

THE EFFECT OF ANTIBACTERIAL SOAP ON IMPETIGO INCIDENCE, KARACHI, PAKISTAN

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Abstract. We conducted a study to determine if soap containing 1.2% triclocarban would be effective in reducing the incidence of impetigo. We randomized 162 households in a low-income neighborhood of Karachi, Pakistan, to receive a regular supply of 1.2% triclocarban-containing soap ($n = 81$) or an identically appearing placebo ($n = 81$); 79 households in a nearby neighborhood were enrolled as standard practice controls. After adjustment for household clustering and covariates, the incidence of impetigo among children living in households receiving triclocarban-containing soap (1.10 episodes per 100 person-weeks) was 23% lower than in households receiving placebo soap ($P = 0.28$) and 43% lower than the standard habit and practice controls ($P = 0.02$). The routine use of triclocarban-containing soap by children living in a community with a high incidence of impetigo was associated with a reduced incidence of impetigo.

BACKGROUND

Impetigo is a common condition, particularly in settings with high ambient temperature, high humidity, and poor hygiene.¹ This disease burden translates into health care costs. In the Sindh province of Pakistan, 4% of all diagnoses in government primary health care centers were for skin infection.² Impetigo from nephritogenic streptococci also can lead to acute renal failure from poststreptococcal glomerulonephritis, which in a small percentage of affected patients progresses to chronic renal failure.³

Studies evaluating the effectiveness of antibacterial soap in preventing impetigo and other skin infections produced mixed results. In 2 studies, military recruits in the United States who used older formulations of commercially available antibacterial soap had 44% fewer superficial skin infections compared with recruits who used nonmedicated placebo soap.^{4,5} The most common organism isolated from lesions was *Staphylococcus aureus*.⁴ Despite widespread use of antibacterial soaps among U.S. troops serving in Vietnam, however, rampant impetigo infections contributed to lost man-days. The primary pathogens among U.S. servicemen in Vietnam were *Streptococcus pyogenes*.⁶ Subsequent studies in settings where *Streptococcus* was the primary organism cultured from skin lesions, including a boarding school in Arizona⁶ and 2 rural villages in South Trinidad,⁷ did not show any protective benefit from washing with medicated soap. The one successful impetigo prevention intervention in a developing country was conducted among 304 schoolchildren in Costa Rica. The children were stripped to their underwear and sprayed 5 times a week with 2% chlorhexidine or placebo for the next 6 weeks. Children receiving chlorhexidine had 61% fewer skin infections than children receiving placebo.⁶

The predominate conceptualization that emerged from these studies was that antibacterial soap was most effective against *Staphylococcus* but that *Streptococcus* was likely responsible for the largest burden of impetigo, especially in tropical countries, where impetigo is most common. These prior studies were conducted in extreme conditions—servicemen in military barracks with close supervision of showering or schoolchildren who were stripped and sprayed by adults. We conducted a study to determine if a currently marketed antibacterial soap would be effective in reducing

impetigo when used regularly in a hot environment where impetigo was common.

MATERIALS AND METHODS

Setting. Karachi is the largest city in Pakistan, with an estimated population of 11 million. Of Karachi residents, 40% live in squatter settlements, where water and sanitary infrastructure are limited.⁸ This study was conducted in adjoining multiethnic squatter settlements in central Karachi, Manzoor Colony and Mujahid Colony, in collaboration with Health Oriented Preventive Education (HOPE), a nongovernmental organization that provides community-based primary health care in these communities. Children in these communities routinely wash their skin daily using a “bucket bath.” They remove their clothing, take 1 or 2 cups of water, pour it over their head and skin, lather with soap, and use another 1 or 2 cups of water to rinse off.

Interventions. A medicated bar soap, Safeguard*, which contains 1.2% triclocarban as an antibacterial agent, was provided by Procter & Gamble Company. Placebo bar soap also was provided by Procter & Gamble Company. The placebo soap was identical to Safeguard with the single exception that it did not contain 1.2% triclocarban. The soaps were packaged identically and identified by serial numbers. Participants and the field workers were blinded to the triclocarban content of the soap.

Design. The study was conducted in 2 different neighborhoods, separated by 5 km. Households in Mujahid Colony were randomized to receive a regular supply of either triclocarban-containing soap or placebo soap. Participants were instructed to continue their regular routine of bathing and hand washing but to substitute their usual soap with the study soap. The standard habits and practices control group consisted of households from Mansoor Colony, who received a regular supply of children’s books, notebooks, pens, and pencils to help with their children’s education but no products

* Inclusion of trade names is for identification only and does not imply endorsement by Centers for Disease Control and Prevention or the Department of Health and Human Services.

that would be expected to affect their rate of impetigo. The study included an additional group of households who received a water vessel and chlorine bleach for disinfecting drinking water, an intervention designed to reduce diarrhea. These results were collected over a 12-month period and will be reported later.

Eligibility. Eligible households were located in Manzoor Colony or Mujahid Colony, provided informed consent, had at least 1 child < 5 years old and 2 children < 15 years old living in the household, had sufficient water supply for the children to bathe daily, and planned to continue to reside in their homes for the duration of the study.

Measurements. Trained field workers conducted a preintervention baseline survey identifying hand-washing and bathing practices, soap use, and drinking water storage and purification practices. Field workers distributed the interventions and visited participating households each week for 6 months from May 1 to October 31, 2000. The field workers identified lesions consistent with impetigo among children < 15 years old living in the household. A study physician visited each of the households to confirm the diagnosis of impetigo and referred the family to locally available health care services.

An episode of impetigo was defined as a new skin eruption, confirmed by the study physician to be impetigo. The study subject again could be a candidate for a new episode of impetigo only after the diagnosed episode of impetigo was noted to be cleared by the community health worker on one of the weekly visits.

We defined primary cases as cases occurring in households with no impetigo in the preceding week. Secondary cases were cases of impetigo occurring in households with impetigo in the preceding week. We further subdivided primary cases into solo primary cases and coprimary cases. We defined solo primary cases as cases occurring in households with no impetigo in the preceding week and the identified case was a single new case in the household. We defined coprimary cases as cases occurring in a household with no impetigo in the preceding week but that had ≥ 2 cases develop impetigo in the household during the same week.

Statistics. The primary outcome was the incidence density of impetigo (i.e., the number of episodes of impetigo/person-weeks of observation). We calculated a sample size of 75 households per intervention group, assuming 2.6 episodes of impetigo per 100 person-weeks in the standard habits control group, 25% efficacy of nonmedicated soap in reducing impetigo, 50% efficacy of antibacterial soap in reducing impetigo,

3 children per household, and a 20% loss of power because of clustering of impetigo in households.

We calculated a crude incidence density ratio, comparing the incidence density of impetigo in each intervention group. We next accounted for the possible effects of repeated measurements of single individuals and clustering within households using generalized estimating equations. We assumed an exchangeable correlation structure to estimate serial association between measurements for a single individual and within-household disease transmission and produced adjusted incidence rates, incidence density ratios, 95% confidence limits, and *P* values. We also conducted a survival analysis of time to the first episode of impetigo of each child and a survival analysis of multiple events (i.e., repeat occurrences of impetigo for each child). Both analyses accounted for clustering within households.

Ethics. Community leaders and heads of households provided informed consent. The study protocol was approved by the Ethics Review Committee of the Aga Khan University and an institutional review board of the Centers for Disease Control and Prevention.

RESULTS

Impetigo incidence. We enrolled 241 households; 81 received soap with triclocarban; 81 received placebo soap, and 79 were controls. The 3 groups were similar at baseline (Table 1). There were 319 episodes of impetigo during the 20,364 person-weeks of observation (1.57 episodes per 100 person-weeks). Impetigo incidence peaked in July (Figure 1) and was more common among younger children (Figure 2).

The crude incidence of impetigo among children living in households receiving soap with triclocarban was 30% lower than the incidence in households receiving placebo soap (1.10 versus 1.58 episodes per 100 person-weeks) (Table 2). When these rates were adjusted for clustering within households and significant covariates, including age, father's literacy, and number of persons in the household, the incidence density in households receiving soap with triclocarban was 23% lower than in households receiving placebo soap. This difference in adjusted rates between these 2 groups was not statistically significant (*P* = 0.28) (Table 3).

The incidence of impetigo among children living in households receiving soap with triclocarban was 47% lower than the incidence in the standard habit and practices control households (2.07 episodes per 100 person-weeks). When these rates were adjusted for clustering within households and

TABLE 1
Baseline household characteristics by group, Karachi, Pakistan, 2000

	Soap with triclocarban (n = 81)	Placebo soap (n = 81)	Control (n = 79)	<i>P</i> value
Mean				
Persons per household	7.9	8.4	8.0	0.47
Age of children (y) %	6.1	6.4	5.9	0.34
Study children < 5 years old	48	46	51	0.53
Households owning a refrigerator	44	32	37	0.26
Maternal literacy	37	39	49	0.28
Paternal literacy	72	68	68	0.86
Household income > 4,000 rupees/mo	26	23	33	0.34
Households that bought soap in the 2 wk before the study	65	63	52	0.18

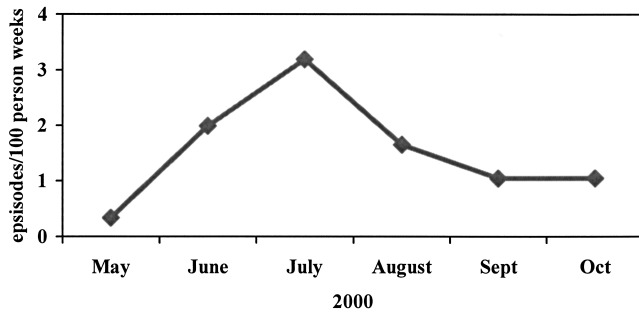


FIGURE 1. Incidence of impetigo by month, Karachi 2000.

significant covariates, including age, father's literacy, and number of persons in the household, the incidence density of impetigo in households receiving soap with triclocarban was 43% lower than in control households. The difference in adjusted rates between these 2 groups was greater than would be expected by chance ($P = 0.02$) (Table 3).

The incidence of impetigo among children living in households receiving placebo soap was 24% lower than the incidence in control households (1.58 versus 2.07 episodes per 100 person-weeks). When these rates were adjusted for clustering within households and significant covariates, including age, father's literacy, and number of persons in the household, the incidence density in households receiving placebo soap was 25% lower than in control households. This difference in adjusted rates between these 2 groups was not statistically significant ($P = 0.21$) (Table 3).

Most impetigo cases (76%; $n = 241$) were primary cases; 24% ($n = 78$) were secondary cases. Of all impetigo cases, 52% ($n = 166$) were solo primary cases; 24% ($n = 75$) were coprimary cases. Coprimary impetigo occurred 64% less frequently among children living in households receiving soap with triclocarban than in households receiving placebo soap (0.18 versus 0.50 episodes per 100 person-weeks) (Table 2). When these rates were adjusted for clustering within households and the only significant covariate, refrigerator ownership, the incidence density in households receiving soap with triclocarban was 59% lower than in households receiving placebo soap. This difference was of borderline statistical significance ($P = 0.09$) (Table 3).

Duration of impetigo. Impetigo episodes that occurred among children receiving soap with triclocarban lasted a mean of 1.89 weeks versus a mean of 1.99 weeks among chil-

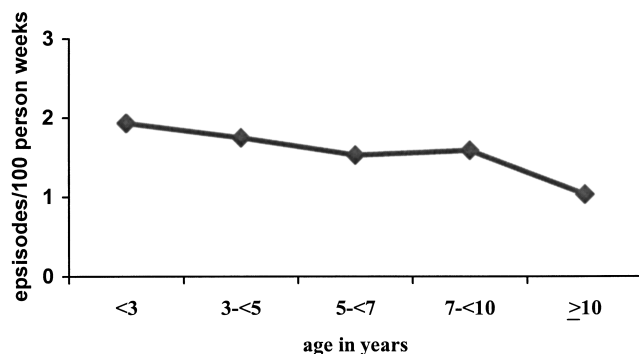


FIGURE 2. Impetigo incidence by age group among children age 0 to 15 years, Karachi, 2000.

dren receiving placebo soap and 2.59 weeks among control children. The difference in episode duration between soap with triclocarban and placebo was no greater than would be expected by chance ($P = 0.68$), but the difference in duration between soap with triclocarban and control ($P = 0.01$) and between placebo and control ($P = 0.04$) were both greater than would be expected by chance.

Households as unit of analysis. Using households as a unit of analysis, the incidence of impetigo was 3.3 per 100 household weeks among soap with triclocarban households, 4.1 among placebo soap households, and 4.7 among control households. There was a 20% reduction in impetigo in the soap with triclocarban versus placebo soap households (incidence density ratio, 0.80; 95% confidence interval, 0.57 to 1.13; $P = 0.21$) and a 30% reduction in impetigo in the antibacterial soap households versus control (incidence density ratio, 0.70; 95% confidence interval, 0.50 to 0.98; $P = 0.04$).

Survival analysis. In the time to first episode of impetigo survival analysis, age was the only covariate significantly associated with impetigo. When controlled for age, the hazard ratio for soap with triclocarban versus placebo soap was 0.78 ($P = 0.28$); for triclocarban soap versus control, 0.56 ($P = 0.008$); and for placebo soap versus control, 0.71 ($P = 0.13$). In the survival analysis for multiple events, age and father's literacy were the only covariates significantly associated with impetigo. When controlled for age and father's literacy, the hazard ratio for soap with triclocarban versus placebo was 0.71 ($P = 0.16$); for antibacterial soap versus control, 0.60 ($P = 0.03$); and for placebo soap versus control, 0.84 ($P = 0.45$).

DISCUSSION

Children living in squatter settlements in Karachi who received a regular supply of soap with triclocarban and encouragement to use it as part of their regular daily bathing developed impetigo 47% less frequently than control children who did not receive supplemental soap and encouragement. This difference was greater than would be expected by chance and was consistent across several methods of analysis.

The study suggests that including 1.2% triclocarban in soap contributed to the reduction in impetigo incidence. Children living in households that received soap with triclocarban had crude and adjusted rates of impetigo lower than children who received placebo soap. Chance could not be excluded confidently as the explanation for these differences, but the differences were persistent across many methods of analysis. Although the difference in incidence between children receiving soap with triclocarban versus control was consistently statistically significant, the difference between children receiving placebo soap versus control was not. Children living in households who received triclocarban-containing soap had 64% fewer episodes of coprimary impetigo than persons receiving placebo soap. This difference was of borderline statistical significance ($P = 0.09$).

Impetigo develops in children who first are colonized with an organism capable of causing impetigo, who then suffer minor trauma (e.g., insect bites or abrasions), which allows the organism to gain access beneath the epidermis and cause infection.^{6,9} Triclocarban is deposited on the skin after washing with a triclocarban-containing soap.¹⁰ The likely mecha-

TABLE 2
Incidence of impetigo by study group, Karachi, Pakistan, 2000

	Soap with triclocarban	Placebo soap	Control
Total impetigo episodes	79	107	133
Person-weeks of observation	7,161	6,784	6,419
Crude incidence per 100 person-weeks	1.10	1.58	2.07
Adjusted* incidence per 100 person-weeks	1.02	1.47	1.95
Primary impetigo episodes	63	89	89
Person-weeks of observation	6,726	6,349	5,704
Incidence per 100 person-weeks	0.94	1.40	1.56
Adjusted* incidence per 100 person-weeks	0.94	1.42	1.59
Secondary impetigo episodes	16	18	44
Person-weeks of observation	435	435	715
Incidence per 100 person-weeks	3.68	4.14	6.15
Adjusted* incidence per 100 person-weeks	2.15	3.08	4.91
Solo primary impetigo episodes	51	57	58
Person-weeks of observation	6,726	6,349	5,704
Incidence per 100 person-weeks	0.76	0.90	1.02
Adjusted* incidence per 100 person-weeks	0.76	0.90	1.02
Coprimary impetigo episodes	12	32	31
Person-weeks of observation	6,726	6,349	5,704
Incidence per 100 person-weeks	0.18	0.50	0.54
Adjusted* incidence per 100 person-weeks	0.18	0.48	0.53

* Adjusted for clustering within households.

nism of activity of triclocarban is that children who regularly use soap containing triclocarban are more resistant to colonization with organisms that are prone to cause impetigo. If a person who was actively shedding an impetiginous strain of *S. aureus* visited a household, children having sufficient triclocarban on their skin might resist colonization. With this lower rate of colonization, multiple simultaneous episodes of impetigo (i.e., coprimary episodes) would be relatively uncommon.

Studies from the 1970s suggested that most impetigo in warm environments was due to *Streptococcus* that was not prevented with available antibacterial soaps.^{6,7} Why might soap with triclocarban have been effective in preventing im-

petigo in Karachi in 2000? Possibilities are that *Staphylococcus* was a significant contributor to impetigo in Karachi, as has been noted in some settings,^{4,5} and that 1.2% triclocarban prevented colonization with impetiginous *Staphylococcus*. Another possibility is that *Streptococcus* was the primary pathogen but that the formulation of soap used in 2000, which contained a higher concentration of triclocarban than soap evaluated in prior studies, was sufficiently different that it prevented colonization with impetiginous strains of *Streptococcus*. Although the minimum inhibitory concentration of triclocarban is lower against *Staphylococcus*, triclocarban is active against *Streptococcus in vitro*.^{11,12} Another possibility is

TABLE 3
Comparison of adjusted impetigo incidence rates by intervention groups, Karachi, Pakistan, 2000

	Soap with triclocarban versus placebo soap	Soap with triclocarban versus control	Placebo soap versus control
Total impetigo episodes			
Adjusted incidence density ratio*	0.77	0.57	0.75
95% confidence limits	0.48–1.24	0.36–0.92	0.47–1.18
P value	0.28	0.02	0.21
Primary impetigo episodes			
Adjusted incidence density ratio*	0.70	0.64	0.91
95% confidence limits	0.44–1.12	0.41–1.00	0.58–1.42
P value	0.14	0.05	0.67
Secondary impetigo episodes			
Adjusted incidence density ratio [†]	0.70	0.44	0.63
95% confidence limits	0.25–2.00	0.16–1.19	0.28–1.42
P value	0.50	0.10	0.26
Solo primary impetigo episodes			
Adjusted incidence density ratio [‡]	0.94	0.82	0.88
95% confidence limits	0.60–1.47	0.54–1.26	0.57–1.35
P value	0.78	0.37	0.55
Coprimary impetigo episodes			
Adjusted incidence density ratio [§]	0.41	0.36	0.89
95% confidence limits	0.15–1.14	0.14–0.93	0.39–2.05
P value	0.09	0.03	0.79

* Adjusted for clustering within households and significant covariates, including age, father's literacy, and number of persons in the household.

[†] Adjusted for clustering within households. No covariates were significantly associated.

[‡] Adjusted for clustering within households and significant covariates, including age, father's literacy, number of persons in the household, and number of children in the household.

[§] Adjusted for clustering within households and 1 significant covariate: refrigerator ownership.

methodologic differences between studies. In Karachi, the incidence of impetigo was considerably higher than in the Arizona boarding school.⁶ In Trinidad, point prevalence of impetigo was > 30%, and weekly point prevalence was the major outcome.⁷ In Karachi, we evaluated incident cases and found the greatest difference between groups receiving medicated and nonmedicated soap was in prevention of coprimary episodes, a difference that a prevalence-based analysis could not evaluate. In Trinidad, the prevalence of impetigo when persons were using medicated soap was lower than when these same persons were using nonmedicated soap, but different soaps were used during different months, and the differences in prevalence were not statistically significant.

Impetigo does not cause the same degree of severe morbidity and mortality that diarrhea, a different disease that washing with soap can interrupt, causes in these and similar communities. Even in this exceptionally dry year, however, impetigo was remarkably common—319 episodes in 241 households in one summer. Mothers in the community were keenly interested in preventing the morbidity and temporary disfigurement of impetigo in their children. If the findings from this study are confirmed, communicating the benefit of preventing impetigo may be an effective way to encourage more skin and hand washing in these communities, which in turn may reduce the incidence and mortality from diarrhea.

There are 2 principal limitations to these data. First, there were an insufficient number of events to evaluate the primary comparison of impetigo incidence in the soap with triclocarban versus the placebo group. During the study, Karachi experienced its driest summer in 30 years. The incidence of impetigo was 40% lower in the control group than we had predicted based on a pilot study during the summer of 1998 that had normal rainfall. A further problem with statistical power was that we had increased the targeted sample size by 20% to account for the loss of power from clustering, but the data showed a higher level of clustering than we anticipated. The design effect was 1.69, suggesting that a 70% increase in sample size would have been more appropriate.

The second limitation to the study is that the standard habits and practices control group, which received no soap, was separated geographically from the groups receiving soap. Differences between the standard habits control group and the soap groups may be a result of differences between the communities. We considered the risk factors that are known to be associated with impetigo. Humidity and season were identical, and the level of literacy, income, and material possessions was similar across the groups. Multivariate analyses that adjusted for these potential confounding variables suggested that the disease experience was related to the intervention group and not to these differences between communities.

Despite these similarities, it remains possible that the exposure to impetigo pathogens was not sufficiently uniform across these similar neighborhoods for a valid comparison. It is possible that each season impetigo concentrates in certain high-risk neighborhoods and avoids others high-risk neighborhoods. There may have been several focal outbreaks of impetigo in the standard habits and practices neighborhood, but because of different population mixing patterns, different rates of unnoticed minor trauma, or some other unmeasured difference, the disease never spread to the soap intervention neighborhoods. We do not have specific evidence of these phenomena, but there was enough geographic separation be-

tween the neighborhoods that identical exposure between the 2 neighborhoods cannot be ensured.

The prior study in Costa Rica schoolchildren who were sprayed 5 times a week with 2% chlorhexidine showed that consistent application of an agent with activity against gram-positive organisms can reduce endemic impetigo.⁶ The present study suggests that routine use of a commercially available soap containing 1.2% triclocarban also may reduce the incidence of impetigo. Additional studies would be useful to define the relative contribution of increased body washing with soap and specific antibacterial compounds in preventing impetigo.

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