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Journal

International Journal of Clinical Pharmacy, 34(6)

ISSN

2210-7703

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Publication Date

2012-12-01

DOI

10.1007/s11096-012-9709-0

Peer reviewed

Published in final edited form as:
Int J Clin Pharm. 2012 December ; 34(6): 803–806. doi:10.1007/s11096-012-9709-0.

Pharmacists as providers of HIV pre-exposure prophylaxis

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Abstract

The efficacy of HIV pre-exposure prophylaxis (PrEP) has been demonstrated in four clinical trials to date; however, the success of PrEP is largely dependent on high levels of medication adherence. Due to their extensive experience and expertise in medication adherence counseling, as well as their ability to monitor and manage medication adverse effects and drug–drug interactions, clinical pharmacists are well-equipped to play a key role in effective PrEP utilization. Here we discuss reasons favoring the establishment of a protocol-based, pharmacist-run PrEP clinic.

Keywords

Adherence; HIV/AIDS; Pharmacist Pre-exposure prophylaxis; Prevention; PrEP

Introduction

With 2.5 million new infections worldwide in 2011 [1], the prevention of HIV continues to be a crucial priority. Currently, several new biomedical prevention approaches, such as vaccines, topical microbicides, and pre-exposure prophylaxis (PrEP), are being examined and evaluated. PrEP is an approach to prevent HIV acquisition and involves the use of antiretroviral (ARV) medications by HIV uninfected individuals as a method of reducing their risk of infection. The idea for this approach stems from prior clinical studies showing efficacy of ARV medications in preventing HIV infection, such as the use of ARVs in the prevention of mother-to-child transmission and post-exposure prophylaxis (PEP). PrEP has been shown to be effective in four clinical trials to date [2–5]. These trials have uniformly revealed the positive correlation between adherence to PrEP and HIV-1 prevention. While there is increasing evidence that PrEP may serve as a tangible method of HIV-1 prevention, there are trials that have been stopped early due to futility [6–8]. This disparity has primarily been attributed to differences in product adherence.

The efficacy of PrEP in reducing HIV acquisition was shown to be as low as 44 % in 2,499 individuals in the iPrEx study and as high as 92 % in subjects with detectable drug levels [3]. Therefore, in order for PrEP to be successful, numerous factors, namely medication adherence, require close attention, counseling, and monitoring. Based on prior research, the majority of an HIV clinical pharmacist's functions involve providing ARV adherence

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Conflicts of interest
None.

counseling and instructing on the use of adherence-enhancing tools, detecting drug–drug interactions, monitoring for adverse drug reactions, providing patient education, and selecting or modifying an ARV regimen [9]. Therefore, clinical pharmacists are well-positioned to play a key role in the effective roll-out of PrEP. Here we review some of this expertise and experience as they pertain to the successful use of PrEP.

Importance of medication adherence counseling and monitoring

Despite other potential explanations for the divergent results of PrEP trials, such as the contribution of variable drug concentration at the exposure site, integrity of the vaginal epithelium, and the impact of acute infection, medication adherence is considered to be the "Achilles heel" of HIV PrEP and the major driver in the success of PrEP [10]. In the iPrEx, TDF2, Partners PrEP, and CAPRISA004 studies, the risk of HIV-1 transmission was strongly correlated with low adherence to tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), oral TDF, or vaginal tenofovir (TFV) [2–5]. Similarly, low levels of adherence to oral TDF/FTC in the FEM-PrEP study and to oral TDF and vaginal TFV in the VOICE trial is considered to have been the most important reason for the unfavorable results leading to their early discontinuation [6–8, 10].

Numerous studies have shown that HIV clinical pharmacists' interventions and clinical care activities significantly improve medication adherence and virologic outcomes in HIV-positive individuals [9]. It has also been reported that pharmacists' direct patient care significantly improves patient's knowledge, medication adherence, and quality of life [11]. Pharmacists can minimize missed doses by spending sufficient time to educate patients on the importance of adherence and the various methods that can maintain high levels of adherence to new medication regimens (including pill boxes, refill reminders, beepers, alarms, medication schedules, blister packs, medication diaries, etc.), by monitoring adherence, and by providing counseling on approaches to help overcome adherence barriers throughout medication treatment.

Most methods for improving adherence entail a multitude of interventions, require tailoring, and can be labor-intensive [12, 13]. Methods that may lead to adherence improvement vary depending on patient preferences and particular reasons for non-adherence, but may include programming medication reminders through mobile telephone automated text messages, alarms, promoting the use of pillboxes, providing individualized or group counseling and education, and assisting patients in incorporating their medications into their daily routines [13, 14]. Additionally, with more data on PrEP 2 or the next generation of PrEP, in the coming years, more innovative methods of tailoring PrEP regimens will become available [15].

By educating patients on the safety, efficacy, precautions, and correct use of PrEP, as well as developing personalized methods of reducing missed doses, clinical pharmacists are in an ideal position to help abate PrEP non-adherence. Clinical pharmacists, who have experience and expertise in adherence counseling, are likely to be an essential member of the multidisciplinary care team for the long-term success of PrEP.

Close follow-up is necessary and time consuming

Although the results of several PrEP trials are highly promising, one of the main criticisms of PrEP is the need for frequent monitoring and follow-up [16]. During the iPrEX study [3], participants were monitored every 4 weeks over a median follow-up time of 1.2 years for drug dispensation, pill counts, adherence and risk reduction counseling sessions, HIV testing, and adverse effect reporting. In addition, laboratory analyses, such as an electrolyte panel, complete blood count, and liver function tests, were performed every 4 weeks for the

first 24 weeks and then every 12 weeks thereafter. This close follow-up is likely to have resulted in higher adherence and increased efficacy in comparison to what may been seen in a real-world setting.

It is unclear whether this intense follow-up is feasible for clinics that are over-extended and for physicians who may be unable to provide sufficient amount of time to simulate study protocols or ensure adequate patient follow-up. Increasing administrative duties and cost constraints are impinging on the amount of time physicians are able to spend with patients. Studies have found that the average physician visit duration is as short as 12.8 min [17]. In order to thoroughly counsel and monitor a patient before and during PrEP use, a provider will need to have sufficient time to discuss the important issues surrounding PrEP, which may include building rapport with the patient, discussing the importance of good patient-provider communication, introducing the PrEP medication(s), explaining potential adverse effects, defining and emphasizing the importance of medication adherence, discussing and addressing potential barriers to adherence, scheduling follow-up laboratory and clinic appointments, and counseling on risk-reduction strategies. These components will likely necessitate a physician appointment duration that is substantially longer than what currently exists. However, clinical pharmacists, who typically spend more time with patients and frequently review important medication information such as drug dosing, adverse effects, drug–drug interactions, medication storage, missed doses, adherence, etc., will likely have the ability to conduct similarly detailed and thorough counseling and follow-up sessions.

Monitoring for and recognizing potential adverse effects and drug–drug interactions

Although the appropriate use of PrEP has the potential to have a tremendous impact on the HIV/AIDS epidemic by reducing the number of new HIV-1 infections [18, 19] it is not without risks. Use of TDF in HIV-positive individuals has been associated with an increased risk of acute kidney injury, the most severe cases resulting in Fanconi syndrome [20]. Although the risk of this syndrome is low, there is increasing evidence that TDF exposure can more commonly lead to subclinical proximal tubular injury [21]. Most recently, a large observational study found that each year of exposure to TDF was associated with a 34 % increased risk of proteinuria, 11 % increased risk of rapid kidney function decline, and 33 % increased risk of chronic kidney disease [22].

Pharmacists have extensive experience in monitoring and preventing drug–drug interactions or adverse drug reactions [9]. In one study, HIV-infected patients who were managed by pharmacists in a drug optimization clinic demonstrated significant improvement in drug-related toxicities, including renal dysfunction [23]. With the potential use of TDF for PrEP in clinical practice, the clinical pharmacist is an appropriate individual who is able to anticipate, monitor, and manage potential adverse effects, such as changes in renal function. Despite the fact that TDF has few drug–drug interactions, future PrEP regimens may require closer attention to this detail and necessitate the attention of clinicians with medication expertise.

Success of pharmacists in other disease states

In addition to having more time for patient interactions and having extensive experience in adherence counseling and adverse effect monitoring, pharmacists have already proven to be successful in following clinic-based protocols to aid in the management of numerous disease states. Pharmacist-directed care has also been shown to be beneficial in reducing cardiovascular risk factors, such as blood pressure, total cholesterol, low-density lipoprotein cholesterol, and smoking [24]. A recent meta-analysis found pharmacists' management of

hemoglobin A1c, LDL cholesterol, blood pressure, and adverse drug events to be favorable over comparative services [11].

In a protocol-based pharmacist-run HIV PrEP clinic, the pharmacist can conduct frequent and periodic HIV testing to ensure that patients are HIV-negative prior to and during PrEP use, counsel on safer sex and the need for continued condom use and treatment of sexually transmitted diseases, screen for hepatitis B infection, monitor for adverse effects such as TDF's impact on bone mineral density and renal function, support high levels of adherence, order appropriate tests (such as drug resistance testing) and link those who become HIV infected to care, and develop transition mechanisms for those who wish to discontinue PrEP [25]. The Center for Disease Control and Prevention has published interim guidance on the determination of eligibility before PrEP initiation, beginning PrEP, following up, and discontinuing PrEP [26]. This guidance can be used to establish the protocol for a pharmacist-run PrEP clinic. Given the expertise of clinical pharmacists and their ability to successfully manage various disease states in a protocol-based setting, these clinicians are likely to be the appropriate health care professionals to manage PrEP use in settings where sufficient well-trained and equipped clinical pharmacists are available.

Conclusions

The consideration of how and to whom PrEP will be prescribed and who will bear the responsibility of patient follow-up and management over the period of PrEP usage is a timely matter as the U.S. Food and Drug Administration has recently approved the use of Truvada® (TDF/FTC) for HIV-1 PrEP. Truvada® is the first agent indicated for the prevention of HIV-1 in HIV seronegative individuals. Although PrEP has the potential to have a dramatic effect on the incidence of HIV [27], it is not without risks. Negative outcomes could include drug toxicities, drug resistance, and increased risk compensation; all of which can diminish the benefits of PrEP [28–30]. Therefore, it is critical that the provisions of PrEP be carried out correctly and meticulously. Given that the majority of requirements for appropriate PrEP use (i.e., medication knowledge, adherence counseling, and adverse effect monitoring) fall within the scope of clinical pharmacists' expertise, it is critical to note that these clinicians can play a significant role in the successful use of PrEP. In spite of the fact that PrEP is likely to evolve to regimens requiring lower frequency of administration and less toxicity, the need for adherence counseling, adverse effect monitoring, and medication expertise will remain central to the appropriate use of PrEP. We believe that a protocol-based, pharmacist-run HIV PrEP clinic can provide comparable levels of efficacy to those seen in clinical trials. With improvements in technology, these clinics can be centralized and offered remotely using teleconferencing and the same level of high quality care can be presented uniformly to a wide array of settings.

Acknowledgments

The project described was supported by NIH award numbers F32MH086323 and K23MH097649.

Funding None.

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