

the last 7 days and having no concomitant febrile illness, were included in the study. Patients agreeing with written consent to stay in hospital for 8 days and allowing daily blood slide examination were included and followed up on day 14, 21, and 28. Patients failing to attend for follow-up were visited in their homes. Drug administration was supervised. Clinical and parasitological responses were recorded on a pre-designed scale. The results were analyzed, using the EPI INFO 6 software.

Results: Complete data on 212 patients were available for a mid-term evaluation, of which 8 patients were lost to follow-up. A sensitive clinical response was observed in 22 (17.32%) of the 81 patients in the CQ group, 59 (77.63%) of the 76 patients in the Q3+SP group, and 47 (100%) of the 47 patients in the Q7 group. An early treatment failure was observed only in the CQ group (45.67%), and all the failures with Q3+SP were due to late treatment. The parasitological response was almost similar except that two patients in the Q7 group had asymptomatic parasitaemia on day 28. The groups were comparable in respect of all other variables.

Conclusion: The highly significant difference in sensitivity led to the termination of the trial. If similar sensitivity pattern is observed in other parts of the country, modification of national recommendations would be required. Mefloquine may be considered the second choice of treatment if not the first.

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Molecular Analysis of Toxigenic *Vibrio cholerae* Strains Isolated in Bangladesh During 1961-1996: Relationship Between Continual Emergence of New Toxigenic Clones and Epidemics of Cholera

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Objective: Analyze virulence-associated genes, and study clonal relationships among toxigenic *Vibrio cholerae* strains isolated in Bangladesh during 1961-1996 to establish whether seasonal epidemics are caused by repeated emergence of the same strains or by diverse clones of toxigenic *V. cholerae*.

Methodology: Three hundred seventy-eight *V. cholerae* isolates obtained from cholera patients or from surface water were included in the study. Molecular analysis of virulence-associated gene clusters, including the CTX genetic element, *tcpA*, *tcpI*, and *ToxR* was performed using specific probes or PCR assays. Comparative analysis of serotype-specific *rfb* gene clusters in selected *V. cholerae* O1 and O139 strains was performed by multiple PCR assays using primers corresponding to defined regions of the *rfb* genes. Clonal relationships among strains were studied by computer-assisted numerical analysis of restriction fragment length polymorphisms in conserved rRNA genes. Induction and propagation of the lysogenic bacteriophage-encoding cholera toxin (CTX?) were studied both in animal models and under laboratory conditions.

Results: Analysis of toxigenic *V. cholerae* strains isolated during 1961-1996 revealed clonal diversity among the strains isolated during different epidemics. This study demonstrated the transient appearance and disappearance of more than 6 different clones among classical vibrios, at least 5 clones of El Tor vibrios, and 3 different clones of *V. cholerae* O139. Different clones of strains belonged to different ribotypes and often to different CTX genotypes resulting from differences in the copy number of CTX element and variations in the integration site of CTX in the chromosome. Studies on the induction of lysogenic CTX? revealed that 37.95% of the strains tested could be induced with mitomycin-C to produce infectious extracellular CTX? particles which infected recipient strains under conditions conducive to the expression of *tcp* genes.