Trial from Niger finds village-wide prophylactic antibiotics contained spread of meningitis

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Distribution of single doses of the oral antibiotic ciprofloxacin to residents of rural villages in the African meningitis belt reduced the number of meningitis cases during a 2017 meningitis epidemic, according to a new study in *PLOS Medicine* by Matthew Coldiron and colleagues from Epicentre and Médecins Sans Frontières in France, Switzerland and Niger.

Antibiotic prophylaxis has been used to limit the spread of meningococcal meningitis, mainly in high income countries. This strategy is especially useful for scenarios where vaccines (e.g. *Neisseria meningitidis serogroup C*) or other prophylactic measures are not yet widely available.

In the current cluster-randomized trial, conducted during a meningococcal meningitis outbreak in the Madarounfa District, Niger, villages with detected cases of meningitis were randomly assigned to one of three intervention arms: standard care (control, without prophylactic medication), a single dose of oral ciprofloxacin for household contacts, or village-wide distribution of ciprofloxacin. The investigators compared the number of new cases in each village and household in each of the antibiotic arms to those in the village populations without antibiotic prophylaxis.

Between April and May 2017, 49 villages were included in the trial. A total of 248 meningitis cases were reported in the study. The rate of new meningitis cases was 451 per 100,000 persons in the control arm; 386 per 100,000 persons in the household prophylaxis arm (t-test versus control p=0.68); and 190 per 100,000 persons in the village-wide prophylaxis arm (t-test versus control p=0.032). The ratio of new meningitis cases between the village-wide prophylaxis arm and the control arm was 0.40 (CI [0.19?0.87], p=0.022), and the ratio between the household prophylaxis arm and the control arm was 0.94 (CI [0.52-1.73], p=0.85). One limitation of the study was the small number

of cerebrospinal fluid samples sent for confirmatory testing.

The study results showed that at the end of the epidemic, the number of new meningitis cases was 60% lower in villages receiving village-wide prophylaxis whereas household prophylaxis reduced the rate of subsequent meningitis cases by only a non-significant 6%.

The authors conclude that "the persistence of seasonal meningococcal meningitis epidemics in the African meningitis belt can ultimately be broken only with an effective and affordable conjugate vaccine. In the interim, mass prophylaxis with ciprofloxacin as an epidemic response could be a valuable tool, and should continue to be evaluated."

In a linked Perspective, Keith Klugman and Rasa Izadnegahdar from the Bill and Melinda Gates Foundation in Seattle discuss results of the current trial and consider potential benefits and risks associated with antibiotic chemoprophylaxis on a broader scale in settings where vaccines are not yet available.

More information: Coldiron ME, Assao B, Page A-L, Hitchings MDT, Alcoba G, Ciglenecki I, et al. (2018) Single-dose oral ciprofloxacin prophylaxis as a response to a meningococcal meningitis epidemic in the African meningitis belt: A 3-arm, open-label, cluster-randomized trial. *PLoS Med* 15(6): e1002593. doi.org/10.1371/journal.pmed.1002593

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