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Evaluating Herbal Medicine for the Management of *Herpes zoster* in Human Immunodeficiency Virus–Infected Patients in Kampala, Uganda

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ABSTRACT

Objective: This study was carried out to evaluate the potential effectiveness of herbal treatments used for *herpes zoster* (HZ) by a great number of people living with acquired immunodeficiency syndrome (PLWAs) in Uganda.

Setting: Kampala, Uganda. Clinics of indigenous traditional healers, at the Department of Medicine of Mulago Hospital, Makerere University, and at The AIDS Support Organization (TASO) Clinic, providing primary care to people living with HIV and AIDS.

Design, patients, and participants: Nonrandomized, nonplacebo controlled, observational study in two phases. Inclusion criteria included HIV seropositivity and a recent HZ attack. In phase 1, 52 patients were enrolled, treated, and followed for up to 3 months at three healers' clinics, and compared to 52 TASO Clinic controls receiving ambulatory care. Phase 2 was similar in design to phase 1, but lasted longer (6-month follow-up) and involved 154 hospital outpatients treated with herbal medicine and 55 TASO controls. In both phases, healer patients were given herbal treatment according to healers' prescriptions, while controls received either symptomatic treatment or acyclovir.

Results: Healer patients and controls experienced similar rates of resolution of their HZ attacks. Fewer healer patients than controls experienced superinfection in phase 1 (18% versus 42%, $p < 0.02$) and fewer healer patients showed keloid formation in either phase. This difference was not statistically significant.

In both phases, zoster-associated pain resolved substantially faster among healer patients with a higher degree of significance in phase 2 where the progression of pain over time could be seen because of the longer follow-up (phase 1: maximum p value (p_{max}) $< p_{max} < 0.02$ at 1 month, $p_{max} < 0.005$ at 2 months, $p_{max} < 0.0001$ at 3 months).

Conclusion: Herbal treatment is an important local and affordable primary care alternative for the management of HZ in HIV-infected patients in Uganda and similar settings.

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INTRODUCTION

The Joint U.N. Program on AIDS estimates that two-thirds or 21 million of the 30 million people living with human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) today are in sub-Saharan Africa (UNAIDS, 1998). Uganda has been one of the countries first and most afflicted by the pandemic, with HIV prevalence rates reaching nearly 30% in some urban centers (Uganda Ministry of Health [MOH] 1998). Although these rates have been declining in recent years, the overall prevalence remains at a very high level (9%) representing an estimated 1.5 million people living with HIV or people living with AIDS (PLWAs) (Uganda MOH, 1996, 1998).

In sub-Saharan Africa, traditional medicine remains the first line of care for the vast majority of people from both urban and rural areas, for reasons of preference, access, or affordability (Staugaard, 1985, 1991; Green, 1992, 1994, 1995). Because African traditional medicine covers a broad range of practices, the term "healer" refers to practitioners specialized in various traditional approaches to health and illness, including spiritualists, priests, diviners, mediums, faith healers, bone setters, and herbalists, among others. This specialization does not preclude the use of two or more methods by a given practitioner. This study focuses on the effect of medicinal plants that a great majority of healers of various specialties use in treating their patients. Thus, the healers mentioned in this article all have in common the practice of herbal medicine.

In Uganda, as in many countries of the same region, it has been estimated that the density of indigenous healers is around 1 per 100 inhabitants, compared to a ratio of 1 Western-trained physician to 20,000 or more people (Green, 1994). With the recognition of the HIV epidemic in 1985, traditional healers in Uganda started to see an increasing number of patients presenting with AIDS-related symptoms, which symptoms appeared no different than those they had been treating for generations. These symptoms included diarrhea, fever, respiratory and skin diseases, sexually-transmitted diseases (STDs) as well as other opportunistic infections for which they continue to be consulted by many PLWAs in both urban and rural settings.

Herpes zoster (HZ), also called Varicella zoster virus (VZV), typically causes varicella during childhood, and can reemerge later in life in immunocompromised hosts as an acutely painful condition, which usually prompts patients to seek early treatment (Ghebrekidan et al., 1999; Stewart et al., 1995). HZ infection can occur at all stages of the HIV infection (Edhonu-Elyetu, 1998; Stewart et al., 1995) and the incidence of recurrent HZ has greatly increased with HIV (Donahue et al., 1995). In African patients, it is often seen as an early manifestation of HIV disease (Pitche et al., 1997; Tyndall et al., 1995; Van de Perre et al., 1988) and has been reported to be a clinical predictor of HIV infection (Edhonu-Elyetu, 1998; McNulty et al., 1997; Mahae et al., 1996, Colebunders et al., 1988).

Acyclovir is the recommended treatment for HZ, but it is rarely available through the public sector in Uganda, and few individuals can afford to buy it from pharmacies. Patients presenting at government health facilities are usually given symptomatic treatment, which includes analgesics, antiseptics, and topical desiccants such as calamine. However, a large proportion of patients seek the help of traditional healers and herbal medicine for this and many other diseases because access to care services remains limited in Uganda, and because popular belief holds that healers have more efficient means than modern medicine to treat skin conditions in general and HZ in particular.

The government of Uganda was one of the first to acknowledge the severity of the HIV threat openly in Africa. It quickly recognized the important role of traditional healers, and supported their involvement into the National AIDS Control Programme through fostering collaboration between healers and modern health practitioners, in the area of prevention, care, and research. Traditional and Modern Health Practitioners Together Against AIDS (THETA) is a nongovernmental organization that was initiated in 1992 to establish such collaboration (THETA Participatory Evaluation 1998, unpublished report).

The first THETA study aimed to research herbal medicines as alternatives to expensive or unavailable treatments for AIDS-related conditions. The present study set out to evaluate the clinical effectiveness of herbal preparations used for the treatment of HZ in HIV-infected patients, among other conditions. It was conducted in Kampala, where the HIV prevalence was approximately 27% of the sexually active population at the time of the study (Uganda MOH 1992, 1994). HZ was selected for its high specificity among HIV-infected individuals (Edhonu-Elyetu, 1998; Pitche et al., 1997; Tyndall et al., 1995), for the scarcity and high cost of the recommended treatment (acyclovir) (Lamont et al., 1996; Strauss, 1993), as well as for the claims made by many healers about the effectiveness of herbal remedies for HZ.

We present the results of two consecutive observationl studies comparing the clinical progression of HZ patients treated with herbal medicine to a group of controls who received medical treatment at The AIDS Support Organization (TASO) Clinic, an ambulatory care center for PLWAs located in Mulago Hospital in Kampala. Variables monitored included the progression of the herpes papules, vesicles, pustules, and scabs (Runne and Ochsendorf, 1993) as well as the proportion of patients who experienced complications over time, including superinfections, zoster-associated pain, and keloid formation on the shingles area.

STUDY PARTICIPANTS AND METHODS

This study was a collaboration between traditional practitioners and biomedical health workers from TASO and THETA Organizations as well as Mulago National Hospital. The study was not blinded, because it was not possible to prepare placebos without altering the herbal formulations used by participating healers. Thus, the primary intent of the study was to assess the effect of herbal medicine as a class of treatments for HZ rather than evaluating specific herbal ingredients. This was, therefore, a nonrandomized, nonplacebo controlled observational study carried out in two phases. Phase 1 consisted of a pilot study conducted with healer clients at the healers' clinics while phase 2 was an attempt to validate phase 1 findings with hospital patients in a clinical research setting.

STUDY CRITERIA

Healers were informed about the study through informal visits to their homes and clinics by project nurses and doctors. In the course of these visits, they were asked to answer a structured questionnaire about their background, as well as their knowledge and practices regarding HIV and AIDS (King et al., 1993). After these initial contacts, a series of seminars was organized for interested healers and researchers to share basic AIDS information and establish the objectives, methods, requirements, and constraints of the study. None of the healers had previously participated in clinical research. By the end of these seminars, the following conditions were adopted by all participants to guide the collaborative study:

(1) Only patients presenting with HZ and who tested positive for HIV antibodies would qualify for the study.
(2) Healers would maintain the same herbal treatment for a given patient throughout follow-up and would inform investigators of any change in preparation and/or dosage.
(3) Healers would not mix synthetic medicine in their preprations.
(4) Healers would not coerce, lure, or select patients into joining the study but rather explain its objectives, advantages and constraints to all eligible patients, and let them decide freely.
(5) Healers or doctors would not divulge results or make claims about the study before its completion.
(6) Doctors would respect healers' rights of ownership over their preparations and not inquire about or divulge any particular formulation without the knowledge and approval of the healer(s) concerned.

Evidently, some of these conditions posed a reliability problem, especially regarding the maintenance of a given treatment (point 2) and the mixing of synthetic drugs (point 3). These positions were nevertheless adopted not only because it was impossible to test the healers' preparations without their full participation in the study, but also because it was essential to establish a mutually trustful relationship between doctors and healers for this and future collaborations. Point 6 (respect of intellectual property rights) also represented a challenge to the study because it implied that research was to be conducted without knowing the active ingredients involved in the herbal treatments used by the healers. Again, this paradigm was adopted for two reasons. First, at the time of this study, there was no patenting mechanism in Uganda that would have allowed the protection of healers' proprietary rights over any active components had they been identified. Furthermore, this clause demonstrated to participating healers that investigators were willing to respect their rights fully, independent of any commercial interests. The issue of trust was indeed of paramount importance to this study as it has greatly hampered traditional practitioners' confidence to collaborate with Western doctors both in Uganda and elsewhere in the world (THETA, unpublished report; Milliken, 1997).

Selection of healers and patient enrollment

Phase 1. Thirty-one (31) healers were invited to participate in preparatory seminars and information sessions regarding the study. Among them, only three had sufficient clientele presenting with HZ to participate in phase 1. These healers were asked to screen patients for enrollment among their regular clients according to the following procedures.

Only patients presenting with HZ within 2 weeks of onset were eligible for enrollment. Patients selected in this way were seen by the project nurses and a clinician to confirm their eligibility and were then given pretest- and posttest counseling for the HIV antibody test. Only those testing positive on two different enzyme-linked immunosorbent assay (ELISA) tests were enrolled in the study.

Controls were selected from the regular clients of the TASO Clinic who had all been tested for HIV. Inclusion criteria and enrollment procedures were the same as for healer patients.

All patients were informed of the study objectives in their own language and when willing to participate, signed a consent form.

Phase 2. Phase 2 was carried out to validate phase 1 findings. The three healers from phase 1 were assigned a consultation room in the Clinical Research Building of the Department of Medicine, at the University of Makerere Medical School in Kampala, where they saw patients on separate days of the week. In this phase, healer patients were not recruited from their own clientele but were referred from the hospital outpatient clinics. Referral was made by project nurses who regularly informed hospital outpatients about the study. In this phase, only healer patients or controls presenting with HZ within 1 week of onset were recruited. Other phase-2 enrollment procedures were as in phase 1.

Follow-up

All patients were seen at enrollment by a study doctor to verify the clinical diagnosis of HZ. Follow-up was standardized through a regular schedule and a specific clinical checklist as described below:

(1) Phase 1 patients were seen three times in the first week (day 0, 4, and 7), weekly for the following 3 weeks, and monthly for the next 2 months. At each visit, patients were seen by a project nurse under the supervision of a study clinician, in addition to the caring healer for healer patients,
(2) In phase 2, healer patients were seen at the Department of Medicine and the controls at the TASO Clinic. The first 3-month follow-up was as in phase 1, and was extended for 3 additional monthly visits (6 months in total).

Treatments

Herbal medications were supplied and prescribed by the healers or their assistants, both orally and in the form of topical applications to the affected body parts. Preparations were code-named by each healer and given to their patients according to the healer's prescribed regimen. Each healer used his own formulation in varying combinations, sometimes adjusting the mix according to the progression of symptoms.

Medical treatment was supplied by TASO, prescribed by the study doctors, and dispensed to control patients by nurses. Symptomatic treatment consisted of calamine lotion, antibiotics, and painkillers as required (Rowbotham, 1994). When available, acyclovir was given orally at a dose of 200 mg, five times a day for 5 days, which is lower than the recommended dose (800 mg, five times a day for 7 days). This prescription was not modified in order to compare herbal treatments to the actual dosage commonly used in Uganda. Only part of the control group received acyclovir because the supply of this drug depended on donations to TASO, and no patient could afford to buy it on their own. Patients who received this drug were so recorded in their follow-up files.

Clinical progression

The number of days it took for each patient to report to the healer or hospital as well as for pustules and scabs to resolve was recorded, counting from the day herbal or medical treatment was initiated. When pustules did not develop, nurses recorded the time it took for papules or vesicles to resolve. In addition, the presence of superinfections, zoster-associated pain, and keloid scar formation was noted at each visit.

Statistical analysis

Data were analyzed using the EpiInfo statistical package. Group comparisons were based on analysis of variance (ANOVA), Fisher exact test, and χ^2 analyses, using Yates correction when expected cell values were less than 5. Comparisons were made both between individual control and healer patient groups as well as between consolidated healer patients and control groups.

RESULTS

Patient enrollment and follow-up

In both phases and in most groups, the majority of patients enrolled in the study were women (Table 1). In phase 1, on average, women represented 65% of enrolled healer patients and 73% of controls. This difference was not significant. In phase 2, however, the proportion of women among controls (85% [n = 55]) was significantly greater than the proportion of women among any healer group, which ranged between 53% (Healer 3, n = 49) and 63% (Healer 2, n = 60) ($0.0003 < p < 0.008$).

Nearly half of all patients were between 26 and 35 years old while approximately one-third were aged 18 to 25 years and the remaining 10% to 20% belonged to the 36 to 45 age bracket (Table 1). There was no significant difference in the average age of patients enrolled at the healers or TASO Clinics in either phase.

As shown in Table 1, 52 patients and 52 controls were enrolled in phase 1 at the three healers' clinics and at the TASO Clinic respectively. Healer 2 was not able to enroll more than five patients in this phase because he did not have herbal treatments for HZ available at the time. In phase 2, 154 healer patients and 55 TASO clients were recruited into the study.

Table 1 also shows the number of patients who completed or were lost to follow-up, as well as those who died during the course of the study. Healer patients and controls were monitored for an average of 10 and 4.5 weeks in phase 1, respectively, and for an average of 16 and 17 weeks in phase 2, respectively. Eighty-one percent (81%) of enrolled healer patients and sixty-three percent (63%) of TASO controls completed at least 4 weeks of follow-up in phase 1 ($p = 0.049$) as compared to 81% and 58%, in phase 2 respectively ($p = 0.0007$).

Overall, losses to follow-up were greater among controls than among healer patients in both phases, although significantly so only in

TABLE 1. ENROLLMENT AND FOLLOW-UP OF HEALER PATIENTS AND CONTROLS

	Phase 1					*Phase 2*				
Gender	Healer 1	Healer 2	Healer 3	All healers	Controls	Healer 1	Healer 2	Healer 3	All healers	Controls
Female	16	3	15	65%	38 (73%)	28	38	26	60%	47 (85%)*
Male	7	2	9	35%	14 (27%)	17	22	23	40%	8 (15%)
Age	Healer 1	Healer 2	Healer 3	All healers	Controls	Healer 1	Healer 2	Healer 3	All healers	Controls
18–25	8	1	6	29%	18 (35%)	14	18	17	32%	20 (36%)
26–35	13	3	14	58%	25 (48%)	24	30	20	48%	26 (47%)
36–45	2	0	4	11%	7 (13%)	6	9	8	15%	8 (15%)
46+	0	1	0	2%	2 (4%)	1	3	4	5%	1 (2%)
Follow-up	Healer 1	Healer 2	Healer 3	All healers	Controls	Healer 1	Healer 2	Healer 3	All healers	Controls
≥4 wks	16	4	22	81%*	33 (63%)	31	58	36	81%*	32 (58%)
2–3 wks	1	—	1	6%	5 (10%)	1	1	1	2%	4 (7%)
Lost[a]	6	1	1	13%	14 (27%)	13	1	12	17%*	19 (35%)
Died	(1)	—	—	(2%)	— (0%)	(2)	—	(1)	(2%)	— (0%)
Average follow-up in weeks	6.6	14.5	11.9	9.9	4.5	15.8	18.0	12.3	15.8	17.0

[a]Any patient monitored for less than 2 weeks was considered to be lost to follow-up.
*$p < 0.01$

The numbers of patients enrolled and followed-up in each phase are shown by gender, age and follow-up category for each healer's patient group (healer 1, healer 2, and healer 3), all healer patients (All healers), as well as for the hospital (TASO Clinic), controls. The numbers of patients followed-up are grouped in four categories: those who were followed-up for 4 weeks or more (≥ 4 wks); for less than 4 weeks but at least 2 weeks (2–3 wks); those who were lost to follow-up, i.e., monitored for less than 2 weeks (Lost); and those who died. The number of patients who died during follow-up are in parentheses to indicate that they were included in the follow-up category they belonged to at the moment of their death. Average follow-up in weeks (Average follow-up) is indicated for all patient groups. Percentages indicate the proportion of all healer patients (All) and Controls enrolled and monitored in the categories indicated.

phase 2 ($p = 0.006$). Finally, there were no differences in the death rate of study participants in either phase.

Clinical course of HZ lesions

The progression of HZ lesions is summarized in Table 2 for each healer and control group. This table shows that except for Healer 2 group in phase 1, it took consistently between 4 to 5.5 days for patients to consult a doctor or a healer after the appearance of first symptoms. The average time for papules, vesicles, or pustules to resolve ranged for all patients between 4.5 and 11 days in phase 1, and between 6.6 and 11.2 days in phase 2, with no significant differences among healer patients and controls. A similar observation applies to the average time it took for scabs to disappear, which ranged between 12.2 and 23.7 days in phase 1 and between 17.5 and 27.9 days in phase 2, with no significant differences between the 2 phases or among the different treatment groups.

Complications

The most common complications associated with VZV infection are bacterial superinfections of the zoster-affected area, the formation of keloid on the scar, and chronic pain persisting after cutaneous healing also referred to as postherpetic neuralgia or zoster-associated pain (Pasero and Davies, 1998; Kost and Straus, 1996; Carmichael, 1991).

Table 3 shows that the occurrence of bacterial superinfections in phase 1 was lower among healer 2 and 3 patients than among controls. The difference between these healer groups and the acyclovir-treated controls was significant ($p = 0.023$), but was not observed in phase 2, where 31% to 56% of all patients groups experienced superinfections.

Keloid formation tended to be less frequent among healer patients than among non–Acyclovir-treated controls, in both phases (Table 3). This difference was significant for all healer patients taken together in phase 2 ($p = 0.04$), but

TABLE 2. PROGRESSION OF *HERPES ZOSTER* LESIONS

	Phase 1						*Phase 2*					
					Controls						*Controls*	
Treatment groups:	*Healer 1*	*Healer 2*	*Healer 3*	*All healers*	*No acyclovir*	*Acyclovir*	*Healer 1*	*Healer 2*	*Healer 3*	*All healers*	*No. acyclovir*	*Acyclovir*
No. of patients	17	4	23	44	10	28	32	59	37	128	27	9
Average no. of days:												
—from HZ onset to initial visit	4.6	13.0	4.9	5.5	5.3	3.9	5.7	5.0	5.4	5.3	4.7	3.9
SD	(2.2)	(7.9)	(2.9)	(3.5)	(2.9)	(2.8)	(3.4)	(3.0)	(4.7)	(3.7)	(2.5)	(1.1)
—from initial visit to resolution of:												
Papules/vesicles	7.3	9.0	7.7	7.7	nd*	nd*	8.8	6.6	9.3	7.7	6.7	10.2
(%)	(41%)	(50%)	(48%)	(45%)			(41%)	(58%)	(41%)	(48%)	(26%)	(44%)
Pustules	11.0	4.5	6.0	7.7	8.0	7.9	8.8	10.6	9.7	9.7	11.2	7.2
(%)	(53%)	(50%)	(57%)	(55%)	100%	100%	(56%)	(34%)	(54%)	(45%)	(44%)	(56%)
Scabs	18.9	12.2	13.1	14.9	23.7	17.4	22.6	17.5	21.9	20.0	27.9	20.4
(%)	100%	100%	100%	100%	100%	(96%)	100%	100%	(97%)	(99%)	100%	100%

*Not done: Phase 1 controls were not monitored for the development of papules or vesicles. Only pustules and scabs were recorded.

Progression of *Herpes zoster* (HZ) lesions are shown in each phase for the number of patients (No. of patients) from each healer group (healer 1, healer 2, and healer 3), all healers (All healers), as well as from the hospital (TASO Clinic) controls. Controls were further categorized in those who received acyclovir and those who received symptomatic treatment (No acyclovir) as described in the text. Numbers shown below the row labeled "Average no. of days" indicate the average number of days for the time it took: (1) for patients to report to the healer or hospital clinic from the time of first symptoms of HZ (from HZ onset to initial visit). Figures in parentheses indicate standard deviation (SD) of the average and (2) for HZ papules/vesicles, pustules, or scabs to resolve after initial visit (from initial visit to resolution of). Figures in parentheses indicate the proportion of patients (%) whose HZ lesions went through the corresponding stages.

TABLE 3. COMPLICATIONS OF *HERPES ZOSTER* LESIONS

	Phase 1						*Phase 2*					
					Controls						*Controls*	
Treatment groups:	*Healer 1*	*Healer 2*	*Healer 3*	*All healers*	*No acyclovir*	*acyclovir*	*Healer 1*	*Healer 2*	*Healer 3*	*All healers*	*No acyclovir*	*Acyclovir*
No. of patients	17	4	23	44	10	28	32	59	37	128	27	9
Superinfection	7	0	1	8	4	12	10	21	15	46	12	5
	41%	0%	4%	18%*	40%	43%	31%	35%	41%	36%	44%	56%
Cheloids	0	2	1	3	2	1	2	2	5	9	6	2
	0%	50%	4%	7%	20%	4%	6%	3%*	14%	7%	22%	22%

*$p < 0.03$

Complications of *Herpes zoster* (HZ) lesions are shown in each phase for patients (No. of patients) from each healer (healer 1, healer 2, and healer 3), all healers (All), and the hospital (TASO) clinic control group (Controls). Controls were further categorized as those who received (Acyclovir) or did not receive Acyclovir (No acyclovir) as described in the text. Numbers shown indicate the number of patients in each category who experienced superinfection, and/or keloid formation on their HZ lesion. Percentages indicate the proportion of patients who experienced the corresponding complication in each treatment group.

individually, only healer 2 group exhibited significantly fewer keloid formation than the controls who did not receive acyclovir treatment ($p = 0.017$).

Postherpetic neuralgia (PHN) is difficult to define because any specific endpoint is arbitrary and likely to introduce a bias (Pasero and Davies, 1998; Kost and Straus, 1996; Dworkin and Portenoy, 1996; Wood, 1995; Johnson 1995). We therefore looked at the progression of herpetic neuralgia or zoster-associated pain over time (Fig. 1). In phase 1, fewer healer patients than controls appeared to have residual pain at 1 month of follow-up, with a significant difference between healers 1 and 3 patients and the acyclovir-treated control group ($p = 0.045$ and $p = 0.0035$, respectively). The loss of controls to follow-up after this time made it impossible to confirm this result in phase 1. In phase 2, the difference between healer and control groups showed clearly throughout the first 3 months of follow-up. At the end of this period, only 11% of all healer patients still experienced chronic pain (range 7% to 16%) compared to 63% of controls (no acyclovir treatment) ($p < 0.0001$), and 33% of the acyclovir-treated controls ($p = 0.157$). The differences between individual healer groups and controls (no acyclovir treatment) were all significant ($p < 0.0001$).

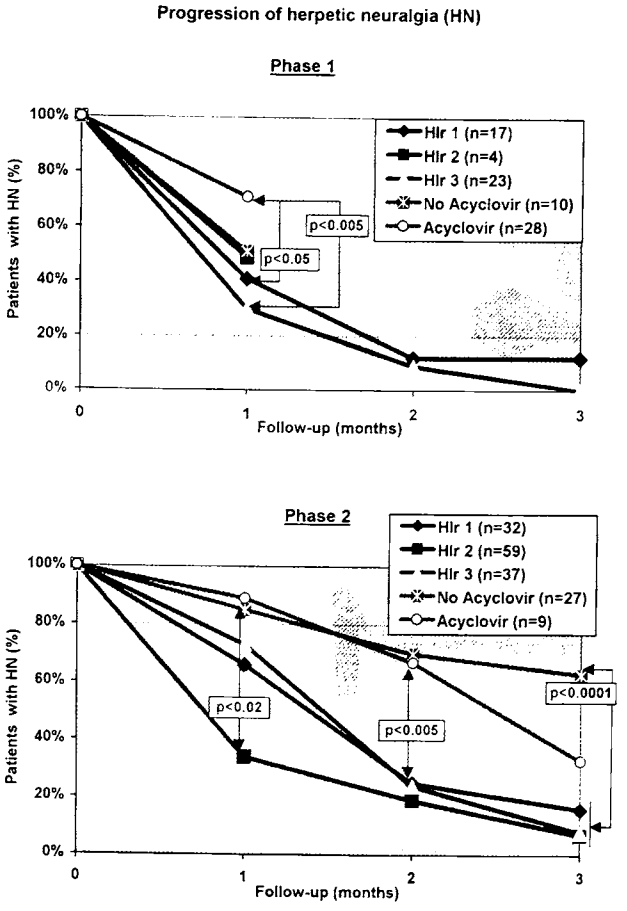

FIG. 1. Progression of herpetic neuralgia (HN). The proportions of phase 1 and 2 patients with zoster-associated pain during follow-up are shown for all patient groups, including Healers 1, 2, and 3 (Hlr 1, Hlr 2, and Hlr 3), as well as hospital (TASO) Clinic controls who either received acyclovir (Acyclovir) or not (No Acyclovir). Patient group sizes are indicated in parentheses in the chart legends. p values indicate significant differences between treatment groups.

DISCUSSION

The predominance of women among study participants reflects the general trend of healer attendance in Kampala (Homsy and King, 1996). In both phases, losses to follow-up were higher among controls than among healer patients. One possible explanation for this observation is that TASO controls received meals as a form of support in phase 1 but not in phase 2. In contrast, dry food rations were given in both phases to healer patients as an incentive for their participation in the study. TASO discontinued its food support to clients between phase 1 and 2 for reasons external to the study, possibly reducing patients' motivation to comply with the longer follow-up of phase 2.

The progression of HZ lesions over time was similar for healer patients and both control groups in both phases (Table 2). This result is interesting as it points to the possibility that neither acyclovir nor the herbal treatments significantly changed the course of the zoster attacks in either patient group.

Differences among healer patient and controls were more marked regarding complications of the zoster lesions (Table 3). Significant differences in the proportion of patients who developed superinfections were observed in phase 1 but not in phase 2. One possible explanation for this discrepancy is that phase 2 healer patients were selected from among hospital outpatients and treated within the hospital. As healer patients tend to go to the hos-

pital when herbal treatments have failed, phase 2 healer patients may have included such cases, who would be more prone to complications. Lastly, the hospital setting may have increased the risk for nosocomial infections.

Keloid formation appeared to be less frequent among healer patients although the number of patients with this complication was small in all groups in both phases. This possibly explains the lack of significance of the differences observed between healer and control groups. However, the fact that the trend was consistent in both phases suggests that herbal preparations may have contributed to this result. Further research is warranted to verify this possibility.

Herpetic neuralgia (HN) is the most frequent complication of HZ infection. It can be crippling for patients and is difficult to treat with conventional drugs, including acyclovir (Johnson, 1997; Volmink et al., 1996; Lancaster et al., 1995). This is especially true for persons with HIV infection for whom only high doses may offer significant survival benefit (Ioannidis et al., 1998; Whitley, 1996; Glesby et al., 1995; Bernhard and Obel, 1995; Colebunders et al., 1994; Balfour et al., 1994, Wallace, 1993). The lack of data for controls beyond 1 month of follow-up in phase 1 make the results difficult to interpret for this phase. In addition to the reason mentioned above, this loss to follow-up may have resulted from an unblinded study bias that allowed controls to find out about the effects of healer treatments on fellow patients, prompting them to switch to herbal medicine. The difference in the proportion of patients with HN at 1 month of follow-up observed between phase 1 and phase 2 could be ascribed to a number of factors. First, group sizes were substantially different in both phases. Moreover, as mentioned above, phase 2 healer patients were recruited from the hospital, thus, could have included a greater number of resistant cases. Healers may also have used different treatment preparations and/or dosage in phase 2 or still, may have exerted different "placebo" effects on their clients. In any case, these fluctuations point to the need for a more strictly controlled design in future studies in order to account for these variables.

Acyclovir has been reported to accelerate cutaneous healing, alleviate pain at high dose, and reduce the severity of PHN when given at high dose within 24 to 72 hours of the herpetic rash (Ioannidis et al., 1998; Jackson et al., 1997; Chasuk, 1997; Kost and Strauss, 1996; Wood et al., 1996). In this study, most patients reported to the healer clinic or the hospital 4 days or more after the onset of the herpetic attack (Table 2). In addition, acyclovir was given to controls whenever available and below the recommended dose, reflecting the reality of hospital care in Uganda. This situation translated into a wide fluctuation in the number of controls who received acyclovir from one phase to the next. It may also have contributed to the emergence of acyclovir-resistant HZ virus strains. Taken together, these conditions probably largely account for the inconsistencies in the differences in PHN progression observed between the acyclovir- and symptomatically-treated controls between phase 1 and 2, thus, these differences cannot be used to either support or contradict the reported effect of acyclovir on PHN.

In summary, phase 2 findings are more reliable in terms of follow-up data and patient group sizes and suggest that healer patients experienced faster resolution of PHN than either control groups over time, particularly symptomatically treated controls.

CONCLUSION

Current optimal treatments for HZ and PHN, which include antivirals, certain antidepressants, and opioid drugs are far from perfect and are mostly unavailable and unaffordable to the great majority of patients in sub-Saharan Africa. In this part of the world, patients have few options of care other than hospitals, public dispensaries, or traditional healers. This study represented the first attempt in Uganda to document the clinical effectiveness of herbal medicine versus that of commonly available biomedical treatments for HZ among HIV-infected patients in Kampala. Its completion illustrates that

collaborative research involving traditional healers and medical doctors is feasible and can yield useful information for the many persons living with HIV infection who regularly consult both types of practitioners in this country (King and Homsy, 1997, Green, 1994).

The observations reported here cannot be interpreted as a rigorous demonstration of efficacy given the lack of randomization or blinding of the study, and the lack of standardization of the herbal or medical treatments and their administration. It is thus evident that further research is required to confirm our findings. Yet, the trends observed in both phases of this study suggest that herbal treatments may be at least as effective as available biomedical treatments for HZ in Uganda, including acyclovir. This preliminary result cannot be overlooked, not only because of its public health relevance for Uganda and other countries facing similar care challenges, but also because of the increasing emergence of acyclovir-resistant HZ infections, especially among HIV-infected patients. We therefore propose that, within the Ugandan context of care, these herbal treatments can be used as a viable local alternative to acyclovir and other palliative biomedical treatments for HZ infection as long as access to other safe and effective treatments for HZ are not available.

This article has presented a relatively simple and inexpensive clinical approach to evaluating herbal medicine, in comparison to long and costly laboratory research, which eventually requires clinical confirmation. It is hoped that this effort will encourage similar work in the region and beyond in order to further document the potential of traditional medicine and reduce the dependency of an ever-increasing number of patients in developing countries on unaffordable imported drugs (Pécoul et al., 1999).

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