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Breastmilk transmission of HIV

Ruth Nduati

Nine out of every ten HIV infections in childhood result from mother-to-child transmission of the virus. Young women of childbearing years are disproportionately affected by the HIV/AIDS epidemic.[1] In addition to young age, risk factors for HIV infection in women include number of lifetime sexual partners, commercial sex, herpes simplex type 2 infection, hormonal contraception, being married, having an older partner and lack of circumcision of the male partner.[2] The prevalence of HIV among girls aged 15–19 years is 4–7 times that in young men of the same age. In this age group the convergence of biological and behavioural factors greatly heightens the risk of infection.[1] In sub-Saharan Africa this group shows extremely high prevalence rates of HIV – 30–40% in Southern Africa, 20–30% in Central Africa, and 10–20% in East Africa.[3] The grave consequences of this high HIV infection rate in women include large numbers of HIV-exposed children, mother-to-child transmission of HIV, increasing child mortality, and a growing number of children orphaned by AIDS.

Mother-to-child transmission of HIV

HIV-infected women can infect their babies during pregnancy, at the time of delivery, and postnatally through breastfeeding; however, most babies born to HIV-infected women do not have HIV infection. The absolute rate of HIV transmission during pregnancy is 5–10%, plus 10–20% during delivery, while the rate of postnatal HIV transmission to the infant varies with the duration of breastfeeding – 5–15% in women who breastfeed for ≤6 months and 10–20% for women who breastfeed for >6 months.[4,5]

At all stages of pregnancy, delivery, and lactation a high viral load in the woman increases the likelihood that her infant will become infected. Women have high HIV viral loads during primary infection and also during the advanced stages of HIV infection (when they are immunosuppressed). In regions of high HIV prevalence, a substantial proportion of the population will be living in HIV-discordant relationships[6] – that is, one partner infected, the other not. In the absence of interventions, the uninfected partner will be at high risk of infection; and, if it is the mother, her baby will then be at special risk from the high viral load of primary infection.

Whatever the viral load, a low CD4 lymphocyte count in a woman increases the likelihood of HIV transmission to her infant.[7] Other factors associated with mother-to-child transmission include low maternal vitamin A, cervical and vaginal shedding of HIV, prolonged rupture of amniotic membrane (>4 hours), amnionitis secondary to sexually transmitted infections, and high-risk sexual behaviour.[7,8] Clinical trials have indicated that supplementation with vitamin A does not prevent mother-to-child transmission of HIV and may even increase breastmilk transmission of the virus.

Prevention

In breastfeeding populations 30–50% of all infant HIV infection is attributable to breastfeeding.[4,5,8,9] If women and their health providers are to make informed choices regarding infant feeding, they require explicit information on all aspects of HIV transmission and its prevention. A randomised clinical trial of breastfeeding versus formula feeding among infants of HIV-infected women was conducted in Nairobi, Kenya. The objectives were to determine the frequency of HIV-1 transmission in breastfed and formula-fed infants, to describe the correlates of transmission, and to determine the morbidity and mortality of these infants after stratification by HIV-1 infection status. The average duration of breastfeeding was 17 months. This study estimated the rate of breastmilk transmission of HIV to be 16% (95% confidence interval 6.5%, 25.9%).[10] A previous meta-analysis had estimated the risk of breastmilk transmission of HIV to be 14% (95% CI 7%, 22%).[9]

The current technology in infant HIV testing does not allow us easily to delineate the contribution of the closely related exposure points of late pregnancy, delivery, and early breastfeeding. The randomised design of this study provided for the first time an accurate description of the timing of breastmilk transmission. Most breastmilk transmission of HIV took place in the first few weeks of life – 63% by 6 weeks, 75% by 6 months and 87% by 1 year. However, infants continued to be at risk of infection as long as they were exposed to breastmilk.[10,11]

Risk factors for breastmilk transmission of HIV include high maternal plasma and breastmilk viral loads, low CD4 lymphocyte count, duration of breastfeeding, cracked bleeding nipples, subclinical and clinical mastitis, and breast abscess.[8,12]

Anti-retroviral drugs can effectively prevent mother-to-child transmission of HIV.[4] These drugs act by decreasing viral replication in the mother and thus reducing HIV viral load in plasma and other body secretions and also by protecting the infant during and after exposure to the virus. In developing-country settings shorter courses of anti-retroviral drugs have given a more modest reduction (about 37–47%) of mother-to-child transmission of HIV.[4] Although the efficacy of these drugs was maintained in long-term follow-up there was a steady increase in HIV infection among the babies who continued to be exposed to breastmilk.

Breastfeeding versus formula

In normal circumstances, exclusive breastfeeding is considered the best way to feed an infant for the first 6 months of life. Breastmilk contains anti-infectious factors which are beneficial to the baby in early life and decline over time as the baby's immune system matures.[13] For HIV-infected mothers, however, avoidance of all breastfeeding is recommended – provided that replacement feeding is acceptable, feasible, affordable, sustainable, and safe.[14] There is now evidence that, if provided with adequate supplies of infant formula, with health education, and with support, HIV-infected women in developing-country settings can safely feed their babies with formula.[15] In the Nairobi trial at 2 years 70% of the children in the formula arm were alive and free of HIV compared with 58% in the breastfeeding arm ($p < 0.05$).[15]

In poor countries of the world where supplies of milk and clean water cannot be guaranteed, avoidance of breastfeeding is difficult and may be associated with substantial risks for the child; therefore infant feeding options for an individual HIV-infected woman need to be carefully weighed against the risks.[14] When breastmilk avoidance is not feasible, because of economic constraints or because of difficulties with disclosure of HIV infection status, exclusive breastfeeding is the recommended mode of infant feeding. The risks of transmission of HIV can then be reduced somewhat by support for exclusive breastfeeding, ensuring appropriate infant feeding techniques to prevent cracked nipples and mastitis, and shortening the duration of breastfeeding. There is evidence from one study that exclusive breastfeeding is associated with lower breastmilk transmission of HIV than mixed feeding.[16]

Breastfeeding is not entirely risk-free to the woman herself. The randomised clinical trial of breastfeeding versus formula in Nairobi found that breastfeeding HIV-infected women had a 3-fold higher mortality than formula-feeding women. The probability of death by 2 years post-delivery in breastfeeding women was 10.5% compared with 3.7% in formula-feeding women.[17]

Conclusions

Breastmilk transmission of HIV remains a serious issue in public health and contributes 30–50% of the 800 000 new childhood cases of HIV infection each year. Ultimately the best way to prevent breastmilk transmission of HIV will be primary prevention of infection in women of childbearing years. Health workers should not lose sight of the fact that most women attending maternal child health clinics are not HIV infected. This group of women should be encouraged to feed their babies exclusively with breastmilk and to protect themselves from future HIV infection. Since most babies at risk of breastmilk transmission of HIV are unlikely to avoid breastfeeding there is an urgent need to evaluate other interventions to prevent transmission by this route. Other possible strategies now being explored are an anti-retroviral drug for the baby during breastfeeding and anti-retroviral treatment of the mother.

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Hormone replacement at menopause and after

Halida Hanum Akhter

A woman's reproductive life begins and ends with distinctive events – menarche and menopause. In many cultures menarche is an occasion for celebration, whereas menopause marks a less happy transition. Although amenorrhoea and infertility will often come as a relief, the symptoms due to loss of ovarian function can be unpleasant and can be hard to distinguish from the effects of ageing and mid-life stress. Issues related to menopause are now seen as an important component of women's reproductive healthcare. In this article I concentrate on management of symptoms arising in the perimenopause – the phase that begins about two years before menopause and ends one year after it. I also refer to the possible influence of long-term hormone replacement therapy (HRT) on bone fracture rates and the incidence of cardiovascular disease.

Common symptoms

The average age at menopause is about 51 years in developed countries and tends to be lower in resource poor societies. When ovarian function ceases, oestrogen deficiency can affect every organ system of the body (see Panel 1); but the experiences of individual women vary greatly and the only symptom common to all is the cessation of menstrual periods. This may be abrupt, or heralded by changes in frequency or volume of flow. Other symptoms can be categorised as vasomotor, psychological, urogenital, and dermatological; however, only menstrual, vasomotor, and urogenital symptoms can be directly attributed to the reduction of hormone secretion.

Panel 1: Symptoms of menopause

Vasomotor	– Hot flushes
	– Sweats
	– Palpitation
	– Headaches
Psychological	– Irritability
	– Lethargy
	– Emotional lability
	– Forgetfulness
	– Loss of libido
Urogenital	– Vaginal dryness
	– Dyspareunia
	– Urethral syndrome
Skin	– Dryness
	– Brittle nails
	– Dry hair

Typical vasomotor symptoms in the perimenopause are hot flushes, palpitations, and night sweats. Psychological symptoms include depression, irritability, poor concentration, and loss of libido. When night sweats are troublesome, some of these symptoms may simply be due to insomnia. The likelihood of hot flushes and night sweats differs between cultures and is lower in Japanese than in European women. A possible explanation is the high content of phyto-oestrogens (plant compounds with oestrogenic activity) in the Japanese diet. Another factor that seems to affect the rate of symptoms is physical activity: a Swedish study in women aged 45–55 indicated that hot flushes and night sweats were only half as common in those who were physically active as in controls.

Other possibly psychological effects are paraesthesiae in the hands and feet, and giddiness – but like insomnia these are not clearly separable from vasomotor effects. In well-adjusted and well-informed women, the psychological changes typically amount to no more than a short phase of increased emotional lability.

The main urogenital effect of oestrogen withdrawal is atrophic vaginitis. The vaginal mucosa becomes thinner, with loss of lubrication and consequent dyspareunia. Simultaneous atrophy of the urethra and bladder predisposes to urinary symptoms such as dysuria, nocturia, frequency, and stress/urge incontinence.

The skin changes associated with, but not necessarily caused by, menopause include thinning, a decline in collagen content, flakiness and transparency, and easy bruising.

Treatment

In resource-poor settings, only a small proportion of women with menopausal symptoms will seek advice; and, even in these women, the demand for HRT will probably be low. Cost is only one factor. Some women are frightened of cancer; some are worried that the treatment means a resumption of uterine bleeding. Whatever the setting, rich or poor, all that some women require is an opportunity to voice their feelings, to receive an explanation, and to be reassured. For some, simple psychotherapy or relaxation training can be helpful. In the past, symptoms were sometimes dealt with piecemeal – for example, sedatives for insomnia, beta-blockers for palpitations, tranquillisers for agitation. However, a hormonal approach will almost invariably be preferable. An exception is the use of non-hormonal lubricants for vaginal dryness, which can give satisfactory results.

Some women will seek advice on "natural" alternatives to HRT such as soy flour containing phyto-oestrogens. There is evidence of modest benefit from such products – for example, in a 12-week study, soy flour reduced hot flushes by 40% compared with a 25% reduction with wheat flour (presumably inactive). However, until there are good data on safety and efficacy, dietary agents should be used cautiously if at all for perimenopausal symptoms and not for long-term prevention.[1]

For troublesome symptoms, the treatment of choice will usually be HRT. However, the decision must be made carefully with every woman in the light of her personal risk profile. The treatment is now safer and more convenient than formerly. With the original preparations, lacking a progestogen, there was an increased hazard of endometrial cancer. This was first eliminated by addition of cyclical progestogens, which induced regular withdrawal bleeding – unwanted by many women. Now, continuous regimens are available that lack this disadvantage. The most important risk to discuss with the client is venous thromboembolism – rare, but about doubled in HRT-users. Breast cancer is another consideration with hormonal agents, but the evidence on continuous HRT preparations is at present reassuring.[2] Cardiovascular disease is discussed later.

HRT can be expected to work against all the symptoms in Panel 1, with the possible exception of skin changes. In some instances, however, a woman will appreciate additional help in dealing with the stresses of this time of life: counselling or simple psychotherapy may be an important adjunct to HRT.

Late effects of menopause and their prevention

Bone

Osteoporosis is a major public health problem in many countries. It is characterised by reduced bone mass and loss of bone architecture which leads to enhanced bone fragility and consequent increase in fracture risk. The primary fracture sites are vertebrae, hips, and wrists. In the USA alone, some 1.3 million people experience osteoporotic fractures every year. After osteoporotic fracture of the hip, 12–20% of patients are dead within a year. Loss of bone tissue accelerates at menopause and the risk of fracture increases progressively. In theory, we might expect HRT to decrease these risks.

The likelihood of osteoporosis and related fractures depends to some extent on peak skeletal mass achieved at the end of linear growth. This is under genetic control, but adequate physical activity and dietary intake of calcium during the teenage years are also very important. Measures to prevent osteoporosis should start early in childhood and continue into old age. In postmenopausal women, calcium supplementation with or without vitamin D has been shown to reduce bone loss,[3] and a daily intake of 1000–1500 g is recommended in some countries for women past menopause. Most of the calcium in the diet comes from dairy products (70–75%). Regular, moderate, weight-bearing exercise is recommended not only for its effects on bone but also for its wider benefits in terms of physical fitness.[4]

What of hormone treatment for prevention of osteoporosis? The evidence from clinical trials is not straightforward. Although controlled trials demonstrate that HRT maintains bone mineral density in the spine, wrist, and hip, not all show a reduction in fractures. The benefit stops when treatment is withdrawn; thus, to prevent hip fracture, women will probably need to continue until age 70 or even 75 – the time of highest risk. In a systematic review Collins[2] concludes that the evidence is not sufficiently strong to warrant HRT solely for fracture prevention; other strategies, possibly including HRT as a supplement, need to be evaluated in controlled trials.

Cardiovascular disease

Women tend to develop cardiovascular disease ten years later than men, and oestrogen is a likely cause of this difference. At menopause, various cardiovascular risk

factors worsen, including serum cholesterol and insulin resistance. Oestrogen, as prescribed in HRT, might be expected to reverse this adverse trend through beneficial effects on lipid metabolism, arterial tone, coagulation, and insulin resistance. Many retrospective and cohort studies have indeed reported that the use of HRT can decrease the incidence of coronary artery disease by 30–70%. HRT seemed to reduce the risk of cardiovascular disease in obese women, those with hypertension, and those with previous myocardial infarction. However, the whole scene was changed by two randomised controlled trials – the Heart and Estrogen/Progestin Replacement Study (HERS), involving 2763 women with coronary artery disease[5]; and the Women's Health Initiative (WHI), a study of primary coronary prevention in about 27 000 women.[6] In the HERS study, HRT had no effect whatever on the incidence of myocardial infarction or death; and the WHI investigators, after two years' follow-up, issued a warning that hormone-treated women were at increased risk of cardiovascular events, stroke, and venous thromboembolism. An American Heart Association panel[7] looked at these results and concluded:

- There are insufficient data to suggest that HRT should be initiated for the sole purpose of primary prevention of cardiovascular disease
- HRT should not be initiated for the secondary prevention of cardiovascular disease
- If a woman develops an acute cardiovascular event while receiving HRT, it is prudent to consider discontinuing the HRT or instituting thromboembolism prophylaxis to cover the period of immobilisation.

In his systematic review Collins[2] judges that "the cardiovascular events experienced in the WHI trial were not sufficient to recommend discontinuation of HRT by those who were active participants in the trial. This policy appears to be appropriate for clinical practice". I agree.

Conclusion

Globally, almost 90% of women live long enough to experience menopause. In resource-poor settings HRT will not always be an option, but women can be much helped by simple advice and counselling. For those troubled by the symptoms of oestrogen deficiency, HRT offers convenient relief, now obtainable without the need for withdrawal bleeding. The treatment is generally safe, but the advantages and disadvantages will differ for every client and must be judged individually. Whether HRT is useful for long-term prevention of osteoporotic fractures and cardiovascular disease is at present uncertain; therefore it should not be prescribed solely for these purposes.

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News

Child rape and the virgin cleansing myth

In sub-Saharan Africa there is growing concern about sexual abuse of girls – not least in relation to the hazard of HIV infection. Jewkes and co-workers,[1] from Pretoria, South Africa, have assessed the frequency of rape in a nationally representative study of 11 735 women. Now aged between 15 and 49 years, these women were asked whether before the age of 15 they had been "forced to have sexual intercourse against their will by being threatened, held down, or hurt in some way" or "persuaded to have sexual intercourse when they did not want it". 153 (1.6%) reported such an incident. 85% of the assaults had occurred between the ages of 10 and 14 years; in order of frequency, the rapists were most commonly schoolteachers, then relatives (21%), strangers or recent acquaintances (21%), and boyfriends (10%). The fact that rape in childhood was much less often described by the older women may point to an increase in incidence, though reporting bias cannot be ruled out as an explanation. The role of schoolteachers in child rape is a scandal that has already prompted action in South Africa; sexual activity between staff and students, even when consensual, is now an offence for which teachers are dismissed.

In an accompanying editorial, Pitcher and Bowley,[2] from Johannesburg, discuss the practice of infant rape in South Africa. A cluster of recent cases has generated much anger, and a particular cause for concern is the notion that some incidents are prompted by the virgin cleansing myth – the idea that intercourse with a virgin infant will rid the perpetrator of HIV/AIDS or other sexually transmitted infections. Pitcher and Bowley believe that the myth, which seems to have begun in Central Africa and moved southwards with the HIV pandemic, is relevant to an apparent increase in cases of infant rape. However, responding to the editorial, Jewkes and her colleagues[3] deny that the virgin cleansing myth is an important factor. There is no evidence, they say, that infant rapes are increasing in South Africa; moreover, if the cleansing myth were gaining ground, one would expect the HIV seroconversion rate in child victims in Cape Town (most of whom do not receive anti-retroviral therapy) to be higher than the present 1%. In their opinion, infant rape should be seen not separately but as part of the spectrum of violence against women and girls associated with sex inequalities, a culture of male entitlement, and a climate of relative impunity for rape.

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