

Review

Sperm washing techniques address the fertility needs of HIV-seropositive men: a clinical review



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Abstract

It is estimated that nearly 40 million people worldwide are infected with HIV. HIV/AIDS prevalence among young people is high, with youth under age 25 years accounting for approximately half of all new infections. Nearly 1 million Americans are HIV-seropositive. Today, HIV-seropositive individuals live active and productive lives despite their illness, largely a result of prescribed highly active antiretroviral therapy (HAART). Most individuals are of reproductive age, and many desire to have children. Various assisted reproductive techniques have been used to reduce or eliminate infectious elements known to be present in semen so that isolated spermatozoa can be safely inseminated or used for intracytoplasmic sperm injection into oocytes. Presently, several European centres and a few US groups offer assistance to HIV seropositive men and their seronegative partners by performing either intrauterine insemination (IUI) or IVF. Since 1987, more than 3600 published attempts have been reported in which processed spermatozoa from HIV-seropositive men were used to establish pregnancy in HIV-seronegative women. Although the data remain observational, sperm washing techniques appear to be relatively safe and effective, offering HIV-serodiscordant couples an opportunity to have children.

Keywords: HIV, IUI, IVF–ICSI, serodiscordant, sperm washing

Introduction

It is estimated that nearly 40 million people are presently infected with HIV. Most are under the age of 25 years (UNAIDS, 2004). HIV infection occurs primarily in young, reproductively healthy individuals. The epidemic has affected hundreds of thousands of American men (CDC, 2001). Although many of these men are gay, others are engaged in heterosexual relationships and may desire children. A report of 2864 HIV-infected adults in the United States interviewed as part of the HIV Cost and Services Utilization Study confirmed this presumption, with approximately one-third of participants stating a strong desire to have children (Chen *et al.*, 2001). However, safe sexual practices require the constant use of condoms, which reduces the risk of transmitting virus to the uninfected partner, yet also precludes any hope of pregnancy.

Reproductive choices for HIV-serodiscordant couples are limited. Providing assisted reproductive care to couples in whom the male partner is known to be HIV-seropositive remains a subject of intense controversy (Anderson, 1999; Englert *et al.*, 2001; Sauer, 2003). Donor sperm insemination and adoption represent the only recommended 'safe' options for couples wishing to have a family. Yet, reproductive drive is very strong, and patients are known to take unreasonable risks in order to have a baby. It is therefore not surprising that HIV seroconversions of uninfected partners have occurred as a result of timed intercourse without a condom.

Sperm washing and insemination techniques

Sperm preparation techniques, commonly referred to as 'sperm washing', followed by intrauterine insemination (IUI),

has been suggested as a means of reducing the likelihood of horizontal transmission of HIV. Its clinical use in HIV infected men was first reported over a dozen years ago (Semprini *et al.*, 1992). Although subsequent published results from Milan (Semprini *et al.*, 1997, 1999) were encouraging, few practitioners in the United States were willing to offer IUI therapy for fear of infecting the seronegative partner and child. Early on, the Centres for Disease Control (CDC) recommended against treating HIV-serodiscordant couples following an alleged seroconversion in a woman inseminated with 'washed' spermatozoa from her HIV-seropositive husband (CDC, 1990). That position was recently reiterated (Duerr, 2003). Renewed calls for prohibition relate more to concerns regarding the safety of sperm washing and its quality control, as well as the relative absence of long-term follow-up data on outcomes. In many locales within the United States, intentionally inseminating a woman with spermatozoa from an HIV-seropositive man constitutes a criminal act. Unfortunately, many prohibitions were based upon information regarding the natural history of HIV infection prior to 1990, a time in which the disease was typically considered to be a terminal illness. Thus, the professional, civil, and possible criminal liabilities associated with treating HIV-serodiscordant couples continue to dissuade many clinicians from providing care.

Processed spermatozoa for IUI have been used in Europe, and numerous series (**Table 1**) document pregnancy success without HIV seroconversions (Brechard *et al.*, 1997; Semprini *et al.*, 1997; Vernazza *et al.*, 1997; Marina *et al.*, 1998; Tur *et al.*, 1999; Bujan *et al.*, 2001; Daudin *et al.*, 2001; Marina, 2001; Weigel *et al.*, 2001; Delvigne *et al.*, 2003; Gillling-Smith *et al.*, 2003). The large number of patients successfully treated is impressive, and these results may have influenced the American College of Obstetricians and Gynecologists (ACOG) and the American Society for Reproductive Medicine (ASRM) to revise earlier statements against caring for HIV-

serodiscordant couples. Both groups now recommend adopting more tolerant policies of non-discrimination (ACOG Committee Opinion, 2002; Ethics Committee of the ASRM, 2002).

Separating virus from spermatozoa

The basis for IUI treatment rests on the premise that isolated motile spermatozoa used in washed inseminations do not carry HIV. Spermatozoa lack the CD4 receptor and the CCR5 and CXCR4 co-receptors needed for the virus to gain entry into the host cell. Non-motile cells, particularly CD4 positive lymphocytes and macrophages, are known to exist in seminal plasma, and are principle targets for infection with HIV (Van Voorhis *et al.*, 1991; Quayle *et al.*, 1997). Density gradient centrifugation combined with sperm swim-up has been used in centres offering assisted reproduction for years in order to permit the intrauterine placement of spermatozoa. Washed swim-up techniques effectively separate the motile fraction of spermatozoa from the seminal plasma and non-motile cells, and have been reported to reduce HIV RNA and proviral DNA to undetectable concentrations (Kim *et al.*, 1999; Hanabusa *et al.*, 2000). Most practitioners of fertility care are familiar with the technique, as IUI therapy is commonly performed for the treatment of unexplained infertility.

However, concerns do exist regarding the ability of a HIV surface glycoprotein (gp120) to bind to galactosyl-alkyl-acylglycerol (GalAAG), a glycolipid structurally related to galactosylceramide present on the surface membrane of spermatozoa (Brogi *et al.*, 1998). This molecular complex has been associated with HIV infection in cells that lack CD4, CCR5, and CXCR4 proteins (i.e. neurons and colonic epithelium), and could potentially implicate spermatozoa as vectors of infection. This might also explain the mechanism for how HIV-like particles become associated with spermatozoa when the virus is co-cultured with gametes, as

Table 1. Summary of published results on HIV-1 serodiscordant couples undergoing washed sperm intrauterine inseminations. All values are numbers.

Study	Cycles	Patients treated	Pregnancies	Births	Ongoing	Infection
Semprini <i>et al.</i> (1997)	1954	623	272	242	–	0
Marina <i>et al.</i> (1998; 2001)	458	233	116	86	20	0
Tur <i>et al.</i> (1999)	155	67	32	–	–	0
Gilling-Smith <i>et al.</i> (2003)	92	36	12	10	0	0
Vernazza <i>et al.</i> (1997)	46	16	5	3	1	0
Weigel <i>et al.</i> (2001)	143	64	19	14	–	0
Bujan <i>et al.</i> (2001)	62	28	14	2	11	0
Daudin <i>et al.</i> (2001)	93	39	18	–	–	0
Brechard <i>et al.</i> (1997)	11	–	5	–	–	0
Delvigne <i>et al.</i> (2003)	5	5	4	4	–	0
Total	3019	1111	497	361	32	0

Cycles = attempts at treatment.

Pregnancies = clinical pregnancies established, including miscarriages and ectopic pregnancies.

Births = deliveries post-treatment.

Ongoing = ongoing pregnancies beyond 20 weeks gestation.

Infection = infections with HIV-1 resulting in seroconversions in mothers or offspring.

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