

HIV Infection: A possible complication in corrective Craniofacial surgery

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A. Study Purpose and Rationale

The Honduran Medical Institute (HMI) funds and oversees a Plastic Surgery Training Program in Tegucigalpa, Honduras. The principal investigator (JH) is the president of this Foundation, which was formed with the cooperation of the Honduran Ministry of Health, the University of Honduras and Hospital Escuelas, the main teaching hospital for the medical school. The primary aim of the HMI is to improve the surgical and medical care of children with cleft lip and cleft palate, as well as other craniofacial abnormalities.

Since its inception in the mid-1990's, hundreds of children have undergone surgical repair of their cleft lip and palate abnormalities at Hospital Escuelas. Most of the children's wounds healed well with excellent cosmetic and functional results. A small number of children, despite excellent surgical repair, have been noted to have poorer healing and experienced wound breakdown during the post-operative period. While nutritional factors or trauma may play a role in wound breakdown, underlying systemic illness needs also to be considered. Presently there is no screening for HIV in the infants born with cleft lip and cleft palate in Honduras. We hypothesize that untreated HIV infection is responsible for a significant number of our poor surgical outcomes. Several clinical investigations have demonstrated that AIDS increases the risk of peri-operative morbidity and mortality (Robinson et al., 1987), while other studies have refuted this claim (Jones et al., 2002).

Our goal is to detect whether there is an increased risk of poor surgical outcome in a child who has untreated HIV. Through a prospective observational cohort design we seek to determine if children with craniofacial abnormalities and untreated HIV have increased wound breakdown and peri-operative complications. Children will undergo testing for HIV during a routine pre-operative clinic visit. The results of the HIV test will be withheld until a decision has been made as to whether the child has had a poor surgical outcome. Only after the post-surgical status has been determined will the results of the HIV test be explained to the parents. A mechanism will be set in place for HIV testing of the family should a child's status be confirmed as seropositive. Early detection and treatment of HIV will improve a child's life expectancy, medical, and surgical care.

Honduras has experienced a large increase in HIV infection in the general population and reports 60% of Central America's AIDS cases despite accounting for only 17% of the Central American population (Renjifo et al., 1999). Presently, Honduras is felt to have one of the highest incidences of HIV in Central America (Wheeler et al., 2001). Most of the infection (80%) is felt to occur through heterosexual transmission, putting women at the greatest risk of infection (Trujillo-Garcia et al., 1998). HIV census data is of varying quality and a cheap non-invasive surveillance test such as the saliva ELISA would give public health officials better data regarding the magnitude of the problem. Since newborns are not routinely screened at birth, vertical transmission from the mother to child goes undetected until opportunistic infections arise. Early identification of HIV infected patients would help maintain appropriate CD4 immunity levels and thereby greatly increase the child's life expectancy and ability to fight infection.

The secondary goal of this study is to identify children with HIV and craniofacial anomalies that present to the Craniofacial Clinic and to provide them with longterm care. Pediatric HIV care in Honduras was assessed during a recent visit to the Hospital Escuela. A pediatric HIV infectious disease specialist, Dr. Maricel Rivera, was contacted and stated her willingness to collaborate with the Plastic Surgery Training Team. The Hospital Escuela holds a weekly clinic where it evaluates existing HIV

infected children and monitors patient's triple drug therapy (AZT, 3TC, Efavirenz), CD4 count, and viral load.

Those children who test positive will be referred to Dr. Rivera's pediatric clinic for serum evaluation (Western Blot Confirmation) and medical care before additional surgery is planned. Identifying these children preoperatively should improve postoperative care and healing. In addition, by evaluating the extent of the problem, there will be heightened awareness in caregivers and medical staff of the need for Universal Precautions. At present, Universal Precautions are not standard practice at Escuelas Hospital.

B. Study design and statistical analysis

This study has a prospective observation design and looks for possible associations between HIV infection and poor surgical outcome. This study proposes to screen for HIV infection in children via a non-invasive saliva test. Also 10 ml of venous blood will be collected from each volunteer for traditional HIV testing purposes via ELISA and Western blot. A rigorous pre-operative screening will include the following laboratory analyses: CBC, CHEM 7, LFT's, finger stick, and chest x-ray. All abnormalities will be noted. Careful attention will be paid to signs of malnutrition, uncontrolled diabetes, and neutropenia. This information will be entered into a database for later analysis. The primary endpoint will be surgical complications within 30 days of the operation. Events will be classified as a complication if one of the following events transpires: death, re-hospitalization or return to operating room, intraoperative complication, clinically apparent bleeding, post-operative fever lasting more than 72 hrs, clinical diagnosis of infection requiring antibiotics outside of routine prophylaxis, other clinically significant events such as cardiac arrhythmia or renal failure, and detectable wound breakdown at follow up visit to clinic. Children will be tested at the clinic prior to receiving the surgery (Jones et al., 2002). A blinded third party will evaluate the saliva-ELISA swab.

The methodology of the proposed study is to perform an oral swab-screening test in all cleft lip and palate patients being considered for surgery in the HMI program. This oral testing is highly accurate and has been determined to have nearly a 100% sensitivity and specificity in several clinical trials (van den Akker et al., 1992; Carcaba et al., 1993; Connell et al., 1993; Lu Xs et al., 1994; Emmons et al., 1995; King et al., 1995; Gallo et al., 1997; King et al., 2000). A blinded 3rd party will have the results to the oral swab test within 15 minutes, and will randomly assign patient to a one of surgeons.

The blood samples will be shipped to an outside laboratory for confirmatory ELISA and Western Blot testing.

Triple blind analysis will occur. Power computation shows that 23 subjects are required for both the HIV and non-HIV trial arm to have a power of 81%. This calculation is based on Jones et al., 2002 data, which showed that 70% of untreated HIV patients had complications versus 41% of non-HIV, matched controls.

A two by two table will be created with HIV status compared to surgical outcome. Chi-square analysis will be conducted comparing the two proportions to see if there is a statistically significant difference with a $p < .05$

The secondary outcome will be a cross-sectional study to determine HIV prevalence in those children with Craniofacial abnormalities who present to the Plastic Surgery Clinic. Prevalence studies provide a wide range of descriptive data regarding disease characteristics and patterns, which can later be used to generate hypotheses for more analytical investigations.

C. Study Procedures

A saliva specimen will be collected from each participant in the study after an informed consent is obtained. Pre and post-test counseling will be provided. OraScreen collection swabs and tubes will be used to collect the saliva sample and samples will be kept at 4 degree Celsius until tested via the OraScreen HIV Rapid Test per manufacturer's protocol.

Also 10ml of venous blood will be obtained and shipped to laboratory for ELISA and Western.

D. Study Drugs

N/A

E. Medical Devices

Not Applicable

F. Study Questionnaires

Pre-test screening questions to assess risk factors for HIV and determination of pre-test probability as well as the predictive value of test.

G. Study Subjects

All children who present to Plastic Surgery Clinic and whose parents consent to the HIV testing

H. Recruitment of Subjects

Subject recruitment will be done through the Craniofacial Clinic at Hospital Escuelas in Tegucigalpa, Honduras. Honduran Plastic Surgery residents will discuss the benefits and risks of HIV testing in Spanish during pre and post-test counseling sessions. Patients who refuse testing will be surgically evaluated in a fair and non-biased fashion.

I. Confidentiality of Study Data

Oral swabs and bloods obtained from the patient will be coded by number and kept separate from the medical records at the Plastic Surgery clinic. All patients will be called in for their results and those who test positive will be referred immediately to an HIV infectious disease expert for medical evaluation and if need be a psychiatrist for counseling.

J. Potential Conflict of Interest

None

K. Location of the Study

Craniofacial clinic at Hospital Escuelas located in Tegucigalpa, Honduras.

L. Potential Risks

Pt. and family will become aware will become aware of HIV status if infected.

M. Potential Benefits

Pt. will receive longitudinal HIV care with antiretroviral medication. (AZT, 3TC, Efavirenz) This will improve quality of health and medical and surgical care

N. Alternative Therapies

Not applicable

O. Compensation to Subjects

None

P. Cost to Subjects

Care is through a government hospital at no cost to patient.

Q. Minors as Research Subjects

The study will be submitted to Dr. John Nicholson, Pediatric IRB

R. Radiation

Not applicable

S. References:

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2. King S.D., Wynter S.H., Bain B.C., et al. Comparison of testing saliva and serum for detection of antibody to human immunodeficiency virus in Jamaica, West Indies. *Journal of Clinical Virology* 2000; 19:157-161.
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