marketed as a “single strength” (SS) and “double strength” (DS) tablets: 80 mg TMP / 400 mg SMX as SS; and 160 mg TMP / 800 mg SMX as DS (2).

When doses are provided in the United States, for example, 15 – 20 mg/kg/day of TMP/SMX for the treatment of *Pneumocystis jirovecii* pneumonia (PCP), the dose refers to the TMP component (3). For the “average” 70 kg adult without renal impairment, this would correspond to a dose of 1050 – 1400 mg TMP daily (or, roughly 2 – 3 DS tablets by mouth/intravenously [PO/IV] 3 times a day).

However, not all countries report TMP/SMX doses in the same format. Where a TMP/SMX dose in the United States refers to the TMP component, in other countries, the dose may refer to the combined product of TMP and SMX. Therefore, in the US, TMP/SMX 960 mg twice daily would refer to 960 mg of TMP and 4800 mg of SMX (6 DS tablets) twice daily, whereas in other countries, it would refer to 160 mg of TMP and 800 mg of SMX (1 DS tablet) twice daily. This is a 6-fold difference in dose.

A literature search of PubMed was performed from 1965 through October 13, 2013, with the terms “Bactrim,” “trimethoprim,” “sulfamethoxazole,” “co-trimoxazole,” “peritoneal dialysis,” and “peritonitis.” Additionally, specific organisms such as “listeria” and “nocardia” were searched. All articles and their references were reviewed for case reports of using oral/intravenous TMP/SMX to treat peritonitis, specifically focusing on the dosage used. Intraperitoneal administration was excluded. Initially, 37 reports were identified, but ultimately only 8 provided actual doses (4–11) (Table 1).

Only 4 of the available reports specified that patients were receiving CAPD (4–7) with the most common dose of oral TMP/SMX for the treatment of peritonitis being 1 – 2 DS tablets daily. These doses correspond with the 2000 and 1996 ISPD guidelines (12,13) recommending TMP/SMX 320/1600 mg PO q24–48 h for intermittent dosing of CAPD patients. This equates to 2 DS tablets every 1 – 2 days, which is consistent with the published case reports.

There are 2 discrepancies in the remaining published literature. Ortiz *et al.* list a dose of 320 mg TMP and 3200 mg SMX (10). To my knowledge, SMX is not available as an individual medication. Using a fixed ratio of 1:5 TMP/SMX, the SMX dose may have been 1600 mg, resulting in the overall dose being 2 DS tablets (TMP 320 mg and SMX 1600 mg) every 48 hours. Kendrick-Jones *et al.* only provide their dose as 960 mg of TMP/SMX (8). Again, this may lead to confusion as it can be interpreted as 960 mg TMP (and 4800 mg SMX, or 6 DS tablets) daily; or it could mean 1 DS tablet daily (TMP 160 mg plus SMX 800 mg).

While TMP/SMX is not the only combination product on the market, it is one of the few medications where the US recommended dose refers to only one component of the product. Other combination products, such as ampicillin/sulbactam, piperacillin/tazobactam and quinupristin/dalfopristin, have dosing recommendations that refer to both components (14–16). For example, in the US, ampicillin/sulbactam 3 g IV q6h refers to 2 g ampicillin plus 1 g sulbactam IV q6h; piperacillin/tazobactam 4.5 g IV q8h refers to 3 g piperacillin plus

Clarification of Trimethoprim/ Sulfamethoxazole Dose in CAPD

KEY WORDS: Bactrim; trimethoprim; peritoneal dialysis; CAPD.

Editor:

I would like to clarify a dosing recommendation within the 2010 International Society for Peritoneal Dialysis (ISPD) guidelines (1). In Table 4, for patients undergoing continuous ambulatory peritoneal dialysis (CAPD), the recommended dose for trimethoprim/sulfamethoxazole (TMP/SMX) is 960 mg by mouth twice daily (1). The dose of TMP/SMX 960 mg can be interpreted in 1 of 2 ways: it can be a single double strength (DS) tablet, or it can be 960 mg of TMP/4800 mg of SMX.

Trimethoprim/sulfamethoxazole is a combination antibiotic comprised of a dihydrofolate reductase inhibitor and a folic acid synthesis inhibitor. It is co-formulated in a fixed ratio of 1:5 TMP:SMX. The most common oral formulations are

TABLE 1
Doses of TMP/SMX for the Treatment of PD-Related Peritonitis in the Literature

Reference	Dialysis Type	Organism	TMP/SMX Dose (per day)	Daily Dose in DS Equivalents	Additional Antibiotics
Smith TL (4)	CAPD	MRSA	TMP 160 mg, SMX 800 mg PO	1	Rifampin
Celik A (5)	CAPD	Variable	TMP 320 mg, SMX 1600 mg PO	2	Amikacin
Tzanetou K (6)	CAPD	<i>Stenotrophomonas maltophilia</i>	TMP 160mg, SMX 800 mg IV; TMP 240 mg, SMX 1200 mg PO	1 (IV) 1.5 (PO)	Ceftazidime
Li SZ (7)	CAPD	<i>Nocardia</i> spp.	TMP 320 mg, SMX 1600 mg PO	2	N/A
Kendrick-Jones J (8)	Not specified	<i>N. asteroides</i>	TMP/SMX 960 mg PO	Assume 1	N/A
Machuca E (9)	APD	<i>S. maltophilia</i>	TMP 320 mg, SMX 1600 mg PO	2	Amikacin
Ortiz AM (10)	APD	<i>N. asteroides</i>	TMP 320 mg, SMX 3200 mg IV (q48h)	Assume 2 (q48h)	Amikacin
Gul M (11)	Not specified	<i>Serratia ficaria</i>	TMP 160 mg, SMX 800 mg PO	1	N/A

TMP/SMX = trimethoprim/sulfamethoxazole; PD = peritoneal dialysis; DS = double strength; CAPD = continuous ambulatory peritoneal dialysis; MRSA = methicillin resistant *Staphylococcus aureus*; spp = species; PO = by mouth; IV = intravenous; N/A = not applicable; APD = automated peritoneal dialysis.

1.5 g tazobactam IV q8h; and so forth. These inconsistencies highlight the need for standardization when reporting doses of combination medications.

Previous versions of the ISPD guidelines presented the TMP/SMX dose as “TMP/SMX 320/1600 mg PO q24–48h” which clearly indicated the amount of each component (12,13). The 2010 guidelines present it as “960 mg by mouth twice daily.” In order to standardize and potentially avoid dosing errors, the dose should be clarified to indicate that the 960 mg refers to both components of the medication. Furthermore, authors writing case reports of successful therapy should strive to include exact doses of medications administered. As the above PubMed search illustrates, many of the manuscripts did not provide doses and, therefore, did not help elucidate the optimal dose of TMP/SMX.

DISCLOSURES

The author has no financial conflicts of interest to declare.

M. V. Golik Mahoney

Clinical Pharmacy Coordinator, Infectious Diseases
Beth Israel Deaconess Medical Center
Boston, MA 02215

email: mgolik@bidmc.harvard.edu

REFERENCES

- Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, et al. Peritoneal dialysis-related infections recommendations: 2010 update. *Perit Dial Int* 2010; 30:393–423.
- Sulfamethoxazole and Trimethoprim [Package Insert]. Hauppauge, NY: Amneal Pharmaceuticals of NY; 2012.
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf>. Section accessed 6/19/13.
- Smith TL, Pearson ML, Wilcox KR, Cruz C, Lancaster MV, Robinson-Dunn B, et al. Emergence of vancomycin resistance in *Staphylococcus aureus*. *N Engl J Med* 1999; 340:493–501.
- Celik A, Cirit M, Tünger A, Akçiçek F, Başçi A. Treatment of CAPD peritonitis with oral trimethoprim/sulfamethoxazole and intraperitoneal aminoglycoside combination. *Perit Dial Int* 1999; 19:284–5.
- Tzanetou K, Triantaphyllis G, Tsoutsos D, Petropoulou D, Ganteris G, Malamou-Lada E, et al. *Stenotrophomonas maltophilia* peritonitis in CAPD patients: susceptibility to antibiotics and treatment outcome: a report of five cases. *Perit Dial Int* 2004; 24:401–4.
- Li SY, Yu KW, Yang WC, Chen TW, Lin CC. Nocardia peritonitis – a case report and literature review. *Perit Dial Int* 2008; 28:544–7.
- Kendrick-Jones J, Ratanjee SK, Taylor SL, Marshall MR. *Nocardia asteroides* peritoneal dialysis-related peritonitis: a case of successful treatment and return to peritoneal dialysis. *Nephrol Dial Transplant* 2008; 23:2693–4.
- Machuca E, Ortiz AM, Rabagliati R. *Stenotrophomonas maltophilia* peritonitis in a patient receiving automated peritoneal dialysis. *Adv Perit Dial* 2005; 21:63–6.
- Ortiz AM, Rabaglianti R, Machuca E. Successful treatment of *Nocardia asteroides* peritonitis in a patient undergoing automated peritoneal dialysis and receiving immunosuppressive therapy. *Adv Perit Dial* 2005; 21:66–8.

11. Gul M, Dogan E, Kirecci E, Ucmak H, Dirican E, Karadag A. *Serratia ficaria* isolated from sputum specimen. *Acta Microbiol Immunol Hung* 2011;58:235–8.
12. Keane WF, Bailie GR, Boeschoten E, Gokal R, Golper TA, Holmes CJ, *et al*. Adult peritoneal dialysis-related peritonitis treatment recommendations: 2000 update. *Perit Dial Int* 2000; 20:396–411.
13. Keane WF, Alexander SR, Bailie GR, Boeschoten E, Gokal R, Golper TA, *et al*. Peritoneal dialysis-related peritonitis treatment recommendations: 1996 update. *Perit Dial Int* 1996; 16:557–73.
14. Unasyn (Ampicillin/sulbactam) [Package Insert]. New York, NY: Pfizer, Inc; 2012.
15. Zosyn (Piperacillin/tazobactam) [Package Insert]. New York, NY: Pfizer, Inc; 2012.
16. Synercid (Quinupristin/dalfopristin) [Package Insert]. New York, NY: Pfizer, Inc; 2012.

doi: 10.3747/pdi.2013.00173