Natural Course of Cutaneous Warts Among Primary Schoolchildren: A Prospective Cohort Study

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ABSTRACT

PURPOSE Because cutaneous warts resolve spontaneously and available treatments often fail, family physicians and patients may consider a wait-and-see policy. We examined the natural course of cutaneous warts and treatment decisions in a prospective observational cohort of primary schoolchildren.

METHODS We inspected the hands and feet of children aged 4 to 12 years from 3 Dutch primary schools for the presence of warts at baseline and after a mean follow-up of 15 months. Parental questionnaires at follow-up provided information on inconvenience caused by warts and any treatments used.

RESULTS Of the 1,134 eligible children, 1,099 (97%) participated, of whom 366 (33%) had cutaneous warts at baseline. Among these children with warts, loss to follow-up was 9% and the response rate to the parental questionnaires was 83%. The complete resolution rate was 52 per 100 person-years at risk (95% CI, 44-60). Younger age (hazard ratio = 1.1 per year decrease; 95% CI, 1.0-1.2) and non-Caucasian skin type (hazard ratio = 2.0; 95% CI, 1.3-2.9) increased the likelihood of resolution. During follow-up, 38% of children with warts at baseline treated their warts: 18% used over-the-counter treatment only, 15% used a family physician–provided treatment only, and 5% used both. Children were more likely to initiate treatment if the warts measured at least 1 cm in diameter (odds ratio = 3.2; 95% CI, 1.9-5.3) and especially if parents reported that the warts caused inconvenience (odds ratio = 38; 95% CI, 16-90).

CONCLUSIONS One-half of primary schoolchildren with warts will be free of warts within 1 year. Young age and non-Caucasian skin type enhance resolution. Children with large or inconvenient warts are more likely to start treatment. These findings will be useful in the process of shared decision making with parents and children.

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INTRODUCTION

Cutaneous warts are caused by the human papillomavirus. Small defects of the skin are sufficient to allow the virus to infect the basal layer of the skin, which may lead to benign hyperkeratotic papillomas.[1] Warts are very common in the general population, especially among children. The prevalence of warts among primary schoolchildren is reported to be 22% to 33%,[2,3] while the annual prevalence based on consultations in general practice is about 6%.[4,5] This difference in rates indicates that only a proportion of children seek medical advice or treatment for warts.

Liquid nitrogen cryotherapy and application of concentrated (30%-50%) salicylic acid are treatments most frequently used for warts by family physicians.[6] Less potent over-the-counter (OTC) cryotherapy or salicylic acid (usually 17%) treatments are offered in pharmacies without a prescription.[7] Because warts resolve spontaneously and available treatments often fail, especially in the case of plantar warts,[8-10] a wait-and-see policy may be considered in treatment decisions.[11] Studies on the natural course of warts are scarce and outdated, however.[12-14]

Conflicts of interest: authors report none.

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We therefore undertook a study examining the natural course of cutaneous warts and treatment decisions in a prospective observational cohort of primary schoolchildren.

METHODS

Study Cohort and Procedures

At baseline, we included all children in grades 1 through 7 from 3 primary schools in and around the city of Leiden, the Netherlands. A trained medical student examined the hands and feet of all children for the presence of warts. The details of this baseline examination have been previously reported.[3] One year later, another trained medical student examined the hands and feet of all children who had had warts at baseline (now in grades 2-8), again for the presence of warts. Mean follow-up was 15 months, with a range of 11 to 18 months because of practical reasons and taking into account school vacations. Parents were asked to give informed consent before both examinations. Apart from this requirement, children were free to decline participation during examinations. The study was approved by the Medical Ethics Committee of the Leiden University Medical Center, as well as by the boards of the participating schools.

Presence of Warts

At baseline and follow-up, the type and number of warts were recorded on standard forms with schematic representation of the hands and feet. A distinction was made between plantar warts (located on the sole of the feet) and common warts (located on the hands or the dorsal aspect of the feet). Complete resolution was defined as a complete absence of warts at the follow-up examination. A wart was considered completely resolved when it was no longer visible (skin color and skin lines were reestablished) and could no longer be palpated by hand. More than 5% of both the baseline and the follow-up examinations were supervised by experienced family physicians, with no discordance regarding wart diagnosis or resolution.

Factors Influencing Resolution

During the baseline examination, clinicians recorded the children's demographic and wart factors. The demographic factors were age (split on the median: 4-7 years vs 8-12 years), sex (female vs male), and skin type (coded according to Fitzpatrick[15] as Caucasian vs non-Caucasian). The wart factors assessed were type (plantar vs common), number (single vs multiple), and size (<1 cm vs ≥1 cm).

Treatment Decisions

Before the follow-up examination, parents were asked to complete a questionnaire about the inconvenience caused by warts present at any time during the follow-up period and which treatments, if any, were initiated for these warts. The following factors were recorded. Inconvenience of warts was characterized according to type (pain, irritation, unsightly appearance, opinion of others) and amount (on a scale from 0 [no inconvenience] to 4 [considerable inconvenience]). Initiated treatment was classified according to family physician involvement (OTC vs family physician provided) and specific type (cryotherapy vs salicylic acid application vs other).

Statistical Analyses

We calculated resolution rates with 95% CIs, dividing the number of children with complete resolution by the sum of the person-time of children at risk (person-years at risk). To calculate person-time at risk, we considered the date of resolution to be halfway through the follow-up period. In addition, we calculated resolution rates for plantar and common warts individually, as well as the resolution rate when only baseline warts were considered, that is, new warts that developed during the follow-up period were disregarded.

We used Cox proportional hazards models to identify factors enhancing resolution. Univariate analysis was performed for demographic, wart, and treatment factors to estimate hazards ratios (HRs) with 95% CIs. We performed multivariate analysis with all factors to assess which relations were independent. In subgroup analysis, HRs were calculated for children with plantar warts separately. In addition, we used a logistic regression model to explore factors related to the decision to treat warts. Odds ratios (ORs) with 95% CIs were calculated for demographic, wart, and inconvenience factors.

RESULTS

Study Cohort

Of 1,134 eligible children at baseline, 1,099 (97%) participated: 23 children (2%) were absent from school at the time of baseline examinations, and for 12 children (1%), parental or child consent was not given.

At baseline, 366 children (33%) had warts on examination. Overall, 33 (9%) of this group were lost to follow-up: 24 children (7%) left school, and for 9 children (2%), parental or child consent was not given for the follow-up examination. At baseline, the median age of the 333 children included in the follow-up was 8 years (interquartile range = 5-10 years), 49% were male, and 15% had a non-Caucasian skin type, originating from Morocco, Turkey, China, the Netherlands Antilles, or Surinam (Table 1). In total, 42% of the children

had common warts and 70% had plantar warts; 43% had multiple warts, and 37% had a wart measuring at least 1 cm in diameter.

Resolution of Warts

The complete resolution rate was 52 per 100 person-years (95% CI, 44-60). When newly developed warts were excluded, the resolution rate of baseline warts was even higher: 90 per 100 person-years (95% CI, 79-100). Rates were similar for both common warts and plantar warts individually.

Factors Influencing Resolution

The likelihood that warts would resolve was higher for younger children (HR = 1.1 per year decrease; 95% CI, 1.0-1.2, $P = .003$) and non-Caucasian skin type (HR = 2.0; 95% CI, 1.3-2.9, $P = .001$), whereas the type, number, and size of the warts did not predict resolution (Table 2). Multivariate analysis showed almost the same results, with the only difference being that in this model, the likelihood of resolution increased slightly with the number of warts (HR = 1.1 per each additional wart; 95% CI, 1.0-1.2, $P = .04$). Subgroup analysis of children with plantar warts and the analysis considering only warts present at baseline yielded results similar to those of the primary analysis considering all warts, including those that developed during follow-up.

Treatment Decisions

Of 333 parental questionnaires distributed, 276 (83%) were returned. Within this group, parents of 73 children (26%) reported that the warts caused inconvenience, and parents of 106 children (38%) reported that the warts were treated with OTC or family physician–provided treatments during follow-up (Table 3). Two children were referred to a dermatologist. Initiated treatments were similar for common warts and plantar warts. Treated children were less likely to have resolution of warts than nontreated children (HR = 0.6; 95% CI, 0.4-0.8); the finding was similar for family physician treatment (HR = 0.7; 95% CI, 0.4-1.1) and for OTC treatment (HR = 0.5; 95% CI, 0.3-0.8).

Table 1. Baseline Characteristics of the Children With Warts Included in the Follow-up (n = 333)

Characteristic	Value	Characteristic	Value
Age, median, y	8 (4-12)	Type of warts, No. (%)	
Sex, No. (%)		Common only	100 (30)
Male	162 (49)	Plantar only	192 (58)
Female	171 (51)	Both	41 (12)
Skin type, No. (%)		Number of warts, No. (%)	
Caucasian	284 (85)	1 wart	191 (57)
Non-Caucasian	49 (15)	2 warts	63 (19)
School, No. (%)		3-5 warts	52 (16)
School A, 28 classes	219 (66)	≥6 warts	27 (8)
School C, 8 classes	27 (8)	Presence of warts ≥1 cm, No. (%)	
School D, 12 classes	87 (26)	No	209 (63)
		Yes	124 (37)

Table 2. Univariate Associations of Demographic and Wart Factors at Baseline With the Resolution of All Warts

Potential Risk Factor	No. of Cases/ Person-Years	Resolution Rate per 100 Person-Years	HR (95% CI)[a]	*P* Value
Demographic factors				
Age in years				
8-12	80/176	45	1.0 (ref)	
4-7	82/137	60	1.5 (1.1-2.0)	.02
Age, per year decrease	–	–	1.12 (1.04-1.20)	.003
Sex				
Female	76/164	46	1.0 (ref)	
Male	86/149	58	1.3 (0.9-1.7)	.13
Skin type				
Caucasian	129/274	47	1.0 (ref)	
Non-Caucasian	33/39	85	2.0 (1.3-2.9)	.001
Wart factors				
Type				
Common only	50/94	53	1.0 (ref)	
Plantar only	96/181	53	1.0 (0.7-1.4)	.88
Both	16/38	42	0.7 (0.4-1.2)	.19
Number				
Single	90/184	49	1.0 (ref)	
Multiple	72/129	56	1.1 (0.8-1.4)	.71
Number, per additional wart	–	–	1.03 (0.96-1.10)	.43
Size				
≥1 cm	55/117	47	1.0 (ref)	
< 1 cm	106/194	55	1.2 (0.9-1.6)	.29

HR = hazard ratio; ref = reference group.

[a] Generated by univariate Cox proportional hazards model.

The decision to initiate treatment of warts during follow-up (OTC and family physician treatment combined) was not related to age, sex, skin type, or wart type at baseline, but was related to the size of the wart at baseline (OR for ≥1-cm vs <1-cm diameter = 3.2; 95% CI, 1.9-5.3, P <.001), persistence (OR not resolved vs resolved warts at follow-up = 2.0; 95% CI, 1.2-3.3, P = .01), and the reported inconvenience caused by warts (OR inconvenience vs no inconvenience = 38; 95% CI, 16-90, P <.001) (Table 4). Multivariate analysis with all of the above factors showed comparable results.

DISCUSSION

One-half of primary schoolchildren found to have warts at a given time will be free of warts 1 year later. Among young children and children with non-Caucasian skin type, resolution rates are even higher. During follow-up, 38% of children and their parents decided to treat the warts, a decision that was more likely when warts were bigger and bothersome.

Comparison With Other Studies

The most cited study on the natural course of cutaneous warts reported that 113 of 168 children (67%) were free of warts after 2 years.[12] None were treated during follow-up; however, that study was conducted in 1963 in an institutionalized mentally disabled population. Another study conducted in 1959 finding a complete resolution after 1 year in 77 of 136 patients (57%) included only hand warts in Dutch primary schoolchildren,[13] and a more recent cohort of British children aged 11 years showed a 5-year resolution rate of 337 of 364 cases (93%) but did not provide data on a shorter follow-up.[14] Despite all the methodologic limitations, the natural course in these latter studies is roughly in line with that in our study.

Although the full complexity of the relationship between the persistence of warts and immunologic responses is not yet entirely elucidated,[16] the current study shows that age and ethnic factors play a role in the resolution of warts. In agreement with others, we found that the location and size of warts do not seem to influence this outcome.[12,13] Associations with the number of warts are not consistent in other studies,[10,12,13] and we could not provide clear evidence on this issue either.

Strengths and Limitations

This study with a participation rate of 97% shows the natural course of warts in a current primary school population in western Europe. Although the data did not allow us to draw conclusions on time to resolution

Table 3. Inconvenience Caused by Warts and Treatments Initiated[a] (n = 276)

Inconvenience and Treatment	No. (%)
Any inconvenience caused by warts	73 (26)
Pain	23 (8)
Irritation	28 (10)
Unsightly appearance	38 (14)
Bothered by opinion of others	10 (4)
Initiated treatment	106 (38)
OTC treatment only	49 (18)
Family physician treatment only	41 (15)
Both	16 (5)
Specific OTC treatments[b]	
Dimethylether/propane cryotherapy	28 (10)
Low-dose (17%) salicylic acid	37 (13)
Duct tape	2 (1)
Other	12 (4)
Family physician treatments[c]	
Liquid nitrogen cryotherapy	49 (18)
High-dose (40%-50%) salicylic acid	14 (5)
Other	3 (1)

OTC = over the counter.

[a] Response to parental questionnaires was 276 of 333 (83%).

[b] Initiated treatments were comparable for common warts and plantar warts.

[c] More than 1 option possible: 23 children reported more than 1 type of inconvenience, 13 children used more than 1 OTC treatment, and 9 children used more than 1 family physician treatment.

Table 4. Univariate Associations of Demographic and Wart Factors at Baseline and Inconvenience With the Decision to Treat Warts (n = 276)

Factor	OR (95% CI)[a]	P Value
Demographic factors		
Age (per year increase in age)	1.1 (0.9-1.2)	.33
Female sex	1.3 (0.8-2.1)	.28
Caucasian skin type	1.6 (0.8-3.2)	.24
Wart factors		
Plantar location	1.1 (0.7-2.0)	.66
Number (per additional wart)	1.1 (1.0-1.2)	.08
Size ≥1 cm	3.2 (1.9-5.3)	<.001
Warts not resolved at follow-up[b]	2.0 (1.2-3.3)	.01
Inconvenience caused by warts[c]		
Yes	38 (16-90)	<.001
Type of inconvenience[d]	11 (5.6-23)	<.001
Pain	21 (4.8-91)	<.001
Irritation	27 (6.3-118)	<.001
Unsightly appearance	20 (6.7-57)	<.001
Opinion of others	16 (2.0-126)	.01

OR = odds ratio.

[a] Generated by univariate logistic regression model.

[b] Proxy for persistent warts.

[c] OR per unit on a scale from 1 (little inconvenience) to 4 (considerable inconvenience).

[d] Reported retrospectively by parents.

or wart growth, resolution rates after 1 year were objectively established by physical inspection of hands and feet. Warts on other parts of the body were potentially missed, but they account for less than 4% of all warts.[17]

We collected information on initiated treatments because treatment effects might play a role in the observed resolution rates. In agreement with a study among Australian schoolchildren,[2] about one-third of children with warts had sought treatment, for which a wide range of OTC and family physician treatments were available. The remaining two-thirds decided to refrain from treatment or were simply not aware of the presence of warts. Parental questionnaires completed before the baseline examination showed that approximately one-half of all children had warts that had not been noticed earlier by their parents.[3] The present study shows that on a yearly basis, family practice encounters only 20% of all children with warts. These children have larger and more inconvenient warts with poorer resolution rates than children who did not seek treatment. Further interpretation of these findings is limited, however, because selection and recall bias are probably involved. We had no information on the duration of warts at baseline; moreover, retrospectively, the parents of children with persistent warts may more easily have recalled treatments and inconvenience than the parents of children with resolved warts. In a recent randomized controlled trial in a family practice population, the resolution rate in children after a wait-and-see policy of 3 months was 29% (95% CI, 17%-45%).[10]

Implications

Warts are a persistent problem for some children, regardless of treatments. Age and skin type influence the odds of resolution. Our findings will be useful in the process of shared decision making with parents and children. Patients and family physicians should weigh the benign natural course, the adverse effects of treatments, and the costs on the one hand, and the effectiveness of treatments and the risk of spreading untreated warts on the other. Future research needs to more precisely establish the time to resolution of warts and identify subgroups of patients with relatively low natural resolution rates and high treatment response rates.

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Key words: cutaneous warts; schoolchildren; natural course; primary care

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