Pre-Exposure Prophylaxis

Introduction

Since the emergence of human immunodeficiency virus (HIV) in the 1980s, more than 35 million lives have been lost and without available curative therapy, currently, 1.8 million persons are newly diagnosed every year, worldwide (World Health Organisation, 2018). Moreover, it is estimated that up to 70% of persons are unaware of their HIV positive status, leaving a significant proportion of individuals undiagnosed and therefore, prone to unintentional transmission and others at risk of acquisition (Riddell et al., 2018). In the UK, HIV confers a relatively minor epidemic, with a prevalence of 1.6 per 1000 people and a 18% reduction in new diagnoses that was observed in the year 2016. However, HIV continues to disproportionately affect men who have sex with men (MSM) and black ethnic groups, who frequently undertake unsafe and high risk sexual practices, including condomless anal intercourse, that significantly increases the chance of HIV transmission (AVERT, 2018).

Prevention Strategies and Pre-Exposure Prophylaxis

Various health strategies to reduce the probability of HIV transmission and infection have been reported in the literature, such as education about safe sexual behaviours, large scale HIV testing, male circumcision, and the use of highly active antiretroviral drugs (Cohen et al., 2011). Additional prevention strategies include the use of pre-exposure prophylaxis (PrEP), which involves the use of antiretroviral drugs, including tenofovir and emtricitabine (Truvada) in HIV negative individuals who are at high risk of HIV acquisition, which can significantly reduce HIV transmission rates, particularly in MSM and other high risk groups (Riddell et al., 2018). In 2012, the Food and Drug Administration approved PrEP for use in individuals at high risk of HIV, following research data that confirmed its safety and efficacy. In the year 2017, a trial of PrEP was commenced in England, involving 10,000 people deemed to be at risk of HIV acquisition. These actions were preceded by courts declining funding for PrEP despite efforts by National Health Service England supporting its positive impact, but this decision was recently overturned (AVERT, 2018).

On an individual level, the use of PrEP confers a significant advantage as a treatment strategy, as it prevents the acquisition of infection, thus ensuring individuals are protected from the morbidity and mortality associated with HIV (Riddell et al., 2018). In a study of the morbidity and mortality related to HIV, persons infected with HIV have a poorer health burden than the general population, with higher rates of intermittent infections, cardiovascular disease, cancers, and disability adjusted life-years (AVERT, 2018). Evidence from the use of PrEP in the United States shows that 99% of users were MSM, who were thus, as a subgroup, increasingly likely to partake in high risk sexual practices. Of this group, 30% of PrEP users were diagnosed with a range of sexually transmitted infections (STI), such as chlamydia, gonorrhoea and syphilis, but importantly, there were no new HIV diagnoses during the 388 person-years follow-up (Volk et al., 2015). The fact that individuals seek PrEP paradoxically increases the likelihood of HIV

infection, but more evidently, the acquisition of other STIs. Other evidence related to the benefits of PrEP include the potential reduction in condom use, that confers a benefit to sexual pleasure, which is seen as an important factor influencing individuals wellbeing, particularly among MSM (Fortenberry, 2013). A proportion of persons living with HIV have reported that the use of condoms is deleterious to their wellbeing, as it reduces arousal, sensation and intimacy, and has been reported to act as a 'penalty' when using them for infection prevention purposes. PrEP is therefore, thought to avoid this issue and can thus, improve psychological wellbeing by enhancing pleasure, if persons taking PrEP choose not to use barrier protection methods, such as condoms (Calabrese and Underhill, 2015). The constitution of the World Health Organisation champions the enjoyment of the highest quality of health and regards it as being a fundamental human right and that strategies to minimise adverse stereotypes are essential to ensuring that this problem does not cloud the views of medical professionals, policymakers, insurers and PrEP service users. The constitution also states that health is a holistic state whereby physical, psychological and social wellbeing are as important as the absence of disease or illness. This suggests that the non-medical aspects of a person's wellbeing should also take equal priority as the treatment of disease, and with this in mind, PrEP can offer a solution to these factors among persons with HIV (World Health Organisation, 2006).

Despite PrEPs relatively favourable side effect profile, the use of Truvada can be associated with nephrotoxicity, due to proximal tubular mitochondrial deoxyribonucleic acid damage and resulting, acute kidney injury, Fanconi syndrome or type IV renal acidosis, which has an overall incidence rate of 1.09 per 1000 persons per annum (Herlitz et al., 2010). Other antiretroviral drugs have seen higher rates of renal impairment, but Truvada is mostly well tolerated, with a reported adverse renal effect occurring in 0.5% of patients and alterations in serum creatine concentrations that have been reported in 2.2% of persons. However, studies have shown that this effect can be reversible after drug discontinuation, but this then subsequently impedes the use of PrEP for the prevention of HIV infection, but may protect individuals from other STIs, if they consequently opt to using condoms (Riddell et al., 2018).

The benefits of PrEP to the healthcare sector include its associated cost-effectiveness and reduced requirement and demand on service provision for each case of avoidable new HIV infections (Riddell et al., 2018). However, determinations of the cost-effectiveness of PrEP are complex, requiring consideration of the epidemic context, drug adherence, PrEP population coverage, and PrEP prioritisation. Moreover, the use of PrEP, that can be essentially avoided by the use of barrier methods such as condoms, raises issues and controversy around funding in publicly funded health systems, where resources are limited and budget constraints are in effect (Gomez et al., 2013). In the UK, the cost of an individual living with HIV for their lifetime is estimated to be £360,000 and National Health Service expenditure on HIV therapy exceeds £500 million per annum. Moreover, a one year duration of PrEP with Truvada is expected to cost £3000-4000, but the actual cost per person will be significantly less, given that its use will be intermittent and because it is not a lifelong treatment, although individuals may be encouraged to use PrEP more subconsciously, as a daily medication to prevent HIV infection upon spontaneous sexual contacts (Riddell et al., 2018). Moreover, the ethical principles of distributive equality of health can compete with monetary values, and other principles such as that of utility,

can help support the provision of PrEP in the context of maximising benefit and minimising harm to society (Riddell et al., 2018). Furthermore, PrEP can be utilised as a synergistic HIV prevention strategy, along with behavioural interventions and structural programmes, which can help to maximise HIV prevention efforts among health systems on a global scale (World Health Organisation, 2018).

Societal views of PrEP may be more conservative and involve increased resistance to its fundamental principles, due to conceptions that it promotes high-risk sexual behaviours and a passive individual approach that may seem 'reckless' and of poor self-responsibility (Riddell et al., 2018). In addition, it may seem to be a high cost initiative, when effective prevention already exists in the form of barrier methods, such as condoms and that other services are experiencing budget cuts, which actually require investment to improve the wider healthcare and wellbeing of society. There is also the presence of stigma surround HIV and PrEP, which includes views that the promotion of condomless intercourse is dangerous and an unacceptable motive, as well as promoting high risk sexual practices and behavioural disinhibition. Moreover, several public figures have used the term "Truvada whores" to describe individuals using PrEP, which has contributed to the stigma and comprised its uptake in some settings (Calabrese and Underhill, 2015). These negative associations can lead to erroneous misconceptions among individuals who may be suitable or ideal candidates for PrEP, but may choose to opt out, due to stigma-related fear.

Conclusion

HIV remains a major public health problem and novel initiatives including that of PrEP offer a significant strategy to mitigate the burden of HIV upon high risk populations. Importantly, this includes primary infection prevention, which avoids unnecessary morbidity and mortality for each successful avoidable case. However, the use of PrEP is accompanied by a range of adverse implications, including rare but significant side effects, increasing transmission of other STIs, and stigmatisation, but overall, the efficacy of PrEP renders it a markedly effective prevention strategy. Future PrEP initiatives may observe expansion of the drug formulation, such as that of introducing intravaginal rings containing dapivirine for women, which has reduced the incidence of HIV in Africa, and injections of long-acting integrase inhibitors, such as cabotegravir, which overall, provide a less frequent dosing regime and may confer a better safety and side effect profile than current conventional PrEP therapy (Riddell et al., 2018).