

the left ventricular ejection fraction (LVEF). Of the 23 patients who received deferasirox 10-30 mg/kg/day, for 13.1 ( $\pm 0.78$ ) months; the mean myocardial T2\* measurement was inversely related to myocardial iron content. Deferasirox treatment led to significant reductions in mean serum ferritin concentrations and LICs, while no changes in LVEF were noted [3]. Study conducted by Pathare, *et al.* [4] monitored cardiac siderosis using T2 MRI in 19 heavily iron overloaded patients with  $\beta$ -thalassemia major receiving iron chelation therapy with deferasirox over an 18 months period. Deferasirox therapy significantly improved mean cardiac T2 from a baseline of 17.2 (10.8) to 21.5 (12.8) ms. A concomitant reduction in median serum ferritin, and mean LIC was also noted. Improvements were seen in patients with various degrees of cardiac siderosis, including myocardial iron in those patients with a baseline cardiac T2 of <10ms, indicative of high cardiac iron burden [4].

Studies on long term use, dose, efficacy and safety profile of deferasirox have concluded that deferasirox in doses of 20-30 mg/kg/day could effectively reduce iron burden [5]. Further, efficacy of available chelators on myocardial iron and biventricular function by quantitative MRI in 550 thalasseemics concluded that oral deferasirox has better global systolic ventricular function compared to oral deferiprone and subcutaneous desferoxamine [6].

In the background of such global studies, this prospective, open label, single arm study on 30 patients by Merchant, *et al.* [7] reported good safety profile of deferasirox, and showed that it effectively chelates myocardial iron, more efficacious in moderate to severe cardiac iron overload. In addition, there was a significant decrease in serum ferritin in those patients with cardiac T2\* <10 ms and between 10-20 ms. Similar cardiac findings have also been reported by other researchers

[4]. Although the sample size is small, this study adds that for Indian population, deferasirox is a safe and efficacious iron chelator without any significant adverse effect even with doses of >30 mg/kg/day. Thus, the data shows promising results of deferasirox on cardiac iron and quantifies myocardial iron by non-invasive method. Presently, many thalassemia centers monitor cardiac iron with T2 weighted MRI imaging, but routine application of this technology has not been implemented across all centers.

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#### REFERENCES

1. Michael RD, Jones MF, Vichinsky E. Thalassemia syndrome. *In:* Kliegman RM, Stanton B, Schor NF, St. Geme III JW, Behrman RE, editors. Nelson Textbook of Pediatrics. 19<sup>th</sup> ed. Philadelphia: Elsevier, Saunders; 2011. p.1675-76.
2. Agarwal MB. Deferasirox: Oral, once daily iron chelator- An expert opinion. *Indian J Pediatr.* 2010;77:185-191
3. Neufeld EJ. Oral chelators deferasirox and deferiprone for transfusional iron overload in thalassemia major: new data, new questions. *Blood.* 2006;107:3436-41.
4. Pathare A, Taher A, Daar S. Deferasirox (Exjade ®) significantly improves cardiac T2\* in heavily iron overload patients with  $\beta$  thalassemia major. *Ann Hematol.* 2010;89:405-9.
5. Nisbet Brown E, Olivieri NG, Giardina PJ, Grady RW, Neufeld EJ, Sechaud R, *et al.* effectiveness and safety of placebo controlled, dose escalation trial. *Lancet.* 2003;361:1597-1602.
6. Pepe A, Meloni A, Capra M, Clanciulli P, Prossomariti L, Malaventura C, *et al.* Deferasirox, deferiprone and desferoxamine treatment in thalassemia major patients: cardiac iron and function comparison determined by quantitative magnetic resonance imaging. *Haematologica.* 2011;96:41-7.
7. Merchant R, Ahmed J, Krishnan P, Jankharia B. Efficacy and Safety of deferasirox for reducing total body and cardiac iron in thalassemia. *Indian Pediatr.* 2012;49:281-5.

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## Public Health Significance of Shigellosis

SUJIT K BHATTACHARYA, \*DHIKA SUR AND DILIP MAHALANABIS

*Society for Applied Studies, Salt Lake; and \*National Institute of Cholera and Enteric Diseases, Kolkata, India.*  
*sujitkbhattacharya@yahoo.com*

**S**higellosis is an important intestinal infection of public health concern, accounting for 140 million cases globally per year and 60 000 deaths annually of which 60% occur in children below 5 years of age [1]. The disease can occur as

sporadic, epidemic and pandemic forms. The disease has a short incubation period. In 1969-1970, an epidemic of shigellosis caused by multi-drug resistant *S.dysenteriae* type 1 occurred in Central America and rapidly spread to different parts of Africa and Asia. The epidemic was seen

in Bangladesh in 1970s and in Eastern India in 1974 [2]. The disease is characterized by fever, loose stools mixed with blood and mucus, tenesmus and abdominal cramps. Dehydration is not generally a conspicuous feature. Shigellosis is caused by four species of *Shigella* viz., *S. sonnei*, *S. flexneri*, *S. boydii* and *S. dysenteriae*. *S. sonnei* causes mild dysentery in developed countries, while *S. dysenteriae* type 1 causes severe dysentery in developing countries in patients with poor hygiene, sanitation and improper disposal of human and animal waste and overcrowding. Shigellosis can occur in high risk populations, viz., displaced populations, travellers, in the military and day-care centers. Each of them are subdivided into several serotypes, e.g., *S. flexneri* 1-6, *S. boydii* 1-18, *S. sonnei* phase I and phase II, and *S. dysenteriae* 1-12. Three strains are responsible for causing majority of shigellosis cases, viz., *S. sonnei*, *S. flexneri* 2a and *S. dysenteriae* Type 1.

In the article on school outbreak of *S. sonnei* infection in China in this issue of the journal [3], *S. sonnei* strains exhibited high degree of drug resistance. Usually, shigellosis caused by *S. dysenteriae* type 1 is characterized by multiple drug resistance and high morbidity and mortality particularly in children below 5 years of age [4]. *S. dysenteriae* type 1 may be associated with a number of complications like rectal prolapse, leukemoid reaction, convulsions and hemolytic uremic syndrome (HUS). In this study, the shigella strains were sensitive to ciprofloxacin and third generation cephalosporins. In view of the reported cartilage toxicity of fluoroquinolones in animal model, the drug was not used in China where it is prohibited for use in children. However, in many countries, fluoroquinolones are used in children successfully for the treatment of infections, without any cartilage toxicity being reported [3,6]. High rate of antimicrobial resistance as well as high prevalence of class 2 integrons among *S. sonnei* species was observed in this study. The authors suggest that it is mandatory to continuously monitor the local antibiotic resistance

patterns of *Shigella* species [7]. However, it is imperative to keep in mind that stool cultures are often negative, more so, if the sample has been processed long after collection.

Hand washing with plenty of water with soap or mud, improvement of environmental sanitation, water supply and avoidance of overcrowding are required for prevention of the disease, particularly in slums and refugee camps. Vaccine development for shigellosis is a formidable task as it can be caused by a number of serotypes and immunity to *Shigella* is serotype specific. Several attempts have been made to develop a safe and effective vaccine against shigellosis, but none is yet available for public use.

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#### REFERENCES

1. Kotloff KL, Winckloff JP, Ivanoff B, Clemens JD, Swerdlow DL, Sansonetti PJ, *et al.* Global burden of Shigella infections: implications for vaccine development and implementation of control strategies. Bull World Health Org. 1999;77:651-6.
2. Rahaman MM, Khan MM, Aziz KM, Islam MS, Kibriya AK. An outbreak of dysenteriae type 1 on a coral island in Bay of Bengal. J infect Dis. 1975;132:15-9.
3. Xiao GG, Fan J, Deng JJ, Chen CH, Zhou W, Li XH, *et al.* A school outbreak of Shigella sonnei infection in China: clinical features, antibiotic susceptibility and molecular epidemiology. Indian Pediatr. 2012; 49:287-90.
4. Bhattacharya SK, Sur D. An evaluation of current shigellosis treatment. Expert Opin Pharmacotherapy. 2003;4:1315-20.
5. Bhattacharya SK, Sarkar K, Nair GB, Faruque AS, Sack DA. Multidrug-resistant Shigella dysenteriae type1 in south Asia. Lancet Infect Dis. 2003;3:755.
6. Khan WA, Seas C, Dhar U, Salam MA, Bennish ML. Treatment of Shigellosis: V. Comparison of azithromycin and ciprofloxacin-A double-blind, randomized, controlled trial. Ann Intern Med. 1997;126:697-703.
7. Sur D, Niyogi SK, Sur S, Datta KK, Takeda Y, Nair GB, *et al.* Multidrug-resistant Shigella dysenteriae type 1: forerunners of a new epidemic strain in eastern India? Emerg Infect Dis. 2003;9:404-5.