

Sodium Content of Intravenous Antibiotic Preparations

TO THE EDITOR—We read with great appreciation the recent publication by Frisbee et al [1], which examines a common and perhaps underappreciated phenomenon seen in clinical practice: concurrent treatment for pneumonia in those admitted for acute decompensated heart failure (ADHF). Recent evidence also suggests that incident cardiac complications, primarily new or worsening heart failure, are frequent in those admitted for community-acquired pneumonia (CAP), further complicating the clinical picture [2, 3]. Thus, definitive diagnosis of ADHF versus CAP can certainly be challenging given the similarity in symptoms and can often lead to overprescribing and excessive treatment burden for both the patient and health-care system.

The authors' findings that ADHF patients who received intravenous antibiotics had longer lengths of stay, required more diuretics, and were more likely to be re-admitted compared with ADHF patients who were not exposed to such therapy serve as a caution against unnecessary intravenous antimicrobial therapy in patients who are at low risk for pneumonia.

We believe that an accurate reference for sodium content found in common intravenous antibiotics can serve as a useful tool for antimicrobial stewards in helping convince providers to discontinue antibiotic therapy in ADHF patients who are at low risk for infection. The supplemental table provided by the authors is intended to serve this purpose. However, there are a few aspects about the data that we would like to clarify.

First, sodium restriction is commonly prescribed for patients with heart failure. The amount by which to limit sodium may vary, but the guideline-recommended

values are described in elemental sodium [4–6]. It appears that the authors report sodium content from antibiotics used in their study in terms of “sodium chloride” (eg, vancomycin, doxycycline, and azithromycin), which would overestimate elemental sodium content present in each antibiotic preparation. For example, if a standard 1-gram dose of vancomycin lacking intrinsic sodium content was prepared in 250 mL normal saline (NS), this particular antibiotic-diluent combination would yield approximately 900 mg of elemental sodium, which contrasts with the 2250 mg of sodium reported by the authors.

Second, antibiotics are often prepared in diluents that differ in sodium content and volume. Some are available in ready-to-use preparations from the manufacturer; others are prepared in varying volumes of dextrose 5% in water and NS. For example, with respect to the sodium content reported for linezolid, we are aware of 2 premixed formulations that are prepared in an NS and a dextrose-based solution, containing a sodium content of 1196 mg and 114 mg, respectively [7, 8]. We surveyed common practices across our institutions and developed a table (Table 1) that addresses the above inconsistencies and incorporates more antibiotics to be a more comprehensive antimicrobial stewardship tool in detailing information on the sodium content intrinsic to these antibiotics and in commonly used diluents. We present our data using standard antibiotic doses and report the total sodium content for various volume-diluent preparations on a per-dose basis. We also provide the “total sodium per day of therapy” as a guide for clinicians to better assess the amount of sodium being administered to their patients relative to the “daily” sodium restriction recommendations. The package inserts to which we referred are included in Appendix A.

CONCLUSIONS

In summary, Frisbee et al [1] revisit an important and challenging area of clinical practice and certainly raise awareness of a potentially useful tool that may further support hospital stewardship programs in the discontinuation of inappropriate antibiotic therapy in patients with heart failure. We wholeheartedly agree that “giving patients at low risk of infection antibiotic therapy ‘just to be safe’” may not actually be safe at all, and we hope that our proposed table will provide a more systematic means to conceptualize sodium content of intravenous antibiotic administration.

Acknowledgments

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

APPENDIX A: PACKAGE INSERTS USED IN CREATION OF TABLE 1:

1. Penicillin G Potassium (penicillin g injection, solution) [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2018.
2. PFIZERPEN (penicillin g potassium powder, for solution) [package insert]. New York, NY: Roerig (Division of Pfizer, Inc.); 2019.
3. Penicillin G Sodium (penicillin g sodium injection, powder, for solution) [package insert]. Princeton, NJ: Sandoz Inc.; 2014.
4. Ampicillin for Injection, USP [package insert]. Paramus, NJ: WG Critical Care, LLC; 2017.
5. Ampicillin and Sulbactam (ampicillin sodium and sulbactam sodium injection, powder, for solution) [package insert]. Schaumburg, IL: Sagent Pharmaceuticals, Inc.; 2017.
6. Oxacillin Injection, USP in Plastic Container [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2017.

Table 1. Sodium Content of Intravenous Antibiotic Preparations

Antibiotic	Usual Dose (mg)	Available Diluents	Intrinsic Sodium Content in RTU (mg)	Intrinsic Sodium per Vial (or in D5W) (mg) ^a	Total Sodium Content in 50 mL NS (mg) ^b	Total Sodium Content in 100 mL NS (mg) ^b	Total Sodium Content (mg) in Other Volume of NS	Total Sodium (mg) per Day of Therapy (No. of Doses) ^{c,d}
β-Lactams								
Penicillin G Potassium	4 MU	RTU, D5W, NS	94	272	213.3	390.3	-	2340 (6)
Penicillin G Sodium	4 MU	D5W, NS	-	154.6	340.1	517.1	-	3100 (6)
Ampicillin	2000	NS	-	131.6	-	485.6	-	2910 (6)
Ampicillin-sulbactam	1500	NS	-	115	292	469	-	1880 (4)
	3000	NS	-	230	-	584	-	2340 (4)
Oxacillin	2000	RTU, D5W, NS	184.8	128	375.8	552.8	-	3320 (6)
Nafcillin	2000	RTU, D5W, NS	153.2	132.2	415.4	592.4	-	3550 (6)
Piperacillin-tazobactam	3375	RTU, D5W, NS	195	162	392.1	569.1	-	2280 (4)
	4500	RTU, D5W, NS	260	216	463.8	640.8	-	2560 (4)
Cefazolin	1000	RTU, D5W, NS	48	48	225	402	-	1200 (3)
	2000	RTU, D5W, NS	96	96	-	450	-	1350 (3)
Ceftriaxone	1000	RTU, D5W, NS	83	83	294	471	-	470 (1)
	2000	RTU, D5W, NS	166	166	410.9	587.9	-	1180 (2)
Ceftazidime	1000	RTU, D5W, NS	54	54	231	408	-	1220 (3)
	2000	RTU, D5W, NS	108	108	285	462	-	1390 (3)
Cefepime	1000	RTU, D5W, NS	0	0	212.4	389.4	-	1170 (3)
	2000	RTU, D5W, NS	0	0	212.4	389.4	-	1170 (3)
Aztreonam	2000	RTU, D5W, NS	0	0	-	354	-	1060 (3)
Ertapenem	1000	NS	-	137	349.4	526.4	-	530 (1)
Meropenem	1000	RTU, NS	290.2	90.2	267.2	444.2	-	1330 (3)
	2000	NS	-	180.4	-	534.4	-	1600 (3)
Imipenem	500	D5W, NS	-	375	-	426.9	-	1710 (4)
Fluoroquinolones/Macrolides								
Ciprofloxacin	400	RTU	0	-	-	-	-	0 (2)
Levofloxacin	500	RTU, D5W, NS	0	0	-	-	283 (80 mL)	280 (1)
Azithromycin	500	D5W, NS	-	114	-	-	999 (250 mL)	1000 (1)
Anti-MRSA Agents								
Vancomycin	1000	RTU, D5W, NS	708	0	-	-	885 (250 mL)	3540 (4)
	2000	D5W, NS	-	0	-	-	1770 (500 mL)	3540 (2)
Daptomycin	500	NS	-	0	212.4	389.4	-	390 (1)
Linezolid	600	RTU	114; 1196 ^e	-	-	-	1196 (300 mL)	2390 (2)
Ceftaroline	600	D5W, NS	-	0	247.8	424.8	-	1270 (3)
Doxycycline	100	D5W, NS	-	0	-	389.4	-	780 (2)
Clindamycin	600	RTU, D5W, NS	0	0	177	354	-	1420 (4)
	900	RTU, D5W, NS	0	0	177	354	-	1060 (3)
Sulfamethoxazole-trimethoprim	1875-375 ^f	D5W	-	0 ^g	-	-	-	0 ^h (4)

Table 1. Continued

Antibiotic	Usual Dose (mg)	Available Diluents	Intrinsic Sodium Content in RTU (mg)	Intrinsic Sodium per Vial (or in D5W) (mg) ^a in 50 mL NS (mg) ^b	Total Sodium Content (mg) in Other Volume of NS	Total Sodium Content in 100 mL NS (mg) ^b	Total Sodium (mg) per Day of Therapy (No. of Doses) ^{c,d}
Miscellaneous							
Metronidazole	500	RTU	326	-	-	-	1300 (4)

Abbreviations: D5W, dextrose 5% in water; MRSA, methicillin-resistant *Staphylococcus aureus*; MU, million units; NS, normal saline 0.9% NaCl; RTU, ready-to-use.

^aValues derived from injectable single-dose vial supply; sodium content may vary slightly between manufacturers.

^bIntrinsic sodium content of antibiotic plus sodium content in NS; 177 mg sodium per 50 mL NS; 354 mg sodium per 100 mL NS; if NS is a recommended solvent for reconstitution per manufacturer, sodium content from the solvent is also included.

^cAssumes drug preparation in 100 mL NS or other volume of NS/available diluent with appropriate drug concentration per manufacturer; values are rounded to the nearest 10 mg.

^dTotal sodium content per day of therapy considers maximum number of daily doses seen in clinical practice.

^eRTU formulations available in both NS (1196 mg sodium) and D5W (114 mg sodium).

^fDose based on 5 mg/kg trimethoprim component; weight of 75 kg.

^gSodium content from excipients negligible.

7. Oxacillin (oxacillin injection, powder, for solution) [package insert]. Parsippany, NJ: Wockhardt USA LLC; 2018.
8. Zosyn (piperacillin and tazobactam) injection, for intravenous use [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals Inc. (A subsidiary of Pfizer Inc.); 2016.
9. Piperacillin, Tazobactam (piperacillin sodium, tazobactam sodium injection, powder, lyophilized, for solution) [package insert]. Schaumburg, IL: Sagent Pharmaceuticals, Inc.; 2018.
10. Cefazolin (cefazolin sodium injection, solution) [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2019.
11. Cefazolin (cefazolin injection, powder, for solution) [package insert]. Paramus, NJ: WG Critical Care, LLC; 2019.
12. Ceftriaxone (ceftriaxone sodium injection, solution) [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2018.
13. Ceftriaxone (ceftriaxone injection, powder, for solution) [package insert]. Schaumburg, IL: Sagent Pharmaceuticals, Inc.; 2018.
14. Cefepime (cefepime injection, solution) [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2018.
15. Cefepime (cefepime hydrochloride injection, powder, for solution) [package insert]. Schaumburg, IL: Sagent Pharmaceuticals, Inc.; 2018.
16. Azactam (aztreonam injection) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2018.
17. Aztreonam (aztreonam injection, powder, lyophilized, for solution) [package insert]. Lake Zurich, IL: Fresenius Kabi USA, LLC; 2019.
18. Ertapenem (ertapenem sodium injection, powder, lyophilized, for solution) [package insert]. Chestnut Ridge, NY: Par Pharmaceutical; 2019.
19. Meropenem and Sodium Chloride (meropenem and sodium chloride injection, solution) [package insert]. Bethlehem, PA: B. Braun Medical Inc.; 2019.
20. Meropenem (meropenem injection, powder, for solution) [package insert]. Lake Zurich, IL: Fresenius Kabi USA, LLC; 2019.
21. Imipenem and Cilastatin (imipenem and cilastatin sodium injection, powder, for solution) [package insert]. Lake Zurich, IL: Fresenius Kabi USA, LLC; 2019.
22. Ciprofloxacin (ciprofloxacin injection, solution) [package insert]. Lake Forest, IL: Hospira, Inc.; 2019.
23. Levofloxacin (levofloxacin injection, solution) [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2019.
24. Azithromycin (azithromycin for injection, powder, lyophilized, for solution injection) [package insert]. Weston, FL: APOTEX CORP.; 2018.
25. Vancomycin hydrochloride (vancomycin hydrochloride injection, solution) [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2018.
26. Vancomycin hydrochloride (vancomycin hydrochloride injection, powder, lyophilized, for solution) [package insert]. Lake Forest, IL: Hospira, Inc.; 2019.
27. Daptomycin (daptomycin injection, powder, lyophilized, for solution) [package insert]. Lake Forest, IL: Hospira, Inc.; 2019.
28. Linezolid (linezolid injection) [package insert]. Lake Forest, IL: Hospira, Inc.; 2019.
29. Linezolid (linezolid injection) [package insert]. East Windsor, NJ: AuroMedics Pharma LLC; 2018.
30. Teflaro (ceftaroline fosamil powder, for solution) [package insert]. Madison, NJ: Allergan USA, Inc.; 2019.
31. Doxy 100 (doxycycline injection, powder, lyophilized, for solution) [package insert]. Lake Zurich, IL: Fresenius Kabi USA, LLC; 2019.

32. Cleocin phosphate (clindamycin phosphate injection, solution) [package insert]. New York, NY: Pharmacia & Upjohn Co. (Division of Pfizer Inc.); 2019.
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injection) [package insert]. Rockford, IL: Mylan Institutional LLC; 2018.

39. Metronidazole (metronidazole injection, solution) [package insert]. Deerfield, IL: Baxter Healthcare Corporation; 2018.

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Received 21 October 2019; editorial decision 22 November 2019; accepted 26 November 2019.

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Open Forum Infectious Diseases®

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