolytes were not added)	26,50	
Kanamycin sulfate	C	C	C		17,18,50,51	
Leucovorin calcium	C	C	C		4,5	
Levorphanol tartrate	C	I	I	Emulsion disruption occurs immediately	4	5
Lidocaine HCl	C	C	C	For 2:1, compatible with dextrose 25%/amino acids 4.25% (electrolytes were not added)	26,50	
Linezolid	C	—	—	Compatible with dextrose 20%/amino acids 4.9%; electrolytes were not added	52	
Lorazepam	C	I	I	Partial emulsion disruption occurs in 1 hour	4	5
Magnesium sulfate	C	C	C		4,5	
Mannitol	C	C	C		4,5	
Meperidine HCl	C	C	C		4,5,53	
Meropenem	—	C	C		5	
Mesna	C	C	C		4,5	
Methotrexate sodium	I	C	C	For 2:1, hazy precipitate forms in 0 to 1 hour	5	4
Methyldopate HCl	C	C/I	C/I	For 2:1, compatible with dextrose 25%/amino acids 4.25% (electrolytes were not added); cracked the lipid emulsion in select formulations	26,50	26
Methylprednisolone sodium succinate	C	C	C		4,5	
Metoclopramide HCl	I/C	C	C	Substantial loss of natural turbidity occurs immediately in select formulations	2,5	4
Metronidazole	C	C	C		3,4,5,20	
Mezlocillin sodium	C	C	C		4,5	
Miconazole	C	C	C		4,5,10	

Midazolam HCl	**I/C**	**I**	**I**	White precipitate forms immediately in select formulations	54	4,5,20
Milrinone lactate	**C**	—	—		55,56	
Minocycline HCl	**I**	**I**	**I**	Bright yellow discoloration forms immediately; emulsion disrupts immediately		4,5
Mitoxantrone HCl	**I**	**C**	**C**	Substantial loss of turbidity occurs immediately	5	4
Morphine sulfate	**C**	**C/I**	**C/I**	For 3:1, morphine 1 mg/mL compatible, but 15 mg/mL was not compatible; emulsion disruption occurs immediately in select formulations	3,4,5,20,53	5
Nafcillin sodium	**C**	**C**	**C**		4,5,10,12	
Nalbuphine HCl	**C**	**I**	**I**	Emulsion disruption occurs immediately	4	5
Netilmicin sulfate	**C**	**C**	**C**		4,5	
Nitroglycerin	**C**	**C**	**C**		4,5	
Norepinephrine bitartrate	**C**	**C**	**C**		4,26	
Octreotide acetate	**C**	**C**	**C**		4,5	
Ondansetron HCl	**C**	**I**	**I**	Emulsion disruption occurs immediately	4	5
Oxacillin sodium	**C**	**C**	**C**		10,12,17	
Paclitaxel	**C**	**C**	**C**		4,5	
Penicillin G potassium	**C**	**C**	**C**		3,10,12,17,20	
Penicillin G sodium	**C**	—	—		10,12	
Pentobarbitol sodium	**C**	**I**	**I**	Emulsion disruption occurs immediately	4	5
Phenobarbitol sodium	**C**	**I**	**I**	Emulsion disruption occurs immediately	4	5
Phenytoin sodium	**I**	**I**	—	Heavy white precipitate forms immediately; incompatible with dextrose		2,20
Piperacillin sodium	**C**	**C**	**C**		4,5,10,12	
Piperacillin sodium / Tazobactam sodium	**C**	**C**	**C**		4,5	
Potassium chloride	**C**	**C**	**C**		4,5	
Potassium phosphate	**I**	**I**	**I**	Increased turbidity occurs immediately; emulsion disruption occurs immediately		4,5
Prochlorperazine edisylate	**C**	**C**	**C**		4,5	
Promethazine HCl	**C/I**	**C**	**C**	Amber discoloration in 4 hours in select formulations	4,5	4
Propofol	**C**	—	—	Propofol injection contains approximately 10 gm fat / 100 mL	57	

Ranitidine HCl	C	C	C		3,4,5,20,24	
Sargramostim	C	—	—		58	
Sodium bicarbonate	I/C	C	C	Small amount of precipitate forms in 1 hour in select formulations	4,5	4
Sodium nitroprusside	C	C	C		4,5	
Sodium phosphate	I	I	I	Increased turbidity occurs immediately; emulsion disruption occurs immediately		4,5
Tacrolimus	C	C	C		4,5	
Ticarcillin disodium	C	C	C		4,5,10,12,17	
Ticarcillin disodium-Clavulanate potassium	C	C	C		4,5,20	
Tobramycin sulfate	C	C	C		3,4,5,10, 11,12,13,17	
Trimethoprim-Sulfamethoxazole	C	C	C		4,5	
Urokinase	C	—	—		2	
Vancomycin HCl	C	C	C		3,4,5,10,11,20	
Vecuronium bromide	C	—	—		20	
vitamin K1 - phytonadione	C	C	—		18,59	
Zidovudine	C	C	C		3,4,5	

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