

UC Davis

Dermatology Online Journal

Title

Why sulfonamides are contraindicated in Rocky Mountain spotted fever

Permalink

<https://escholarship.org/uc/item/5j16w527>

Journal

Dermatology Online Journal, 20(2)

Authors

Ren, Vicky
Hsu, Sylvia

Publication Date

2014

DOI

10.5070/D3202021536

Copyright Information

Copyright 2014 by the author(s). This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <https://creativecommons.org/licenses/by-nc-nd/4.0/>

Commentary

Why sulfonamides are contraindicated in Rocky Mountain spotted fever

Vicky Ren MD, Sylvia Hsu MD

Dermatology Online Journal 20 (2): 3

Department of Dermatology, Baylor College of Medicine, Houston, Texas

Correspondence:

Sylvia Hsu, MD
Professor of Dermatology
Baylor College of Medicine
1977 Butler Blvd, Ste. E6.200
Houston, TX 77030
(713) 798-6131
shsu@bcm.edu

Abstract

Sulfonamide antibiotics are not effective for the treatment of Rocky Mountain spotted fever (RMSF). Patients suspected of having RMSF based on history and physical exam should be treated with doxycycline and not a sulfonamide to avoid increased morbidity and mortality.

Keywords: Rocky Mountain, spotted fever, *Rickettsia rickettsii*, sulfa, sulfonamide, cotrimoxazole

Commentary

The ineffectiveness of sulfonamides in the treatment of Rocky Mountain spotted fever (RMSF) was first described in 1939 and 1943 in experimentally infected guinea pigs and rabbits [1, 2]. All sulfa drugs are contraindicated throughout the course of a rickettsial infection [3]. The prompt administration of doxycycline is the treatment of choice for suspected RMSF [4]. We sought to answer the question: Why are sulfa drugs contraindicated in the treatment of RMSF?

Prior to the availability of doxycycline, para-aminobenzoic acid (PABA), an analogue of sulfonamide, was shown to be successful in the treatment of guinea pigs infected with RMSF. However, PABA required frequent dosing and administration of bicarbonate in order to maintain a therapeutic blood concentration and prevent urinary precipitation [5]. Although the rickettsiostatic mechanism of PABA remains unclear and is only of historic interest now, PABA may be associated with the interference of bacterial utilization of para-hydroxybenzoic acid [6].

Sulfonamides (e.g., sulfamethoxazole) are structural analogs and competitive inhibitors of PABA. Sulfonamides bind to dihydropteroate synthetase (DHPS) and inhibit the first step of dihydrofolic acid synthesis. Trimethoprim (TMP), which is administered with sulfamethoxazole (SMX) in the TMP-SMX sulfonamide antibiotic, binds to dihydrofolate reductase (DHFR) and inhibits conversion of dihydrofolic acid to tetrahydrofolic acid. *Rickettsia rickettsii*, the bacterium that is responsible for Rocky Mountain spotted fever, lacks the *folP* gene that encodes DHPS, making it resistant to sulfamethoxazole. Other rickettsial species also lack *folA*, which encodes DHFR. Consequently, rickettsial organisms as a group demonstrate significant resistance to sulfa drugs [7].

Administration of sulfonamides to patients who have not been definitely diagnosed with RMSF leads to further delay in diagnosis and treatment, which results in increased morbidity and mortality. Thus, all patients suspected of having RMSF based on history and physical exam should be treated with doxycycline, preferably within the first five days of symptom development [8].

References

1. Topping NH. Experimental Rocky Mountain spotted fever and endemic typhus treated with prontosil or sulfapyridine. *Pub Health Rep.* 1939 June;54(26):1143-7. [PMCID:PMC1995921]
2. Steinhaus EA, Parker RR. Experimental Rocky Mountain spotted fever: Results of treatment with certain drugs. *Pub Health Rep.* 1943 Feb;58(9):351-2. [PMCID:PMC2016884]
3. Harrell GT. Treatment of Rocky Mountain spotted fever with antibiotics. *Ann N Y Acad Sci.* 1952 Dec;55(6):1027-42. [PMID:13139181]
4. Bratton RL, Corey R. Tick-borne disease. *Am Fam Physician.* 2005 Jun;71(12):2323-30. [PMID:15999870]
5. Ravenel SF. Para-aminobenzoic acid therapy of Rocky Mountain spotted fever; outline of a comprehensive plan of treatment with report of five cases. *J Am Med Assoc.* 1947 Apr;133(14):989-94. [PMID:20288263]
6. Weiss E. Growth and physiology of rickettsiae. *Bacteriol Rev.* 1973 Sep;37(3):259-83. [PMCID:PMC413818]
7. Rolain JM, Raoult D. Genome comparison analysis of molecular mechanisms of resistance to antibiotics in the *Rickettsia* genus. *Ann N Y Acad Sci.* 2005 Dec;1063:222-30. [PMID:16481518]
8. Kirland KB, Wilkinson WE, Sexton DJ. Therapeutic delay and mortality in cases of Rocky Mountain spotted fever. *Clin Infect Dis.* 1995 May;20(5):1118-21. [PMID:7619985]