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How much is not enough? A Community Randomized trial of a Water and Health Education program for Trachoma and Ocular *C. trachomatis* infection in Niger

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Summary

Objective—To determine the impact after two years of a water and health education (W/HE) program on ocular *C. trachomatis* infection and trachoma.

Methods—We randomized 12 trachoma-endemic communities in Maradi, Niger 1:1 to W/HE intervention and control arms and collected data on 10 of the 12 villages. In the intervention villages, at least one clean water well was constructed, and a three-month, modest health education program was provided immediately prior to the two year survey. We censused all households, and 557 children ages 1 to 5 years were randomly selected as sentinel children and examined at baseline and at one and two years from baseline. Trachoma was clinically assessed and a swab taken and analyzed for *C. trachomatis*. Tetracycline eye ointment was provided to all children in either arm during the surveys who had signs of trachoma.

Results—Infection with *C. trachomatis* declined slightly, and not significantly, in the children in the control villages over the two years, from 15% to 11%. The decline in infection was more pronounced, and significant, in the children in the intervention villages, from 26% to 15%. However, the change in infection rates in the intervention villages was not significantly different from the change in infection rates in the control villages (p=0.39, and 0.11 for change from baseline to one year and two year respectively). There was also no difference in the change in overall trachoma rates between the two arms.

Conclusion—These data suggest that the provision of water plus a modest health education program did not result in a significant difference in trachoma or ocular *C. trachomatis* infection in endemic communities in Niger. A more substantial health education intervention is likely necessary to produce change.

Keywords

trachoma; prevalence; intervention; education; water supply; Niger

Introduction

Trachoma, caused by repeated infections with *C. trachomatis*, is the leading infectious cause of blindness with an estimated 84 million in need of treatment (Mariotti 2004). WHO has a

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target for the global elimination of trachoma by 2020 (WHO 1998) and endorsed the SAFE (Surgery, Antibiotics, Face washing and Environmental change) strategy for trachoma control country programs. The full SAFE strategy is felt to have short and long term action against trachoma, the latter by improved hygiene and environmental change to reduce and interrupt transmission of *C trachomatis*.

Whilst several cross sectional studies have linked lack of facial hygiene and unsanitary environments to trachoma, few clinical trials have been done to demonstrate an impact of changes in these factors on rates of disease or infection (Edwards et al. 2006; Emerson et al. 2004; Ngondi et al. 2006; West et al. 1995,2006). The importance of water availability for improving hygiene and the need for health education to promote water use for hygiene are felt to be key factors for changing hygiene behaviors (Alemu & Bejiga 2004; Bailey et al. 1991; West et al. 1989,1995). However, the impact on infection with *C. trachomatis* of water provision with a health education promotion for improving hygiene has not been demonstrated. Moreover, most programs are constrained by resources to deliver minimal health education input at the community level. It is unclear what a minimal amount of input would be to affect change. In the context of a community randomized clinical trial, we aimed to provide data to address the question of the effects of improved water and a modest health education program on infection with *C. trachomatis* and trachoma.

Methods

Villages and sentinel children

As part of the West African Water initiative World Vision, the implementing partner, has a program for clean water well construction in Maradi, Niger. The intervention villages receive at least one well each first, with the control villages to receive wells after the trial was concluded. We randomly selected (Abdou et al. 2007) 12 villages from the Kornaka West area of Maradi to participate in the trial. In summary, we selected villages between estimated size 600 to 1200 persons, based on the last census before the study in 1995. Of the 18 eligible villages, 12 were randomly selected and randomly allocated to intervention or control arms, using a simple table of random numbers. A baseline census conducted by our research team and survey was carried out in December 2005. Two villages were extreme outliers: one had a small population and a low trachoma rate of 3% of children aged 5 years and younger; the other had a very high rate of 82%. These villages were removed from the trial, one from each arm, as they led to extreme imbalance at the outset (Figure 1).

Within villages, we aimed to randomly select 60 children ages 1 to 5 years as sentinel markers of infection and trachoma. The census data from the house-to house survey that we collected was the basis for selection of children. Stratified random sampling was applied to select no more than one child per mother to minimize clustering of children within households. Of 591 children selected, 557 were examined (94%) at baseline. The same sample of children was surveyed for infection one year (January 2007) and two years (January 2008) later. We had estimated a sample size of 60 children per village or 720 children, to achieve α=.05, β=.80, and to observe an Odds Ratio of 0.5, with a design effect of 1.5, prevalence of infection in children under age five at baseline of 30% and loss to follow up of 15% (Diggle et al. 1994).

Survey

All study personnel were trained in proper techniques for taking and storing ocular swabs, and using new sterile gloves for each participant. Swabs were taken of the right conjunctiva after grading for trachoma, using a Dacron swab which was rotated across the surface three times before being stored, dry, in a labeled vial. All swabs were kept frozen with ice packs,

then shipped, on ice packs, to the International Chlamydia laboratory at Johns Hopkins. Swabs were processed for presence of *Chlamydia trachomatis* using Amplicor™ qualitative PCR (Roche Molecular Systems, Branchburg, New Jersey). Samples were processed according to manufacturer's specifications, with positive and negative controls in each run. For these analyses, "infection" was defined as a positive laboratory result. The laboratory personnel were masked to intervention and control status of the swabs received from the field.

Assessment of Trachoma

Prior to each survey, a training program was conducted to assure that the two trachoma graders were standardized against a senior grader (AA), with reliability of kappa=0.65 for TF and for TI. The trachoma grader, wearing 2.5X loupes, assessed the trachoma status of both eyes, using the WHO Simplified grading scheme (Thylefors et al. 1987) for the presence of follicular trachoma (TF) and trachoma intense (TI). Trachoma is defined as the presence of TF and/or TI. All persons grading trachoma changed gloves between examinations. If the child had TF or TI, the mother was given a tube of tetracycline and instructions on proper use. The trachoma grader was masked to the intervention status of the village they were working in, although we cannot exclude their hearing from village residents.

Intervention

Over the two-year period, World Vision completed constructing at least one hand pump well in each intervention village (average=2.4, range 1–3 wells). All villages at the start of the trial were not far from a source of water, although it was not potable (Abdou et al. 2007). The new wells provided potable water using a hand pump system, which was easy to use and an improvement over the old system of relying on ropes or donkeys pulling ropes to reach water where the water table was deep. The pump returned as much water as could be pumped, while the previous system returned a bucket at a time.

The World Vision Health Education component was not implemented until October 2007, three months before the final survey. A two-day training program for village health workers in the intervention villages took place in the second year, which was general but also included information on flip charts on the spread of trachoma through lack of hygiene and flies. The program emphasized building latrines, and using potable water for drinking, as well as hygiene. A dedicated health educator was assigned to the project three months before the two year survey; however, being male, for cultural reasons he was not allowed to talk directly to young women. He organized one to two village meetings in the intervention villages and talked with all who came about the importance of using a latrine to reduce the number of flies and spread of disease, about environmental sanitation and the importance of controlling garbage, and about washing children's faces to minimise transmission of trachoma. He used flip charts and interactive discussions during the one-to-two-hour meetings. The focus was on the F and E component of SAFE, as no antibiotic was available, and surgery was not part of the program.

Over the same time period, other non-governmental organizations had organized trachoma radio messages over the local radio, which would have been available equally to intervention and control villages although most of the radios were owned by males and batteries were scarce in the villages.

Data Analyses

Differences in baseline characteristics between children in the intervention and control arm of the study were tested for statistical significance using logistic regression models adjusted

for age. To account for clustering at village level, standard errors were corrected using the GEE approach.

The pre-specified outcomes were infection with *C. trachomatis* and active trachoma. The prevalence of active trachoma and *C. trachomatis* infection and corresponding 95% confidence intervals are presented for baseline, one year, and two years. Confidence intervals were calculated accounting for the correlation-relevant outcome within children from the same village (GEE approach). For each arm, the McNemar's test for correlated proportions was used to compare changes in disease/infection status in children between baseline and 2 years.

To test for the effect of the intervention over time on infection, models of the following form were constructed:

$$Log\frac{\Pr(Y_{it}=1)}{\Pr(Y_{it}=0)}=\beta_0+\beta_1 x_i+\beta_{21}1(t=1)+\beta_{22}1(t=2)+\beta_{31}1(t=1)x_i+\beta_{32}1(t=2)x_i+\gamma z_{it}$$

Where, Y_{it} = indicator variable for presence infection of the i^{th} child at time t (0,1,2); x_i = indicator variable for the intervention assignment for the i^{th}, t period of observation (0,1,2); and z_{it} additional covariates which can be time dependent. β_1 quantifies the difference in infection rates at baseline between intervention and control; β_{21} and β_{22} the effect of time for years 1 and 2 respectively; β_{31} the additional effect of the intervention at year 1; and β_{32} the additional effect of the intervention at year 2. To account for the within-person serial correlation, standard errors are corrected using the Generalized Estimation Equation approach.

All procedures and protocols were approved by the Johns Hopkins University Institutional Review Board, and the Niger national Ethical Review Committee of the Ministry of Health. The trial is registered at clincialtrials.gov (#NCT00348478).

Results

The study populations in the two arms were mostly similar. The overall baseline prevalences of trachoma were similar in the intervention (43%) and control arms (40%, p=0.75). However, the prevalence of infection with *C. trachomatis* at baseline was 26% in the intervention villages and 14% in the control villages, significantly different (p=0.02) (Table 1). There was no difference by intervention arm in the proportion of female sentinel children, the number of children in the compound younger than 8 years, time to walk and wait to get water, or the size of the village (Table 1). However, there was imbalance in the ages of the sentinel children, with more 1–2 year-olds in the control villages, and more 3–4 year-olds in the intervention villages. The children in the intervention villages were also more likely to live in a compound with waste inside, 70%, compared to children in the control villages, 51% (Table 1).

At one year, we re-surveyed 91% of the original sample (91% in intervention and 91% in the control villages). At two years, we re-surveyed 89% of the original sample (89% in the intervention and 88% in the control villages). The primary reason for loss to follow-up at both times was death of the child or child having left the village.

The change in prevalence of infection over time in the intervention and control arms is shown in Table 2. Infection declined among the children in the intervention villages, and there was a significant change from baseline values (26% to 15%, p<0.001, McNemar's test). Infection declined in the children in the control villages as well, however, the

difference in prevalence between the two arms at two years was not statistically significant (p=0.15). Although the decline of infection appeared greater in the children living in the intervention villages, in a model predicting infection over time, adjusting for baseline status, age and gender, at year 1 and 2 the additional effect of the intervention on reduction of infection was not significant at either time point (p=0.39, and 0.11 respectively) (Table 3).

The prevalence of trachoma in the two arms increased from baseline to two years, with no difference in either the prevalence of trachoma at two years between children in the intervention villages versus the control villages, or in the change of prevalence over time (Table 2).

Discussion

Our study failed to demonstrate a significant impact on infection with *C. trachomatis* or trachoma in children after a water and modest health education program in trachoma endemic villages in Niger. The estimate of the odds show a modest reduction in infection in children living in the intervention villages, which was not statistically significant. There was no difference, in fact an increase, in the prevalence rates of trachoma.

Previous research has shown that trachoma is endemic in communities characterized by lack of water and long distances to fetch water for household use (West et al. 1989). While water availability *per se* does not have a direct biological effect on trachoma or infection, it is likely that transmission of infected ocular secretions is facilitated where lack of water inhibits water use for personal hygiene. We and others have noted previously that just improving access to water without behavior change programs to improve water use for hygiene is unlikely to have an impact on trachoma (Alemu & Bejiga 2004; Bailey et al. 1991; West et al. 1989). Others have also reported that allocation of water to hygiene is the key factor for reducing trachoma rates in households (Polack et al. 2006).

Our data suggest that water provision with only a modest trachoma health education campaign at the village level (training of village health workers, radio program, and 1–2 village meetings) was insufficient to affect our trachoma outcomes. This finding is compatible with provision of water alone having little impact on disease. First, it should be noted that we observed at baseline that most households reported a relatively short time to walk to water and wait to access water (Abdou et al. 2007). 75% of women reported it was less than 30 minutes, and there were no differences between intervention and control households. However, this measure is only a surrogate for access to water, and the provision of pumped water has distinct advantages over hauling water from a deep water table with ropes. Nevertheless, we expected that any differences in infection or trachoma would largely rest on the impact of the health education program to improve use of water for cleaning faces.

However, there are no data on the approach that is ideal for such a program, the timing and length of time for such a program, and when trachoma or infection would decline. The health education program implemented by World Vision in this project was very modest, and not very long (three months immediately prior to the year two survey). The dedicated Health Educator during this time was male, and culturally unable to meet one-to-one with young women, or even groups of women, so we presume uncertain penetration to the mothers in the villages. This approach, plus training of village health workers in general principles of trachoma control and a national radio program, was not sufficient to have an impact. In our previous study in Tanzania, the intervention was community-based, using a participatory approach, and intensive for three months in each village, with monthly follow up for ten months, including building support among the school teachers and local healers

(Lynch et al. 1994). At one year, the proportion of children with sustained clean faces doubled (100% improvement) in the intervention villages, to 35% overall, compared to a 37% improvement in the control villages (26% overall) (West et al. 1995). The higher rate of clean faces in the children in the intervention villages was observed over the 10 month period as well. In that study at one year, the percentage of children with clean faces and sustained clean faces increased significantly in the intervention villages; the odds of any trachoma were 23% higher and the odds of severe trachoma were 60% higher in the control villages than in the intervention villages. Perhaps a program needs to be more intensive, and to result in the proportion of clean faces for a longer period of time, than we observed in Niger, to have an impact.

In a cross-sectional study following three years of implementation of A, F, and E in Sudan, Ngondi and colleagues (2006) reported independent effects of three rounds of azithromycin, a clean face, reported washing faces of children 3 or more times per day, and use of a pit latrine. In that study, 62% of children had a clean face at the time of examination. However, there were huge differences in districts by trachoma status, such that most of the data were contributed by one district. There were also profound differences by whether anyone had had at least one dose of azithromycin, which leads to a dramatic reduction in TI. Thus, it is difficult, even with multiple adjustment, to determine the contribution of the hygiene program.

In Ethiopia, a cluster randomized trial was carried out with radio messages on hygiene and environmental improvements in all areas, activities (non specified) by non-governmental organization partners (Orbis International and World Vision) in ¾ of the areas, and village level videos in vans to further promote health education in ¼ of the areas (Edwards et al. 2006). The investigators found a small reduction in active trachoma (8%) across all three arms of the trial at one year, with no difference between the arms, and no difference in clean faces from baseline to follow up. It is not clear what intervention was actually done in the communities, or that trachoma was assessed masked to intervention status, and infection was not assessed, but in any case no differences were observed.

We observed that infection rates were declining in these Nigerien villages. Children with trachoma during the surveys were given topical tetracycline, which may have had some effect in reducing the burden of infection. This was given out equally to children in intervention and control villages, which had equal rates of disease at baseline, so should not have affected the villages differentially. The provision of topical tetracycline clearly had no impact on clinical disease.

Despite randomizing villages, and achieving balance in trachoma rates and village size, we had small but statistically significant differences in baseline prevalence of *C. trachomatis* in the children in the intervention versus the control villages. This imbalance creates difficulties in analyzing changes over time, as adjustment for baseline prevalences is then critical. If a model only evaluates the difference in outcome at two years, it misses the rate of change from baseline. It is not clear why, when trachoma rates were similar, the differences in infection were significantly different at baseline. There were no differences in positivity rate by study team, and both teams worked in the intervention and control villages, so it is unlikely that the differences were due to technical reasons. At baseline, two of the five control villages had low infection rates, 7%, compared to the prevalence of trachoma, 40% and 54%, suggesting in these villages trachoma was declining but the clinical signs had not yet waned(Abdou et al. 2007). This may have contributed to the disparity in infection at baseline.

We were underpowered to detect differences as subtle as OR=0.79 in our sample. We expected more infection in these children, based on the trachoma rates, and a larger difference at two years, based on our original face washing trial, of OR=0.5. We also planned to enroll 6 villages, but two of the villages clearly were outliers after the trachoma assessment and had to be excluded.

The strengths of the study lie in the high rate of follow up, and the use of infection as our primary outcome, as it was masked to intervention status. The internal consistency of our data in the expected direction was also notable; some evidence for reduction of infection, although again not different from the children in the control villages.

How much is not enough? Our data suggest that accessibility to water, accompanied by a modest health education intervention (two day training of village health workers and 1 to 2 village level meetings prior to the final assessment) was not sufficient to change trachoma or infection with ocular *chlamydia trachomatis* over a two year period. However, we cannot rule out a different outcome if the educational component had occurred earlier and/or been more intensively targeted towards mothers of children. Other studies suggest that higher rates of clean faces, and for a longer period of time, may be more effective; future trials would be useful.

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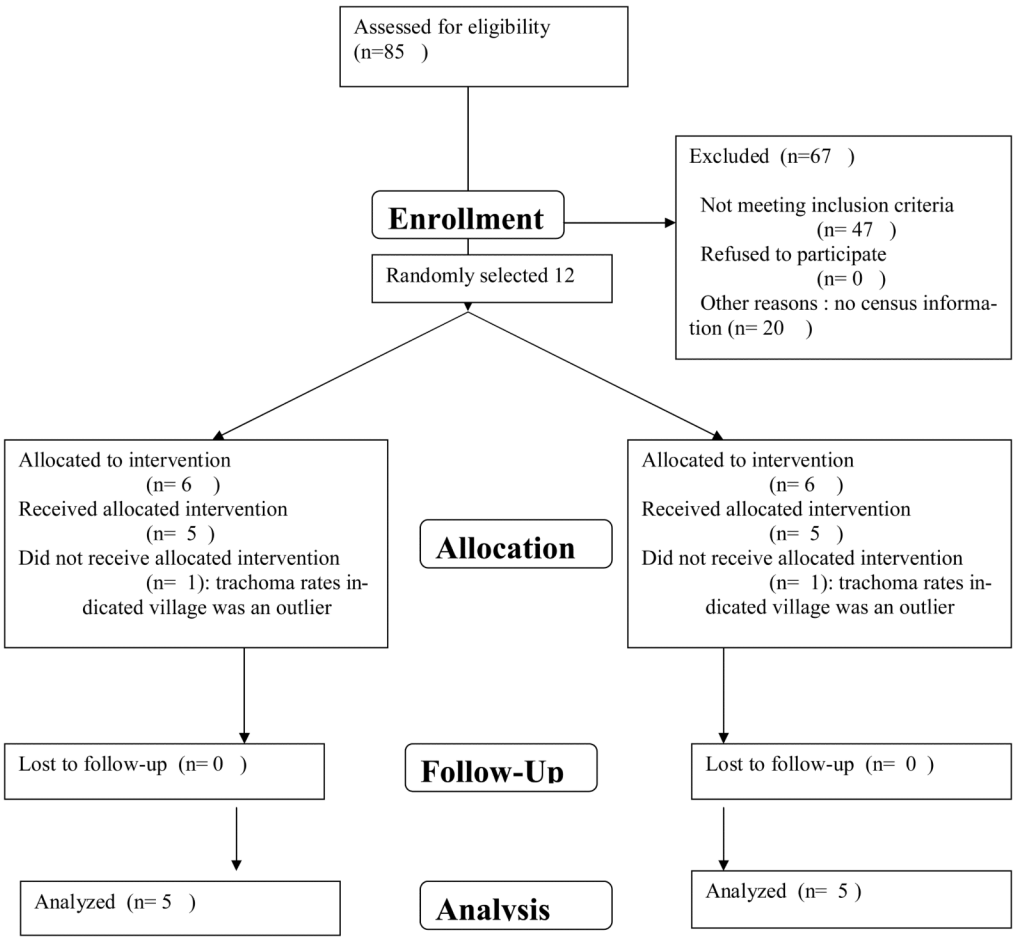

Figure 1.
Flowchart of Villages

Table 1

Baseline Characteristics of children by residence in Intervention or Control village

Characteristic	Intervention N (%) (n=284)	Control N (%) (n=273)	P-value
C. trachomatis infection	73 (26%)	39 (14%)	0.02**
Trachoma[1]	123 (43%)	109 (40%)	0.75**
Age in years			
1	33 (11.6)	60 (22.0)	
2	52 (18.3)	71 (26)	0.01*
3	78 (27.5)	42 (15.4)	
4	68 (23.9)	51 (18.7)	
5	53 (18.7)	49 (17.9)	
Gender			
Male	148 (52.1)	135 (49.4)	0.44**
Female	136 (47.9)	138 (50.6)	
Sib ship size			
% children with 1–3 siblings age <8 years	76 (26.8)	91 (33.3)	0.75**
% children with 4–5 siblings age <8 years	78 (27.5)	54 (19.8)	
% children > 5 siblings age <8 years	130 (45.8)	128 (46.9)	
Proportion of children living in compound where Garbage was observed within	198 (69.7)	136 (50.6)	0.01**
Proportion of children living in compound where time to walk and wait for water was more than 30 minutes	65 (22.9)	82 (30.5)	0.34**
Proportion of children living in villages of size less than 650 persons.	170 (59.9)	167 (61.2)	

* adjusted for Cluster at the village level;

** adjusted for Age, and cluster at village level

[1] Defined as follicular trachoma (TF) and/or inflammatory trachoma (TI)

Table 2

Prevalence of trachoma and *C. trachomatis* infection over time in the cohort of children selected at baseline, by intervention arm

Arm	Outcome	Baseline	One year	Two years
Control	Active Trachoma* (95% CI)**	39.9 (28.4–52.7)	34.2 (29.4–39.6)	49.4 (38.3–60.6)
	Infection (95% CI)	14.4 (8.6–23.3)	13.2 (8.6–19.7)	10.9 (8.2–14.5)
Intervention	Active Trachoma* (95% CI)	43.3 (33.5–53.6)	39.0 (32.8–45.5)	54.3 (44.0–64.3)
	% Infection* (95% CI)	25.7 (23.7–27.8)	20.1 (13.8–28.5)	14.7 (8.9–23.3)

* per 100 children

** Confidence intervals account for the correlation of active trachoma/infection within children from the same village

Table 3

Multiple logistic regression model of Predictors of Infection in children with *C. trachomatis* over two years time

Characteristic	Odds Ratio (95% Confidence Interval)	p-value
Age (per year)	1.17 (1.02–1.34)	
Male	1.00	
Female	1.17 (0.83–1.65)	
Intervention at baseline/Control at baseline	1.97 (1.28–3.04)	
Intervention at year 1/Control at year 1	1.59 (0.59–4.28)	
Additional effect of the intervention at 1 year	0.81 (0.50–1.31)	0.39*
Intervention at year 2/Control at year 2	1.07 (0.39–2.96)	
Additional effect of the intervention at 2 years	0.62 (0.34–1.12)	0.11*

*Effect of the intervention (corresponding to the interaction of time and intervention, comparing 1.97 vs. 1.59, and 1.97 vs. 1.07, for years 1 and 2 respectively)

Standard errors adjusted to account for the within person serial correlation using the GEE approach