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The efficacy of 2 days versus 3 days treatment with Ciprofloxacin, in our cases of multidrug resistant shigellosis

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Background: The annual number of Shigella episodes worldwide was estimated to be 164.7 million, of which 163.2 were in developing countries. Multiple drug resistant strains of Shigella are emerging throughout the world. Shigellosis still represents in average 0.9-1.05% of admissions to the Service of Infectious Diseases at Mother Theresa University Hospital Center in Tirana, Albania. Strains of Shigella isolates were 28.2% resistant to Ampicillin, 25% to Trimethoprim-Sulfamethoxazole, 23.9% to Chloramphenicol, 22.8% to Tetracycline and 13% to Nalidixic acid. All isolates were susceptible to Ciprofloxacin. To our knowledge, this is the first report of multiple drug resistant shigellosis from Albania.

Methods: In a prospective study to evaluate 2 days versus 3 days treatment of shigellosis with Ciprofloxacin, 92 patients comprising 53 females and 39 males, ranging in age from 17 to 55 years old were enrolled in this study (2006-2010). 24 randomly selected patients received Ciprofloxacin, 500 mg twice daily for 2 days and 24 patients (then 44 others) received 500 mg twice daily for 3 days. In addition to routine laboratory examinations, daily stool cultures were obtained. Rectosigmoidoscopy was performed in each patient before and on the third day of treatment.

Results: Sh. flexneri (1b, 2a, 2b) was isolated in 83.7% of stool cultures, Sh. sonnei in 6.5%, Sh. dysenteriae in 5.5% and Sh. boydii in 4.3%. Rectosigmoidoscopy revealed hyperemia, multiple bleeding sites and some purulent secretion. Gastroenteritis was controlled in 88% in 24 hours and in all patients in 48 hours. Apyrexia was observed in 61.9% within 24 hours and in 98.9% within 48 hours of treatment. Stool cultures for Shigella were positive in 36.9% of patients in 24 hours and negative in all patients in 48 hours. Rectosigmoidoscopy revealed a decrease in hyperemia and bleeding sites. There were no relapses in three-month follow up examination of all of them.

Conclusion: Excellent therapeutic results with Ciprofloxacin were observed in 2 days of treatment of multi-drug resistant Shigella in Albania. Although Shigellosis is a self-limited disease, for public health reasons antibiotic therapy is useful in (1) shortening fecal excretion of the Shigella and (2) the clinical course of the disease.

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A possible role of ICAM-1 in OspA mediated borrelial adhesion to BMEC surface

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Background: Neuroborreliosis can arise at any time during the course of Lyme disease. Neurological manifestations are attributed in part to penetration of the blood-brain barrier (BBB) and invasion of the central nervous system. The main prerequisite for successful BBB translocation is stationary adhesion to surface of endothelial cells (BMECs) mediated by ligand:receptor interactions. Our previous studies showed that borrelial OspA is able to interact with host CD40 (1) and upregulate ICAM-1. It can be hypothesized that ICAM-1 can be another potential candidate for borrelial BMEC stationary adhesion.

Methods: To elucidate ICAM-1 contribution in BBB adhesion process, His-tagged ICAM-1 of rat was overexpressed in *Saccharomyces cerevisiae* andpurified with metal affinity chromatography. Further, His-tagged ICAM-1 was immobilized on magnetic-beads (MB-IMAC, Bruker) and hybridized with whole cell lysate of neuroinvasive (SKT-7.1) *Borrelia* strain. After washing of unbound proteins, ICAM-1 and its ligand/s were eluted from beads and proteins were analyzed with MALDI-mass spectrometry. Results showed that ICAM-1 interacted with one protein candidate of the *Borrelia*. This borrelial ligand was further identified as OspA with the help of peptide mass fingerprinting. Binding ability of OspA of SKT-7.1 to ICAM-1 was further confirmed by pull down assay based on His-tagged OspA. To demonstrate importance of ICAM-1 in adhesion of *Borrelia* on BMEC, in situ, BMEC monolayer was incubated first with antibodies against ICAM-1 and then with SKT-7.1. Inhibition of the adhesion was compared to positive control wherein BMECs were not blocked with anti-ICAM-1 antibodies.

Results: Results approved that borrelial adhesion to BMEC can be mediated via OspA:ICAM-1 dyad. Blocking of ICAM-1 on BMECs reduces borrelil adhesion by 82% compared to control.

Conclusion: Taken together, study demonstrated that OspA provides *Borrelia* with an essential function in adhesion to endothelium. It can be concluded that adhesion process is mediated not only via OspA:CD40 dyad (1) but also via OspA:ICAM-1, and this interaction may plays an intrinsic role in borrelial neuroinvasion.

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