

Exploration of pain in children on antiretroviral treatment in a regional hospital in South Africa

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Abstract

Background: Patients with human immunodeficiency virus (HIV) disease on antiretroviral therapy (ART) may experience pain for a variety of reasons, including the effects of the virus itself, associated opportunistic infections and the ART. Studies indicate that pain in adults on ART is frequent, can be severe, and is often undertreated. This study sought to explore the experience, and the prevalence of pain in young children aged 3-13 years on ART.

Method: Primary caregivers of children aged 3-13 years on ART attending a paediatric ART clinic at a regional hospital in Durban participated in the study. Convenience sampling was used. The Wong-Baker FACES™ Pain Rating Scale and a questionnaire adapted from Hirshefeld were used to investigate variables such as age, cluster of differentiation 4 (CD4) count, ART regimen, ART duration, and site, prevalence and impact of pain during activities. Data were analysed using a standard statistical programme.

Results: Four hundred and twenty primary caregivers were interviewed. Most were mothers caring for their HIV-positive children, and the majority of the children were aged 3-7 years. Most children were on a first-line ART regimen, and half reported pain. Nociceptive pain (visceral or somatic) was the most common type of pain, and pain interfered with the daily activities of a third of the children. There was a significant association between CD4 count and pain (p -value = 0.040). Paracetamol was the most commonly used analgesic.

Conclusion: Pain was a common problem, and generally was undertreated with analgesia. A need to improve pain assessment and management in this population group was identified.

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Introduction

In South Africa, human immunodeficiency virus (HIV) remains a major cause of morbidity and mortality among adults and children. In 2009, the estimated adult prevalence of HIV was 5.24 million (meaning that 10.6% of the total population was HIV positive). The estimated number of children under 15 years of age who are HIV infected is 330 000. The annual number of new infections among children is estimated to be 40 000.¹ The number of children in need of antiretroviral therapy (ART) doubled between 2005-2010, and by 2009, it was estimated that 86 270 children were receiving ART.²

HIV is associated with many symptoms, of which pain can be particularly problematic. Pain may be caused directly by the virus, which has a predilection for nerve tissues. Both the peripheral and central nervous systems are frequently affected in patients with HIV.³ Pain can also be caused indirectly by opportunistic infections associated with HIV

and malignancies.⁴ In adults with HIV, pain is a frequently reported symptom throughout all stages of the disease. Patients report headaches, mouth and throat pain, chest pain, myalgia, arthralgia, as well as the pain associated with medical procedures.⁴ Similar to findings on patients suffering from cancer, pain in patients with HIV is frequently not recognised by healthcare providers, and when acknowledged, is often undertreated.⁵

In southern Africa (Botswana, Lesotho, South Africa and Swaziland), a study among 743 adults with HIV disease reported that pain was a common symptom that required care.⁶ A high pain prevalence among adults has been shown to be associated with advanced HIV disease in South Africa. For example, in a hospice-based study among 103 adult patients with World Health Organization Stage 4 acquired immune deficiency syndrome (AIDS), carried out in 2003, 98% of patients reported pain, of whom the majority were not receiving ART.⁷ A rural community-based study, carried out in 2002, indicated that pain was commonly reported

among HIV-infected adults who were not on ART.⁸ Pain has also been found to be prevalent among HIV-positive outpatients, as indicated in a study conducted in Pretoria among 354 HIV-positive outpatients who were not on ART, in which 62% of patients reported significant pain, and 20.9% patients reported severe neuropathic pain, that was assumed to be due to HIV. These patients reported that pain interfered with their quality and enjoyment of life, and their moods and ability to work.⁹

In South Africa, studies on pain prevalence in children on ART have been slow to emerge. In a Western context, Hirschfeld et al reported a pain incidence of 59% in children with HIV infection, as compared to an incidence of 47% in children with cancer.¹⁰ Various types of pain have been recorded in children with HIV, including headaches, abdominal pain, myalgia, peripheral neuropathy, chest pain, and oral cavity pain.¹¹

Barriers to recognition and treatment of pain in children by healthcare providers may be considerable. Despite education and research to the contrary, misconceptions regarding pain perception in children persist.¹² For example, studies indicate that some clinicians believe that young children do not experience pain, as there is an incorrect view that nerve cell myelination is incomplete in infants and young children. Therefore, the belief is that children do not experience the same kind or intensity of pain as adults, and do not need pain prevention or pain relief. A second misconception is that children do not remember painful experiences.¹³ A third misconception around pain in children lies in an assumption that pain is not a prevalent problem, as children cannot describe a source or type of pain. It is true that children may not have the same vocabulary as adults, and may experience difficulty in verbalising issues around pain. However, a clinician can gain awareness of pain in children by studying non-verbal communication.¹⁴ Like adults, children on ART may experience pain due to HIV infection itself, opportunistic infections, the side-effects of drugs and therapeutic procedures.^{10,11,15}

Assessment and management of pain in children on ART should form a major focus of clinical intervention. In 2002, the Paediatric AIDS Clinical Trial Group (PACTG219) found a significant association between pain and mortality in children. The researchers reported that children who reported pain were five times at greater risk of dying, than those who did not report pain.¹⁶

The effective assessment and treatment of pain in children with HIV/AIDS can be challenging. Developing an appropriate pain management strategy may include pharmacological and nonpharmacological therapies, tailored to a child's age, development, culture, type of pain, and past experience. With regard to assessing pain in children, studies have indicated that in the case of a young child, the primary caregiver can report symptoms, including pain, on behalf of a young child, and that there is a strong correlation between

what the caregiver reports, and the child's experience of pain.¹⁰⁻¹⁷ Most studies of pain in children with HIV infection have been conducted in first world countries, and the results of such studies cannot be directly transcribed to a South African setting. This study aimed to explore pain in young children who have HIV disease, and who are taking ART in a South African regional hospital.

Method

This was a descriptive and exploratory study. Ethical permission was granted by the University of KwaZulu-Natal Research Ethics Committee (REC.290408-009). Written permission was obtained from all participants.

Study site

The study was set in an ART clinic that is affiliated to a regional level hospital in KwaZulu-Natal. The paediatric section of the clinic provides ART to children from birth until 13 years of age. This site was chosen as a large number of young children on ART present there.

Subject and sampling

At the time of the study, 1 400 children were receiving ART at the paediatric ART clinic. Caregivers attending the ART clinic with a young child (aged 3-13 years) were given information about the study, and invited to participate. Caregivers with a child who was younger than three years of age, or with a child who was acutely ill, or those who refused to participate, were excluded from the study. The primary caregiver was defined as the person who cared for the child most of the time, and who was 18 years of age or older. On designated days between July and October 2010, the researchers interviewed caregivers at the clinic, until 420 caregivers had been interviewed. A Zulu-speaking nurse explained the nature of the study, provided information on confidentiality and consent, and was available for translation when required. Charts were marked to ensure that caregivers only participated once. Although the sample was convenient in nature, the sample was considered appropriate as this study does not make any claims towards reliability or generalisability. It simply explored whether further study in this topic might be warranted.

Data collection tools

Assessing pain is an essential step when developing a management plan, and a holistic assessment of pain involves observation of the child and discussion with parents and other caregivers. There are numerous formal tools for assessing pain in children that are appropriate for differing ages and development levels.

The Wong-Baker FACES™ Pain Rating Scale (WBFS), which has been tested in many developed and developing countries and is considered to be a valid and reliable pain assessment tool, was used in this study.¹⁸ The WBFS has been developed for children over the age of three, and

depicts six faces that are numbered 0, 2, 4, 6, 8, and 10. The first picture (0) presents a picture of a smiling face, and the last picture (10) presents a picture of a grimacing, distressed face with tears. The tool was initially developed for young preverbal children, so that they could point to a face that they felt best represented the effects of pain. A score of 4 or greater is associated with significant pain.¹⁹ In this study, the caregivers of young children were asked to score their child's pain on the WBFS, and thus the tool was used in a way other than that for which it was designed. The researchers made a decision to focus on the opinions provided by caregivers about the level of pain experienced by their children, rather than those of the children themselves, as the WBFS has not been validated in South Africa.¹⁴ However, other studies have shown that there is good concordance between the caregiver's assessment of a child's pain, and the child's pain score.^{10,17,20} To get a general idea of the pain experienced by young children on ART, the WBFS was incorporated into a questionnaire developed by Hirschfeld.¹⁰ Hirschfeld et al studied pain in children who were HIV positive, and their questionnaire considered a number of variables, including the site and duration of pain, and impact of pain on activity and sleep. In this study, the questionnaire was modified to capture data on the relation of the caregiver to the child, the child's age, CD4 count, ART regimen, and duration of ART. The child's clinic record was used to obtain data on CD4 count, ART regimen and duration of treatment, and an interview was conducted to complete the WBFS and gather other information.

Data analysis

For the purpose of this study, positive responses for pain were tabulated, and point prevalence was calculated. Responses relating to the quality-of-life questionnaire were rated on a five-point scale ("never" = 0, "rarely" = 1, "sometimes" = 2, "often" = 3, and "all the time" = 4). A rating of 2 or more was taken as significant. Data were captured and analysed using the Statistical Package for Social Science®. Data were summarised by descriptive statistics. Inferential analysis was carried out, and a p-value of < 0.05 was considered to be significant.

Results

Four hundred and twenty primary caregivers were interviewed: 226 (53.8%) mothers, and 102 (24.3%) grandmothers, as illustrated in Table I. The age of the children ranged from 3-13 years, with an average of 7.19 years. Most of the children (233: 55.5%) were 3-7 years old, and 187 (44.5%) were 8-13 years old.

Just under half (43.1%) had a CD4 percentage of > 25%. A fifth had a CD4 percentage of < 15% (which implies severe immunosuppression). Most of the children were on a first-line regimen (411: 97.9%), with only nine (2.1%) on an alternative regimen of ART. Most started treatment after 2006 (79.5%).

Table I: Demographic and clinical data summary

Information on the children on antiretroviral treatment	n	Percentage (%)
Primary caregiver		
Mother	226	53.8
Grandmother	102	24.3
Aunt	58	13.8
Other (father, uncle, brother, sister or cousin)	34	8.2
Age of children		
3-7 years	233	55.5
8-13 years	187	44.5
CD4 percentage		
< 15%	86	20.5
15-25%	133	31.7
> 25%	181	43.1
Antiretroviral treatment regimen		
Stavudine, lamivudine, lopinavir/ritonavir	71	16.9
Stavudine, lamivudine, efavirenz	314	74.8
Abacavir, lamivudine, efavirenz	26	6.2
Alternative regimen	9	2.1
Duration of antiretroviral treatment (years)*		
0-3 years	355	79.8%
> 3 years	68	16.4%

* Some data were missing from the records

Under half of the primary caregivers indicated that their children experienced some pain (scored > 2 on the WBFS) at the time of the interview (188: 44.8%). The pain was estimated by the caregiver as greater than 4 on the WBFS in a third of the children (141: 33.5%). Generally, intensity of more than 4 is considered to be significant pain. There was no difference in the mean age of the children who experienced pain, and those who did not: 7.40 and 6.96 years respectively (p-value = 0.123).

Table II summarises the relationship between age and pain > 2 on the WBFS.

Table II: Relationship between age and pain (> 2 on the Wong-Baker FACES™ Pain Rating Scale)

Age in months	Pain > 2 on WBFS	%
36-60 (3-5 years)	86	46
60-84 (5-7 years)	28	15
84-108 (7-9 years)	39	21
108-156 (9-13 years)	35	18
Total	188	100

A third of the caregivers reported that pain was present for at least eight hours during a 24-hour period, and that pain was present while resting. A third of the caregivers (29.3%) reported that pain interfered with daily and physical activities, such as walking, playing and running. In 10.6%, pain was also related to other activities, for example, swallowing.

Table III summarises the temporal aspect of pain, and the effect of pain on daily activities. Table IV summarises the reported sites of pain.

Table III: Temporal aspects of pain and effect of pain on daily activity

Features of pain	n	%
Pain > 2 on WBFS	188	44.8
Pain > 4 on WBFS	141	33.5
Duration of pain > 8 hours	161	38.4
Pain while resting, or sleep disturbance due to pain	151	36.4
Pain during activity	121	29.3
Pain related to swallowing	45	10.6

Table IV: Reported sites of pain

Pain sites described by the primary caregivers	n	%
Headache	58	13.8
Abdominal pain	28	6.7
Chest pain	27	6.4
Body pain	22	5.2
Earache	21	5.0
Nose pain	5	1.2
Painful gums	2	0.5
Mouth pain	1	0.2
Painful limbs and feet (peripheral neuropathy)	16	3.8
Genital pain (warts)	3	0.7
Painful lymph nodes	2	0.4
Backache	1	0.2
Joint pain	2	0.5

Nociceptive pain (visceral or somatic) was most commonly described (40.2%), while painful limbs and feet (which the researcher made an assumption to be neuropathic pain) were found in 16 (3.8%) children.

There was a significant association between CD4 count and pain (p -value = 0.040). Those with a CD4 percentage > 25% reported less pain than those with a CD4 percentage < 25%. Paracetamol was the most commonly used analgesics (66.7%). Among the children with assumed neuropathic pain, only a minority (3%) were on medication that might improve neuropathic pain (such as amitriptyline), and the remainder were not on any pain medication. Other medications that were dispensed as a form of analgesia included the local application of cream, and the use of nebulisation with β_2 agonists for chest pain.

Discussion

A quarter of the caregivers were grandmothers, and this may be reflective of the high proportion of HIV-positive children who are being cared for by elderly caregivers in this population. These caregivers often care for a number of young children,

and ART education, adherence counselling and support must consider that the caregiver may be elderly and have his or her own health issues.²¹

It is of concern that half of the caregivers reported that their children experienced pain, and this finding is comparable with the findings of other studies.^{10,17,20} A limitation of this study is that the data collection tool did not consider the length of time that the pain had been present, and so it is not possible to say whether it was acute or chronic. This distinction is critical, as the management of acute pain differs greatly from the management of chronic pain.²² Acute pain tends to resolve when the acute problem is treated. For example, earache will resolve when otitis media is treated. Chronic pain may be more difficult to assess and treat in young children.

A third of the participants reported that their children experienced pain for at least eight hours in a 24-hour period. Thirty-six per cent reported pain while resting or sleep disturbance, 29.3% reported activity-related pain (either walking or running), and 10.6% reported pain on swallowing. Other studies have shown that typically, pain that is associated with activities limits the participation of children in physical activities, and restricts their social life.²³ Paracetamol, the analgesia that is most commonly used, is graded as a “weak” analgesia on the World Health Organization analgesia ladder.²⁴ The use of a β_2 agonist to manage chest pain requires further investigation, as does the use of creams (assumed to be local analgesia). Pain assessment and management should be an important component of HIV care. HIV care services need to be strengthened, with a particular emphasis on pain recognition and management. Palliative care services stress the importance of healthcare providers having skills and knowledge in pain management, and could be a resource in the management of these children. Reasons for the low use of analgesia, despite a high prevalence of reported pain, must be further investigated.

In this study, pain was not associated with age, and this finding was in contrast with the findings of other studies that documented that younger children experienced more pain than older children.¹⁰ In our study, the duration of time on ART did not affect reported pain prevalence or pain type. However, in studies carried out on adults, it appeared that ART reduced pain.²⁵ Those children with a low CD4 experienced the most pain, and this finding is similar to the findings of previous studies.¹⁶ The majority of children in this study were on a first-line ART regimen, that includes the use of stavudine. The South African National Department of Health’s latest guidelines for ART have replaced stavudine with abacavir,²⁶ due to toxicity which includes peripheral neuropathy associated with stavudine use. These guidelines were rolled out in June 2010, and it is of concern that by December 2010, only nine (2.1%) children were on

the regimen that included abacavir. However, this may be explained by bias introduced by the sampling method used.

The head has been reported as a common site of pain in HIV infection.^{4,7} In this study, too, the most common pain was reportedly that of headaches, according to the caregivers. The sources of headache may be multiple. For example, sinusitis, intracranial infections, referred pain, advanced-stage HIV infection and the side-effects of ART may all cause headaches, and further research is required to clarify the underlying causes. Because of the nature of this study, it was not possible to determine the origin of the headaches. Similarly, further research needs to be carried out to clarify the cause of pain in other sites, e.g. abdominal and chest pain.

Symptoms suggestive of neuropathic pain were found in 15 (3.6%) children. This prevalence is lower than that found in an adult population.⁹ A minority of these children was given analgesia that was specific for neuropathic pain, and this requires further study.

Study limitations

This was an exploratory study, and highlights areas for further research. The study was conducted over a relatively short period, and it may be that, over time, the pain profile alters on ART. For example, in those children who were just starting ART, it was expected that pain due to opportunistic infections would decline as the immune system recovered, and as opportunistic infections were treated. A convenience sampling strategy was employed, and although patients presented in a random order to the clinic, the pain profile of those who were not sampled may differ substantially from the pain profile of those who were. Caregivers was asked to assess pain in children using the WBFS, a tool designed to be used by children to report pain.¹⁹ Although studies have shown that there is concordance between caregiver assessment of pain, and a child's own assessment of pain,^{10,17,20} the use of the WBFS tool in this manner may have introduced information bias. The researchers made several assumptions, including the belief that pain in the limbs and feet was due to neuropathy, which may not have been the case. Other limitations include the fact that no distinction was made between acute and chronic pain, and no follow-up was undertaken to see whether pain was reduced at subsequent visits. The non-distinction between acute and chronic pain impacts greatly on the assessment and management of pain, and it is recommended that future studies focus more on this distinction.

Conclusion

This exploratory study revealed that pain in children on ART is common, and can interfere with their daily living activities. In general, pain was significant, as indicated by the WBFS, and pain was more common in children who had a lower CD4 count. The study indicates that analgesia may

not be appropriate. For example, paracetamol was offered in instances in which pain was reported to be significant. There is a need for further research, and in particular, in assessing whether pain is acute or chronic.

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