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Correspondence concerning this article should be addressed to Professor Robin J Green; Department of Paediatrics and Child Health, University of Pretoria, PO Box 667, Pretoria, South Africa | Phone: +2712 354-5276 | Email: robin.green@up.ac.za

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Disease progression unrelated to passive environmental tobacco smoke exposure in HIV-infected children

Robin J Green (1) *, Piet J Becker (2), Denise Labuschagne (1), Omolemo P Kitchin (1), Refiloe Masekela (1)

1) Division of Pediatric Pulmonology, University of Pretoria, South Africa

2) Biostatistics Unit, South African Medical Research Council, South Africa

* Corresponding Author

ABSTRACT

Background: Studies in adults have shown that smokers have a higher risk of death and a higher risk of developing AIDS. Other studies have shown an increased risk of smoking HIV-positive adults to infections. There is, however, no available data on HIV-related disease progression in environmental tobacco smoke exposed children.

Aim: The aim of this study was to determine if passive ETS exposure is a risk factor for HIV-related disease progression in children.

Methods: An observational, descriptive study of children attending the HIV Clinic at a District Hospital during October 2007.

Results: 127 children were enrolled. 47 (37%) were living in households where adults smoke. There was no difference between passive tobacco smoke exposed children and those not exposed for CD4 percentage ($p=0.66$) or HIV stage ($p=0.70$). HIV-infected children were no more likely to be admitted to hospital if caregivers smoked ($p=0.70$).

Conclusion: This study of HIV-infected children, did not reveal significant differences in objective measures of HIV status (CD4 count and HIV stage), nor increased rates of more severe illness (hospitalization) between children exposed to passive ETS and those not exposed. This is in contra-distinction to adult studies. The small sample size may limit comparison in this study.

Keywords: HIV-infected children, Passive environmental tobacco smoke

Running head: HIV status, environmental tobacco smoke exposure

Background

Cigarette smoking has been associated with increased morbidity and mortality in Human Immunodeficiency Virus (HIV)-infected adults.^{1,2} In the Strategies for Management of Antiretroviral Therapy Clinical Trial, 40.5% of HIV-infected subjects were current smokers and 24.8% were former smokers.¹ The mortality of these individuals was higher in current smokers (hazard ratio (HR)=2.4; $p < 0.001$) and there were more serious illnesses (major cardiovascular disease (HR=2.0; $p = 0.002$), non-AIDS cancer (HR=1.8; $P = 0.008$), and bacterial pneumonia (HR=2.3; $p < 0.001$)), in smokers.¹

In addition to the risks of cigarette smoking it seems that the prevalence of smoking is higher in HIV-infected individuals. This has been clearly shown for African HIV-infected individuals.^{3,4}

Increased morbidity in smoking HIV-infected adults may take many forms. Importantly smoking increases the risk for secondary infection, including tuberculosis,⁵ cardiovascular disease^{1,6} and malignancy.^{1,7}

Studies in adults have revealed that smokers on highly active anti-retroviral therapy (HAART) had poorer viral responses (HR=0.79; 95% confidence interval (CI)=0.67-0.93) and poorer immunologic responses (HR=0.85; 95%CI=0.73-0.99).⁸ A greater risk of virological rebound (HR=1.39; 95%CI=1.06-1.69) and more frequent immunologic failure (HR=1.52; 95%CI=1.18-1.96) were also observed among smokers. There was a higher risk of death (HR=1.53; 95%CI=1.08-2.19) and a higher risk of developing AIDS (HR=1.36; 95%CI=1.07-1.72), but no significant difference between smokers and non-smokers in the risk of death due to AIDS. These authors concluded that 'some of the benefits provided by HAART are negated in cigarette smokers'.⁸

These findings may relate to research demonstrating that chronic exposure of mice and rats to cigarette smoke or nicotine inhibits T-cell responsiveness, which may account for the decreased antibody response to T-cell dependent antigens seen in these animals.⁹

Other studies have confirmed an increased risk of smoking adults to infections. Current smokers were more likely than never smokers to develop bacterial pneumonia (HR=1.57; 95%CI=1.14-2.15; $p = 0.006$), oral candidiasis (HR=1.37; 95%CI=1.16-1.62; $p = 0.0002$).¹⁰ The AIDS dementia complex is also more likely in smoking HIV-infected adults (HR=1.80; 95%CI=1.11-2.90; $p = 0.02$).¹⁰

These increased risks have led authors to call for incorporating advice on smoking cessation into HIV education programs and consultations.¹¹

The natural progression of HIV in children differs from that of adults. Immaturity of the immune system leads to more rapid progression of HIV-related infection.¹² There are various factors that contribute to the rate of HIV progression in children. These include maternal viral load, genetic composition, immunological profile of the child and possibly some environmental factors.¹³

Despite a vast literature on the health effects of cigarette smoking on HIV-infected adults, there is no study demonstrating an effect of passive cigarette smoke exposure on the health of HIV-infected children.

Objective

The main objective of this research was to determine if passive environmental tobacco smoke (ETS) exposure is a risk factor for HIV progression and disease severity in children.

Methods

An observational, descriptive study of children attending the HIV Clinic at Tshwane District Hospital, Pretoria, South Africa during October 2007. A convenience sample of parents attending the clinic for routine follow-up of their children's disease was selected. Each attendee completed a questionnaire relating to their smoking habits and the HIV status of their children. Ethics approval was obtained from the Research Ethics Committee of the University of Pretoria and all subjects signed informed consent and assent where appropriate.

HIV infection was deemed to be present if HIV-enzyme linked immune-sorbent assay (ELISA) was positive in children older than 18 months of age. Children younger than 18 months required both a positive HIV ELISA and positive HIV polymerase chain reaction (PCR).

The World Health Organization (WHO) HIV clinical staging¹⁴ was used to determine HIV stage of disease.

The Architect (Abbott Diagnostics) and MODULAR E170 (Roche Diagnostics), fourth generation HIV ELISA assays (detecting both p24 antigen and HIV antibodies simultaneously), were used for HIV serology. Qualitative HIV PCR was performed using Amplicor HIV-1 DNA assay, version 1.5 (Roche molecular systems). CD4 count measurements were performed on Epics instrument (Beckman Coulter Diagnostics) using a pan leukocyte gating (PLG) method.

Statistical Methods

Stata 10 (eStataCorp LP, 4905 Lakeway Drive, College Station, Texas 77845 USA) was used for computations. The two-sample t test with equal variances was performed for

analysis of continuous variables while the Fischer exact test or Pearson Chi-square test was performed for analysis of categorical variables.

Results

Information was obtained from 127 accompanied HIV-infected children. Of these, 47 (37%) were living in households where adults smoke. There was not a significant difference in the mean age (at the time of the study) between ETS exposed and non-exposed children (4.6 months vs 4.9 months ($p=0.66$)). There was also not a significant difference for age of HIV diagnosis between ETS exposed and non-exposed children ($p=0.50$). 118 (93%) of the children were on HAART. At the time of the study the protocol for HAART was Stavudine, Lamivudine and Kaletra as first line therapy.

ETS exposed children had a 1.1% lower CD4 percentage than children who had no passive smoke exposure. This was not statistically significant ($p=0.59$) (Fig. 1).

There was not a significant relationship between cigarette smoke exposure and HIV-stage ($p=0.70$) (Table 1).

There was not a significant relationship between the number of cigarettes smoked daily by the caregivers and the CD4 count ($p=0.9661$), nor the HIV stage ($p=0.4949$), of the of the ETS exposed children.

Thirty two of the 127 children were hospitalized in the last month. This group included all of the children not on HAART and only 13 of the 32 children that were hospitalized in the last month had care-givers who smoked. The ETS and non-ETS groups did not differ with respect to hospitalization ($OR=1.17$; $95\%CI=0.47-2.86$; $p=0.70$) (Table 2).

The proportion of smokers amongst parents with secondary education does not differ significantly from those without secondary education ($p=0.595$; 38.2% vs 29.4%).

Conclusion

This is the first study reported of the effects of passive ETS exposure on the health of HIV-infected children.

The study reveals that rates of cigarette smoking are higher in parents of HIV-infected children than the South African national average.¹⁵ This may support data available from other studies in Africa demonstrating that smoking was more common in HIV-infected adults.^{3,4}

This study of 127 HIV-infected children attending an HIV treatment clinic did not reveal statistically significant differences in objective measures of HIV status (CD4 count and HIV stage) between children exposed to ETS and those not exposed. This is in contradiction to most adult studies.

In addition there is no apparent effect of ETS exposure on clinical disease severity as indicated by need for hospitalization. ETS exposure has been linked to greater risk of asthma exacerbations in asthmatic children¹⁶ and it seems unlikely that this is not true of disease exacerbations in HIV-infected children. Either the study sample was too small to draw meaningful conclusions or the diseases associated with HIV-infection are of such a nature to render the additional effects of ETS insignificant.

Since most children were on HAART the effect of this form of therapy in relation to ETS exposure could not be assessed. Only a much larger study group would enable teasing out of the effect of cigarette smoke exposure on HIV-infected children prior to

commencement of HAART or the possible effect of ETS exposure on efficacy of HAART.

The small sample size may limit comparison in this study. In addition the range of age in these children would mask some of the consequences of increasing age on HIV progression in individual patients. A large age-stratified study would be useful.

Conflict of Interest:

All authors disclose no financial and personal relationships with other people or organisations that could inappropriately influence (bias) this work.

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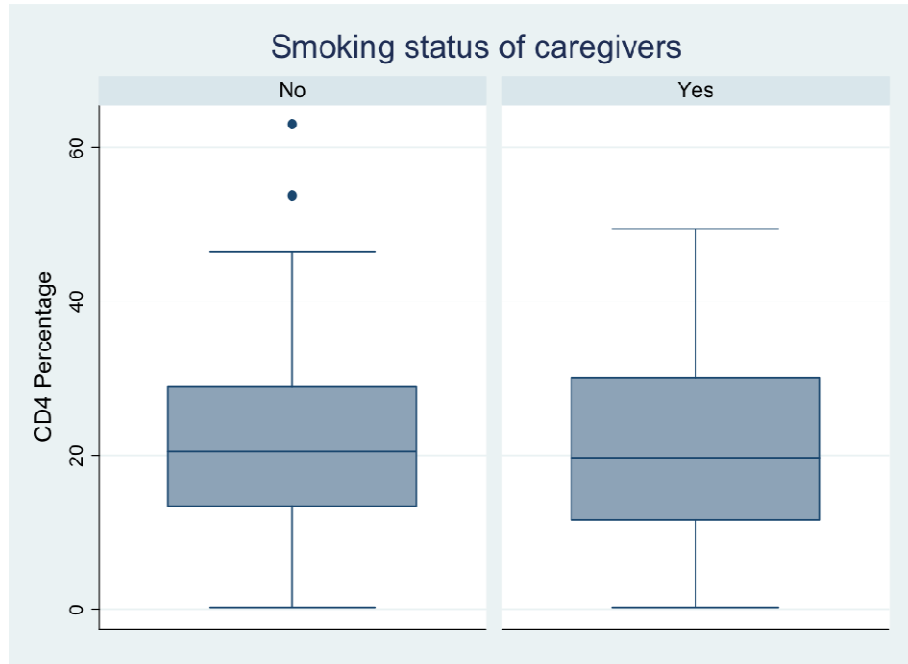


Figure 1: Box and whisker plots for smoking status of caregivers compared to CD4 percentage of their HIV-infected children

Table 1: Smoking status of caregivers versus HIV-stage of children, frequency (%).*

HIV Stage	Smoking		Total
	No	Yes	
1	8 (11·9)	2 (5·0)	10 (9·4)
2	7 (10·5)	5 (12·5)	12 (11·2)
3	38 (56·7)	23 (57·5)	61 (57·0)
4	14 (20·9)	10 (25·0)	24 (22·4)
	67 (100)	40 (100)	107 (100)

* Staging data unavailable on 20 children.

Table 2: Smoking status of caregivers versus hospitalization of HIV-infected children, frequency (%)

		Hospitalization		Total
		Yes	No	
Smoking	Yes	13 (27·1)	35 (72·9)	48 (100)
	No	19 (24·1)	60 (76·0)	79 (100)
		32 (25·2)	95 (74·8)	