ORIGINAL ARTICLE

Oral complication risks after invasive and non-invasive dental procedures in HIV-positive patients

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BACKGROUND: Limited published scientific evidence is available to provide guidance to clinicians on possible increased risks of invasive oral procedures associated with the human immunodeficiency virus (HIV) status of the patient. The aim of this study was to assess postprocedural complications in patients infected with HIV.

MATERIAL AND METHODS: This was a retrospective cross-sectional study of the records of 101 consecutive HIV patients treated at the School of Dentistry of Madrid Complutense University and Sandoval STD Clinic in Madrid between January 2003 and February 2005. Data were gathered by an experienced dental practitioner using a structured epidemiological questionnaire for information on gender, age, HIV transmission category, medical history, hepatitis B virus (HBV) or hepatitis C virus (HCV) coinfection and other diseases, TCD4+ and TCD8+ count, HIV viral load (VL), platelet count, neutrophil count, international normalized ratio and haemoglobin level; tobacco and alcohol intake, highly active antiretroviral treatment and presence of oral lesions. Information was also collected on complications related to dental treatment (invasive or non-invasive) during the previous 6 months. Chisquared test and Fisher's exact test were used to establish statistical significance.

RESULTS: Data were gathered on 314 dental procedures in 101 patients. The overall complication rate was 2.2% (7/314); in 147 invasive procedures, seven complications (4.8%) were documented (one persistent pain, two prolonged bleeding, three infections, one bone sequestrum) including extractions, periodontal scaling, endodontic treatment and biopsy. No differences were found in TCD4+, TCD8+, platelet count, HBV or HCV co-infections or HIV VL between patients with and/or without complications. Patients with complications were mainly in B stage

of HIV disease (P = 0.020). Oral lesions and smoking habit >20 cig day⁻¹ were documented in 83.3% (P = 0.086) and 50% (P = 0.060), respectively, of patients with complications.

CONCLUSIONS: The complication rate was 2.2% overall and 4.8% after invasive dental procedures. Presence of oral lesions, smoking habit or HIV clinical stage B may be predictive factors for oral complications in HIV patients. No relationship was found between complications and virological, immunological or other laboratory values. Studies with wider samples and negative control group are warranted to confirm the absence of an association between HIV positivity and higher risk of oral complications. Oral Diseases (2007) 13, 110-116

Keywords: AIDS; dental care; dental complications; dental treatment; HIV

Introduction

Countries with widespread availability of antiretroviral therapy (North America and Western Europe) have experienced a major reduction in the incidence of new acquired immune deficiency syndrome (AIDS) cases and in the mortality associated with the disease, especially after the introduction of highly active antiretroviral treatment (HAART). As a result, HIV infection is becoming a chronic disease that is generating a greater demand for health care, including dental care (Diz *et al*, 1998; Diz-Dios et al, 1999). Patients' awareness of their infected state commonly increases their concern about their oral health, leading to improved hygiene routines and an increased frequency of visits to the specialist (McCarthy et al, 1996; Vazquez et al, 1997). Most of these consultations are for conventional dental therapy rather than for treatment of oral manifestations of the human immunodeficiency virus (HIV) infection (Porter et al. 1996).

Several authors have evaluated dentists' attitudes towards the treatment of HIV-infected patients

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(Gerbert, 1987; Cohen and Grace, 1989; Moretti et al, 1989; Dove and Cottone, 1990; Kunzel and Sadowsky, 1991). Most studies conclude that a majority of dentists acknowledge their ethical obligation to treat HIVinfected patients but remain reluctant to do so, mainly citing fear of infection and the loss to their practice of seronegative patients (Glick et al, 1994; Sadowsky and Kunzel, 1994). Some professionals have also called for these patients to be treated in specialized centres (Kunzel and Sadowsky, 1991), based in part on the supposition that dental procedures on this patient population may be associated with a higher complication rate (Glick et al, 1994; Vazquez et al, 1996). A related issue of interest is whether patients inform their dentists about their HIV seropositive status before dental treatment. In a survey of a randomly selected sample of 50 HIV-infected patients at Sandoval STD clinic, 65% admitted not informing their dentists for fear of rejection or discrimination (J Campo, J Del Romero unpublished data).

Limited published scientific evidence is available to guide clinicians about the possible increased risks of invasive oral procedures associated with the HIV status of the patient. The aims of this study were to: (i) assess the post-dental procedure complication rates in patients infected with HIV undergoing dental treatment at the Sandoval STD Clinic and School of Dentistry of Madrid, Spain; and (ii) evaluate a possible relationship between oral complications and the main immunological, virological and other laboratory parameters in these patients.

Methods

A retrospective cross-sectional study was conducted at two centres: the Oral Medicine Clinic of the School of Dentistry of Madrid Complutense University and the Sandoval STD Clinic, Madrid. A structured questionnaire was administered to 101 adult HIV-infected volunteers, and their dental charts were reviewed. Laboratory analysis results [viral load (VL), TCD4+ and TCD8+ count, and TCD4+ and TCD8+ percentage, platelet count, haemoglobin level, neutrophil count and, when available, prothrombin time and international normalized ratio (INR)] closest in time to the dental treatment were considered, excluding analyses performed more than 2 months after or before treatment. All patients were tested for HIV antibody using an enzyme-linked immunosorbent assay and positive results were confirmed by Western blot. Serum TCD4+ lymphocyte count was performed by flow cytometry, using a CoulterTM (Epics Profile II Analyzer; Izasa, Spain) and quantitative VL measurements by QuantiplexTM HIV RNA 2.0 Assay (bDNA). All patients were over 18 years old and signed their informed consent to participate in the study. Confidentiality of records was maintained by removing all names and other identifiers in the questionnaires and data bases used.

A structured epidemiological questionnaire was used to gather study variables, grouped as follows: (i) Social and medical variables: age, gender, HIV infection route, antiretroviral treatment (ART; mainly current HAART), consumption of alcohol, tobacco or other drugs, hepatitis C virus (HCV) coinfection and presence of oral lesions (EEC-Clearinghouse, 1993); (ii) Immunological and virological parameters: TCD4 + cell/ percentage, TCD8 + cell/percentage and VL and TCD4 + /TCD8 +; (iii) Other laboratory values: haemoglobin level, platelet count, prothrombin time, INR and neutrophil count; and (iv) Treatment variables: invasive (periodontics, surgical extraction, simple extraction, endodontics, dental implant and biopsy) and noninvasive (prosthodontics, operative dentistry and others) dental procedures.

Invasive procedures were defined as any treatment that broke the mucosal barrier resulting in bleeding. This differentiation between invasive and noninvasive procedures was related to the American Heart Association's guidelines for prophylactic antibiotic medications where there was risk of causing bacteraemia (Glick *et al*, 1994).

All dental procedures with associated complications were recorded. Complications were defined as: excessive bleeding from extraction site at \geq 48 h after extraction reported by the patient or requiring medical attention; infection when pus was visible in the wound after extraction or presence of abscess after endodontics that required antibiotic treatment; postoperative flare-up requiring treatment before the next appointment; dry sockets with > 36 h of postoperative pain and partial or total loss of blood clot from extraction site; delayed postoperative healing, recorded when the wound was not completely epithelialized by day 21; and postextraction complications other than the bleeding and infections already noted, e.g. persistent pain, documented when the patient required repeat analgesic dose at ≥48 h post-extraction (Dodson, 1997a).

Invasive and noninvasive procedures were analysed globally to estimate the overall complication rate. Statistical analysis was performed using the Statistical Package for Social Sciences Software (SPSS 10.0 for Windows 10.0; SPSS Inc., Chicago, IL, USA). Chisquared and Fisher's exact test were then used to compare differences in proportions of study variables (sociodemographic, immunological, VL and laboratory values) between patients with and without oral complications. P < 0.05 was considered statistically significant.

Results

Between January 2003 and February 2005, 101 HIVpositive patients were enrolled in the study cohort. Table 1 shows a summary of descriptive statistics for the study sample, including demographics, medical history [e.g. HCV, hepatitis B virus (HBV) co-infections, syphilis or pneumonia], HIV clinical stage, immunological and virological values, ART (HAART or others) and other data, including tobacco and alcohol usage and presence of oral lesions.

More than half of the patients included in the study (59.4%) were homo/bisexual men; 21.8% had a history

Study variables	n	%
Gender		
Male	82	81.2
Female	19	18.8
Age, years (mean \pm s.d.)	35.31 ± 6.82	
Transmission group		
IDU	22	21.8
Homosexual	60	59.4
Heterosexual	18	17.8
Blood transfusion	1	1.0
HIV clinical stage (CDC, 1992)		
A	58	57.4
В	25	24.7
C	8	7.9
Unknown	10	9.9
HIV CD4 cell count		
stage (CDC, 1992)		
1. $> 500 \text{ CD4 ml}^{-1}$	44	44.4
2. 200–500 CD4 ml ⁻¹	42	42.4
3. $< 200 \text{ CD4 ml}^{-1}$	13	13.1
CD4+, cell mm ⁻³ (mean \pm s.d.)	519.6 ± 349.6	
CD8+, cell mm ⁻³ (mean \pm s.d.)	1176.1 ± 492.7	
$CD4/CD8$ (mean \pm s.d.)	0.48 ± 0.32	
Viral load – median (copies ml ⁻¹)	19493 (range 48-500	
HCV positive	26	25.7
AntiHBc positive	35	34.7
HBAg positive	11	10.9
HBV vaccine	36	35.6
HAV positive	27	26.7
Syphilis positive	17	16.8
Antiretroviral treatment		
Never	74	73.3
Current (HAART)	22	21.8
Previous ^a	4	4.0
Unknown	1	1.0
STI previous – yes	40	39.6
Tuberculosis – yes	6	5.9
Pneumonia – yes	8	7.9
IDU – yes	14	13.9
Non-injected drug users – yes	50	49.5
Alcohol use > 80 cc day ⁻¹	6	5.9
Current alcohol user – yes	63	62.4
Tobacco > 20 cig day ⁻¹	18	17.8
Current tobacco smoker – yes	52	51.5
Oral lesions – yes	47	46.5
Other medications	34	33.7
Preoperative antibiotic use – yes	7	7.7
Postoperative antibiotics – yes	9	8.9

IDU, injection drug users; STI, sexually transmitted infection; s.d., standard deviation; HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HAART, highly active antiretroviral treatment.

^aHAART or other regimen.

of intravenous drug use (IDU); 57.4% were asymptomatic, 39.6% had a history of sexually transmitted infection, 62.4% were current alcohol users and 51.5% were tobacco smokers (17.8% smoked > 20 cig day⁻¹). Only 21.8% of the patients were receiving HAART at the time of the study.

Other medications (e.g. antibiotics, antipsychotics, anxiolytics, interferon or methadone) were being taken by 33.7% of the patients at the time of the study (especially by patients with pneumonia and tuberculosis). Only seven patients received preoperative antibiotics before the dental treatment.

Oral complication rates after dental procedures

Data were gathered on 314 dental procedures in 101 patients. The overall complication rate was 2.2% (7/314). Seven complications were documented (one persistent pain, two prolonged bleeding, three infections and one bone sequestrum) in 147 invasive procedures (4.8%) including extractions, periodontal scaling and endodontic treatment (Table 2). All complications were minor and were managed on an outpatient basis. Postoperative antibiotics were administered to patients with infection after endodontic treatment. No complications were recorded after noninvasive dental procedures.

Relationship of study variables with presence or absence of postoperative complications

Table 3 summarizes the bivariate analysis of the social and medical variables grouped by presence or absence of complications. There were no statistically significant differences in age, gender or infection route (P > 0.293) or in HCV co-infection or (HAART) treatment (P > 0.340) between patients with and without complications.

Eighty per cent of patients with complications were in clinical stage B vs 20% in stage A (P = 0.029). Oral lesions and smoking habit > 20 cig day⁻¹ were documented in 83.3% (P = 0.086) and 50% (P = 0.060) of the patients with complications respectively. Interestingly, the alcohol intake of all patients with complications was <80 g day⁻¹, and preoperative antibiotics were received by 33.3% of patients with complications.

Table 4 shows the relationship between presence of complications and immunological, virological and other laboratory values. The mean TCD4+ cell count for all patients was 519.6 cells mm⁻³ and for patients with complications was 562.4 cells mm⁻³. There were no differences in TCD4+, TCD8+, platelet count or HIV VL between patients with and without complications.

Discussion

Immunologically compromised patients may be incapable of a sustained, controlled and effective immune response to exogenous trauma, implying a high risk of developing postoperative complications (Ficarra, 1992; Yee and Cristou, 1993). Thus, a higher percentage of HIV-positive than HIV-negative patients presented with postoperative infections after surgery for maxillofacial trauma (11.8% vs 4.4% respectively) (Martinez-Gimeno *et al*, 1992), and a higher risk has been hypothesized for HIV-infected patients after oral surgery (Dodson *et al*, 1994; Dodson, 1997a; Diz-Dios *et al*, 1998).

This issue of complications after simple or surgical tooth extraction in the outpatient setting is of special relevance. Various authors have studied the incidence of complications after simple tooth extraction in HIV-infected patients, and they reported similar percentages to those found in uninfected patients (below 5%) (Barr *et al*, 1989; Porter *et al*, 1993). Besides finding a complication rate of 4.1% after simple extraction in these

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Table 2 Complication rates after invasive and noninvasive dental procedures.

	No. persons (%)	No. procedures	No. complications	Complication rate (%)
Invasive dental procedures				
Periodontal therapy				
Prophylaxis	33 (34.4)	45	0	0
Scaling and root planning	8 (8.3)	17	1^{a}	5.8
Surgical therapy	3 (3.1)	4	0	0
Surgical tooth extraction	4 (4.2)	7	0	0
Simple tooth extraction	15 (15.6)	47	3 ^b	6.4
Dental implant	1 (1.0)	4	0	0
Biopsy	1 (1.0)	1	0	-
Endodontics	14 (14.6)	22	3°	13.6
Subtotal	79	147	7	4.8
Noninvasive dental procedures				
Operative dentistry	28 (19.7)	124	0	-
Prosthodontics	11 (16.6)	41	0	-
Other treatments	2 (3.0)	2	0	-
Subtotal	41	167	0	0
Total dental procedures	120	314	7	2.2

^aProlonged bleeding.

^bPain, bone sequestrum and prolonged bleeding. Infections (three cases), treated with antibiotics.

 Table 3 Characteristics of patients according to presence or absence of complications Social and medical variables

	Patients with complications	Patients without complications	P-value
Total	6 (6.2)	90 (93.7)	
Male	5 (83.3)	73 (80.1)	1.000
Age, years (mean \pm s.d.)	38.8 ± 10.9	34.2 ± 8.6	0.293
HIV clinical stage ^a			
Α	1 (20)	53 (65.4)	0.029
В	4 (80)	20 (24.7)	
С	0	8 (9.9)	
HIV CD4 cell count stage ^a			
$1. > 500 \text{ CD4 ml}^{-1}$	3 (60)	41 (43.6)	1.000
2. 200–500 CD4 ml ⁻¹	2 (40)	40 (42.6)	
3. $< 200 \text{ CD4 ml}^{-1}$	0	13 (13.8)	
Infection route			
Homosexual activity	5 (83.4)	52 (57.8)	0.396
HCV co-infection	2 (33.3)	21 (24.4)	0.637
Never received ART treatment ^b	3 (50)	66 (74.1)	0.340
HAART ^c	3 (50)	19 (20)	0.115
Non-injected drug user	3 (50)	45 (59.2)	0.688
Alcohol $< 80 \text{ g day}^{-1}$	6 (100)	84 (95.4)	1.000
Tobacco > 20 cig day ⁻¹	3 (50)	13 (14.8)	0.060
Presence of oral lesions	5 (83.3)	38 (42.2)	0.086
Receipt of preoperative antibiotics	2 (33.3)	5 (5.9)	0.015
Receipt of postoperative antibiotics	3 (50)	6 (7.1)	0.010

Values are expressed as n (%). HIV, human immunodeficiency virus; HCV, hepatitis C virus; HAART, highly active antiretroviral treatment.

^a*P*-value, comparing clinical B stage *vs* clinical A stage and 200–500CD4 ml⁻¹ *vs* > 500CD4 ml⁻¹. ^bHAART or other regimens.

^cHAART at the moment of the study.

patients, Glick *et al* (1994) reported a rate of 11.8% after surgical extraction, similar to the percentage found in HIV-negative patients (Oikarinen and Rasanen, 1991). Although the original aim of the present study was to assess complication rates after dental procedures in patients at all stages of HIV infection, the group in clinical stage C (AIDS) were excluded from the statistical analysis because of the small sample size of these patients. A complication rate of 5.6 % (3/54) was found after tooth extraction. The overall complication rate was

lower in comparison with findings reported by Dodson (1997a), who found rates of 22.4% in HIV-positive and 13.3% in HIV-negative patients after surgical and nonsurgical extractions, although the difference did not reach significance and complications were readily and rapidly treated in the outpatient setting. Furthermore, this difference was smaller when persistent postoperative pain was excluded (HIV-positive rate of 13% vs HIV-negative rate of 9%). Dodson (1997b) analysed variables with possible influence on the complication rate after 113

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	Patients with complications	Patients without complications	P-value
TCD4 + cell count (cell mm-3)	562.4 ± 150.1	504.9 ± 332.3	0.702
TCD8 + cell count (cell mm^{-3})	851.5 ± 358.1	1159.6 ± 492.7	0.222
TCD4 + /TCD8 +	0.57 ± 0.31	0.47 ± 0.32	0.491
Viral load RNA-HIV-1	$9820 \pm 14\ 380$	$53\ 848\ \pm\ 106\ 543$	0.317
(copies ml^{-1})	(10 518) ^b	(18 740) ^b	
Haemoglobin $< 14 (\%)$	1 (16.6)	30 (37)	0.415
Platelet count $< 150\ 000\ (\%)$	2 (33.3)	11 (13.4)	0.214
Prothrombin time $< 20 \text{ s} (\%)^{a}$	3 (100)	41 (95.3)	1.000
INR $< 1.0 (\%)^{a}$	1 (25)	7 (17.5)	0.566
Neutrophil count $< 1000 (\%)^{a}$	ŇA	2 (2.4)	_

 Table 4 Characteristics of patients according to presence or absence of complications: immunological, virological and other laboratory parameters

HIV, human immunodeficiency virus; INR, international normalized ratio; NA, not available.

^aData not available for all patients. ^bMedian value.

surgical extraction in seropositive patients, including delayed wound healing, alveolitis, persistent pain and bleeding. He reported rates above the normal values in the seronegative population, which range from 3% to 10%. Most authors agree that similar complication rates are observed in HIV+ patients at all clinical stages, including those with TCD4+ lymphocyte counts of < 200 cells ml⁻¹ (Porter *et al*, 1993; Glick *et al*, 1994; Ferreira et al, 1996). Moreover, these authors describe these complications as mild and easily managed (Pankhurst et al, 1994). The complications recorded in the present study can also be considered minor (one persistent pain, two prolonged bleeding, three infections and one bone sequestrum), and all were successfully managed without difficulty. The most frequently reported complication in the literature is alveolitis (Glick, 1994) followed by delayed wound healing (Porter et al, 1993). In the present study, the most frequent complication was infection followed by prolonged bleeding, although a larger sample is needed to obtain consistent results and conclusions.

Some authors recommend the routine administration of antibiotic prophylaxis before tooth extraction in patients with AIDS (Ferreira et al, 1996). However, others conclude that patients with CD4 cell counts below 100 cells mm⁻³ and patients on long-term antiretroviral chemotherapy should be evaluated for neutropenia. Patients should receive antibiotic prophylaxis before dental therapy only with absolute neutrophil counts below 500 cells mm⁻³ (Abel *et al*, 2000), who are not receiving prophylactic antibiotic treatment against pneumonia or tuberculosis (Dodson, 1997a). Antibiotic prophylaxis is also recommended in IDUs because they have a high incidence of bacterial endocarditis (Glick, 1995). In the present study, there were three cases of postoperative infections after endodontic treatment. Preoperative antibiotics were received by 33.3% (2/6) of the patients with complications, supporting that antibiotic prophylaxis should not be routinely administered to these patients.

Although thrombocytopenia is relatively common among HIV+ patients, especially among those in advanced HIV stages and with HCV coinfection, haemorrhagic complications after tooth extraction are rarer

(Porter et al, 1993; Glick et al, 1994; Coyle, 1997). Patients with platelet counts higher than 50 000 mm⁻ do not usually suffer postoperative complications, and most surgical treatments are contraindicated in patients with counts lower than 20 000 mm⁻³ due to the risk of spontaneous bleeding, petechiae or gastrointestinal bleeding (Doweiko, 1993; Patton, 1999, 2003). No relationship was found in the present study between a platelet count below 150 000 mm⁻³ and presence of postoperative complications. Some authors have concluded that simple tooth extraction can be performed in HIV-infected patients if they do not present with a coagulopathy (haemophilia or thrombocytopenia) (Dodson, 1997a). Scully et al (2002) found that around 20% of haemophiliacs developed post-oral surgical complications but presence of HIV infection had no notable influence on treatment outcome. Good haemostasis control can be achieved with a 2-min mouthwash of 5% tranexamic acid (10 ml) four times daily for seven postoperative days (Winkler et al, 1989; Borea et al, 1993; Ramstrom et al, 1993) or by the use of topical haemostatics such as absorbable gelatin or fibrin sponges (Patton, 1999).

Nevertheless, in the view of our group, recent haematological and coagulation test results must be obtained before planning surgical tooth extractions (Campo-Trapero *et al*, 2003; Patton, 2003). Caution must also be observed before undertaking extensive surgical interventions in patients with haemoglobin values below 6 g dl⁻¹, as adequate oxygen transport may be compromised and red blood cell transfusion is almost always indicated in this situation (Dental Treatment Considerations, 1995; Glick, 1996; Patton, 1999; Management of Dental Patients Who are HIV Positive, 2001).

The incidence of complications after conventional endodontic treatments is similar between HIV-positive and HIV-negative patients (Porter *et al*, 1993; Glick *et al*, 1994), and these complications can usually be controlled with non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotics. Although some authors advise against the endodontic treatment of molars (Diz-Dios *et al*, 1995), the prophylactic administration of antibiotics or NSAIDs is not necessary in these cases.

Although our results showed a higher rate of infections after endodontic procedures in HIV-infected patients, they were easily managed with postoperative antibiotic treatment.

The sole clinical variable that acted as a statistically significant predictor of post-procedural complications was HIV clinical stage B (CDC, 1992). Presence of oral lesions and smoking habit may also be related to these complications. In a previous study, only the TCD8 + count predicted post-extraction complications, although there was no need to delay treatment in an HIV-positive patient healthy enough to appear for examination as an outpatient (Dodson, 1997a). In the present study, no significant relationship was found between oral complications and immunological, virological or other laboratory values. We highlight that no differences related to HAART administration were observed.

One limitation of this study is the absence of a negative control group receiving the same treatment in the same setting as the HIV-positive group, as recommended by Patton *et al* (2002). The same authors also emphasized the need for substantially wider samples of HIV-infected patients in order to obtain significant results, given the relatively low prevalence of postoperative complications in the general population.

Conclusions

Although presence of oral lesions, smoking habit or HIV clinical stage B may predict oral complications in HIV-infected patients, these are not severe enough to warrant any delay in the dental treatment of these patients. The low overall complication rate after invasive dental procedures (4.8%) in this series indicates that general dentists can safely carry out routine dental care in HIV-infected adults without severe immunosuppression. Preoperative antibiotics should not be routinely administered to all patients, only in patients with neutropenia < 500 cells ml⁻¹ or to IDU patients as a prophylaxis against bacterial endocarditis. Studies with wider samples are required to confirm that HIV positivity alone does not increase the risk of oral complications.

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