HIV MEDICATION ERRORS

Christopher Nguyen, MD

3/16/2016
HIV Medication Errors
[video transcript]

00:00:07

- [Naomi] Good morning everyone, and thank you for participating in today's webinar, HIV Medication Errors. I'd like to introduce our speaker today, Dr. Christopher Nguyen. Dr. Nguyen is an HIV and hepatitis C specialty pharmacist with Duane Reade Walgreens in New York City. He currently practices at Gay Men's Health Crisis, where he works directly with clients on HIV-related issues such as adherence and medication management and provides consults for local practitioners on drug interactions, building adjustments, and HIV and hepatitis C regimen selection. He also helps train Duane Reade pharmacists where he can see HIV specialty network vocations in New York, and is a Pharmacist Champion for the New York State Department of Health AIDS Institute Clinical Education Initiative. Dr. Nguyen received his Bachelor of Pharmacy degree at the University of California, San Francisco, where he currently serves as volunteer faculty and his credentials by the American Academy of HIV Medicine as an HIV pharmacist. So with that, I will pass it over to you, Dr. Nguyen.

00:01:16

- [Christopher] Thank you, Naomi. Good morning. So today we're going to be talking about medication errors that commonly happen in the HIV positive population.

00:01:28

Here are my disclosures.

00:01:32

So we’re gonna discuss some background data and some research on medication errors in this population. We’ll also look at some common types and causes of the medication errors that occur in the HIV population. I'm gonna use some of my patient cases to provide some real-life examples from both the hospital and retail settings that describe some of these errors. And then we're gonna finish up by talking about strategies to prevent medication errors in this population.

00:02:08

Let's start with some background on medication errors. This was a landmark report from the Institute of Medicine that came out in 1999 that looked at the impact of medical errors in the U.S. and the medical errors included medication errors and they estimated up to 98,000 Americans die in hospitals annually from medical errors that are preventable. And as you can see, these errors can be very costly. So it costs between 17 to 29 billion dollars per year.

00:02:46

This was another piece published by the Institute of Medicine as well that shows how common medication errors are and this was published in 2006. What they saw was that there was 17 million errors per one billion prescriptions filled. So that came to about 51 million errors annually. So they translated that to a 1.7 overall error rate in community pharmacies and Amcare pharmacies, and that
means that in a typical pharmacy approximately four errors happened per day for every 250 prescriptions that the pharmacy does. So pretty much on average for a pharmacy that fills 500 prescriptions a day, they are making eight errors somewhere in there per day. They may or may not know that.

00:03:44

So let's look at some literature review here. This was a review of 25 studies looking at errors in the hospital setting only, so no community or Amcare settings were in here. What they saw was from study to study the overall medication error rate ranged from as low as 5.8 percent to a whopping 86 percent of admissions. Now most errors occurred at the time of prescribing, during admission. This is when the patient comes in and the physician sees a drug list and continues prescribing these drugs without really looking at the medications, not doing a med rec. But the errors are also found throughout the hospitalization and also at discharge. The most common types of errors that they found in the hospital? Wrong ART regimen, wrong dosing, wrong frequency, and then also drug-drug interactions that were not caught. Most successful interventions included an HIV or ID clinical pharmacist completing the med rec on admission who reviews the orders daily and also screens the orders at discharge. So you can see the impact that a clinical pharmacist has here in preventing medication errors in the HIV positive population.

00:05:15

So this one, the authors looked at the National Medication Error Database. They reviewed errors reported to the Med Marks Database. So this is a commercial database that tracks both adverse drug reactions and medication errors that are submitted by participating hospitals. So again, this is a review of errors in hospital setting, not in other settings. They looked at 400 errors that involved at least one anti-retroviral. What they saw was three percent of those errors were considered harmful and most of them occurred in the dispensing phase. So unlike the previous study that I showed, the literature review where they saw most of the errors happening on the admission or prescribing phase, this one saw that most occurred in the dispensing phase. And the most common types here were wrong dose and wrong drug. And interestingly, community hospitals were more likely to have prescribing errors than academic hospitals.

00:06:29

So this was one of the first studies done looking at HIV medication errors in the community pharmacy setting and this was done by a couple of clinical pharmacists at UCSF who were former colleagues of mine. So Jennifer Cocohoba and Betty Dong, what they did was they looked at voluntarily-reported errors in an urban, this was in San Francisco, so in a San Francisco-based clinic with experienced HIV providers and using an HIV specialty community pharmacy. So these are specialty HIV providers and pharmacists. So what they saw was, and this is again keep in mind this is only in one clinic and one pharmacy. They saw 37 errors that were reported over three years. 81 percent was classified as a category C with the National Coordinating Council for Medication Error Reporting and Prevention and that means that the error reached the patient, that the error was not harmful enough, no harm was done. The majority of the errors were attributed to lapses in the system of care. So for instance, did the
Pharmacy send a refill request and the refill was not authorized on time and the patient went without meds for a few days? Lapses in insurance and nobody at the clinic was helping the patient to renew or sign up for an insurance quick enough, so there's a lapse of care. So these are in the system of care. The rest of them were attributed to prescribing and dispensing errors. So prescribing wrong doses, wrong drugs, or incorrect dispensing of something that was correctly prescribed. For the dispensing errors, most were the wrong dose directions as I said, one was Combivent was dispensed, instead of Combivir. So the patient went without his Combivir for a whole month until that error was caught. So he was dispensed an inhaler when it was supposed to be an HIV medication. For the prescribing error, many of those were the dosing and directions. A couple of them wrote thrice instead of twice on the prescription so it was given three times a day instead of twice a day. And one was prescribed Rysampen with an interacting drug.

00:09:11

So let's look now at common types and causes of HIV medication errors.

00:09:19

So why is it that we have so many HIV medication errors versus other disease states like hypertension? First of all, there's always new formulations, new changes, new strengths. So if you guys, any of you remember darunavir used to come in 400 milligram strength. So for treatment-naive or treatment-experienced patients with no darunivar RAMs, you would take 800 milligrams boosted with vatonavir or COBI nowadays once a day. So patients used to take two of the 400 milligrams and then they discontinued the 400 milligram strength and put in the 800 milligrams. So at that time there were quite a few medication errors happening because patients were either taking just one pill of the 400 milligrams or two pills of the 800 milligrams when they were confused. It also comes in a 600 milligram strength that is dosed twice daily in patients with darunavir RAMs. So that can be confusing as well. Lopinavir used to come in capsules that had to be refrigerated and they discontinued that so now it only comes in tablets. So these differences in formulations and strengths can create errors. Unlike most other chronic disease states, HIV treatment requires combination therapy. So it's not like starting one drug for hypertension and then slowly add on additional drugs as needed. You start with a combination therapy. And it's not just any random three medications, it's a certain combination. So somebody who doesn't know that can miss that and cause errors. There are some look-a-likes and sound-a-likes, and I'll go over a few of them and I have seen errors resulting from the look and sound-a-likes as well. Confusing names and use of abbreviations. So the use of abbreviations are always discouraged, although we use it in PowerPoint presentations just to make it shorter and more succinct, but in prescriptions themselves, using the three-letter abbreviations can create errors. There are variable dosing for some drugs. As I mentioned, runavir has several dosings based on whether the patient has baseline runavir mutation. Also certain drugs can be dosed once a day or twice a day based on co-medications and they have drug interactions. So there can be variable dosing for some of these ARVs. ARVs overall have a higher drug-drug interaction potential than other medications with themselves and with many co-morbid drugs that the patient may be on. And lastly but not least, there is a lack of training and knowledge from both the provider's side and the pharmacist's side in anti-retrovirals and this can create errors.
So let's look at some of the look-a-likes and sound-a-likes and this is from the Institute for Safe Medication Practices. So this is ISMP's list of confused drug names. So Kaletra can be confused with Keppra. Lamivudine, Lamotrigine. And Indinavir can be confused with Denavir. And this is the most common that I've seen. Ritonavir being confused with Retrovir. If it’s written in handwriting those two look really similar on the piece of paper. And then Saquinavir with Sinequan. The bottom ones are not on ISMP, but I've seen those because they've been made error-wise. Intelen, Isentress, they sound similar. Nelfinavir, Nevirapine. Thankfully neither one of those medications are really used nowadays, especially Nelfinavir so you should not see that. And then as I said before with that one example, Combivir being given Combivent instead.

So another type of error is you could have missing or too many medications and this is because of the combination therapy that I just talked about. There are many FDA-approved agents. Granted, we only really use a handful of them for newly-diagnosed patients but there are many of them available that are FDA-approved. And that combination therapy requirement can confuse somebody who's not an HIV specialist. So that can lead to somebody having monotherapy or just a massive amount of drugs that are unnecessary or overkill. Co-formulations can lead to duplications. So if the provider or pharmacist doesn't realize that a drug has two medications in there and give them another drug that is already inside there, that will lead to duplication. And that tends to happen during a switch in regimen. Some medications should not be combined. Some should. So for instance, in general an active regimen will consist of two NRTIs, especially one that is for a treatment-naive patient. However, two NNRTIs should never be combined together. And if you see that, that is an error. A regimen switch can lead to duplication or too many medications at the pharmacy level. Many times when the provider sends a new regimen to the pharmacy, there's no message on the prescription that says this is a regimen switch, please discontinue previous regimen. So the pharmacist, if he or she is not an HIV specialist, may not know that it is a switch. They may think it is an addition to the current regimen, and that might lead to duplication. It probably does lead to duplication or too many medications. You may have a lack of a booster, a lack of a drug to boost, or too much boosting. There are medications, especially protease inhibitors and the integration inhibitor elvitegravir that requires boosting with either ritonavir or cobicistat. I've seen a protease without a ritonavir boosting because the provider forgot. I've seen ritonavir by itself with nothing to boost, and I've seen too much ritonavir trying to boost a protease inhibitor, causing more side effects in the patient.

Another type of medication error is inappropriate dosing. And this is very common because dosing of ARVs can be tricky. The renal adjustment. This is where some people forget to do. So once your creatinine clearance goes below 50, you would need to really adjust their medications. Tenofovir, TDF, and emtricitabine, FTC, should be every other day when your creatinine clearance is between 30 to 49, for instance. Most of the single tablet regimens are not recommended to be used when your creatinine clearance goes below 50. With the exception of regimens that contain TAF, or tenofovir alafenamide, which can go down to a clearance of 30. The reason is that you need to dose-adjust one or two of the
medications in the STR but you can't dose-adjust that third one. So you would have to break them apart to be able to dose adjust. There could be an incorrect or a lack of dose adjustments due to drug interactions. So many HIV medications that are substrates of a cytochrome 3450 isozyme needs to be dose-adjusted based on what other drugs they're being given with. The most common is maraviroc. I think of maraviroc as a poor victim. It is a pure substrate of 3A4, it does not modulate 3A4. So anything that affects 3A4 is going to increase or decrease maraviroc levels and you would have to increase or decrease a dose accordingly. Atazanavir boosted dosing should be done when TDF or a PPI are on board. So you can't use the unboosted dose of atazanavir when either one of those are on board. And dolutegravir, which is normally dosed once a day, it should be dosed twice a day when you are using it with a potent UGT or 3A4 inducer. And there are certain ones that are listed in the package insert. So some of these medications require dosage adjustment when there is drug interactions involved.

Incorrect dosing. Before when I gave that example of a prescriber writing thrice instead of twice, that led to lopinavir being dosed TID. Three times a day. And also inappropriate dosing in the presence of RAMs, or resistance-associated mutations. Again, duitenivir, which is usually once a day should also be twice a day when there is first generation integrate mutations present in the patient's virus. Darunavir should also be dosed 600 twice a day when there are darunavir mutations present. That needs to be done to overcome some of these mutations.

But the consequences you know very well. Inappropriate dosing where it's too low, we're gonna have a list of virologic failure which can lead to resistance, thus limiting future options for the patient. If it's too high, you're gonna go into toxicity range and if the patient feels toxicity side effects, they're more likely to not be very adherent.

Incorrect drug. So this I've seen quite a few as well. And this is error on both the prescribing and dispensing side. So on the prescribing side, the physician can write down the wrong drug name. Nowadays when we're supposed to all be in e-scribing mode now, the physician can choose the wrong drug in the e-scribing system. Or they can use three letter abbreviations incorrectly if they are writing it and this is why I discourage three letter abbreviations. Now error on the dispensing side. If you try to read the handwriting, you can interpret Combivir as Combivent, so interpreting handwriting incorrectly. You can type the wrong drug or the wrong drug's strength. So same with the prescribing side. When you're typing with the pharmacy system, the computer can give you choices of strength and it can list drugs that may seem similar in name to it and if you choose the wrong one, you just typed out the wrong drug. Or you've done everything correctly, but then you grab the wrong bottle from the shelf during the dispensing phase.

And then there are errors due to drug interactions. As I mentioned before, there is a high likelihood of drug interactions potential with anti-retroviral. So here you really have to watch for this potential. Prescribing interacting drugs due to either the lack of knowledge by the provider because they may not be a specialist, or the provider is unaware that the patient is taking an interacting drug, which means the
patient is taking it over the counter and not telling the provider or they're seeing multiple providers and their primary care physician does not know that. So some of the examples is using rilpivirine with proton pump inhibitors which is contraindicated. Because rilpivirine requires a very thick environment to absorb. Using simvastatin or lovastatin with boosted protease inhibitors or cobicistat that is contraindicated. The levels of simvastatin and lovastatin gets raised incredibly high and the risk of drobdo is quite high. Or the use of rifampin with most HIV drugs. We really don't want to use rifampin. It is a potent inducer. So it will make many of our medications ineffective or less effective. And if the pharmacist is not a specialist either, they may miss the interaction and then the error reaches the patient.

00:22:32

Now here's some contributing factors. We all know that we are busy throughout the day and sometimes things happen and errors do happen. But here's some of the most common contributing factors to errors. Overwhelming workload. Repetitious tasks. Overriding alerts due to de-sensitivity. We see these pop-outs that warn you of a potential drug interaction and if you see it many times and too many times you just click the cancel button and override the alert. And so if the alert is a real one or a significant one, than you just overrode one because you're just too tired of seeing them. You can have momentarily lapse in concentration. You may not be well trained in HIV. So you may not be a specialist. Or there could be a breakdown in the health care system delivery that I've mentioned before.

00:23:24

Okay so let's look at some patient case examples.

00:23:29

So this is an example of an incomplete regimen. So SB is a 35 year old female with a past medical history of HIV, seizures, bipolar disorder, depressive disorder, diabetes, and obesity admitted to the behavioral health unit for suicidal ideation. So she was subsequently transferred from the psychiatric unit to the ICU because she had a seizure so they had to go there for seizure management. The ICU physician continued her medications which is listed there. The ICU clinical pharmacist was a former classmate of mine at UCSF, so she remembered, hey I don't know HIV but Chris does, so let’s call Chris. So she calls me to ask me an opinion. She said Chris, I don't know what a regimen is supposed to be like but I remember in class that it's supposed to not be just one drug. So she was correct. This patient's drug chart only had Isentress. So the patient is lacking a portion of their regimen and the patient is not the best historian so now they have to figure out what the rest of her regimen is by backtracking. Now the ICU physician who is not an HIV specialist did not know that HIV needs to be combo, so he just continued everything that you see there when she was admitted. Good thing that clinical pharmacist knew at least that it is a combination regimen even though she wasn't sure what it was supposed to be.

00:25:13

This was a case of an incorrect boosting of a PI. So NL is a 39 year old female patient participating in a medication therapy management project at her clinic. And this was a MTM project that was done with a local clinic here in New York as well as with the CDC and a community pharmacy where we were
measuring, and I was participating in this project, we were measuring the clinical outcomes of difficult to manage HIV patients when they are followed by a community pharmacist. So the clinic would send me the patient’s labs, two years labs, her chart, and I would sit down with the patient to interview her and talk. So her new PCP gave her prescriptions for darunavir 800 once a day, ritonavir 100 milligram tablets once a day and TDF/FTC once a day. So the med list and labs were sent to me and her provider told me that her main issue was adherence. So I sat down with her to see why she had trouble with her adherence. So she told me that she had GI side effects and she wants to know whether there was a better regimen for her to switch to to not have GI side effects. So when I asked her she tells me she has been taking darunavir one tablet, two ritonavir capsules, and one TDF/FTC tablet all once daily for the last three years. So I said, how come you’re taking two of the ritonavirs? So more questioning I found out that she used to be on darunavir 600 milligrams twice a day with ritonavir 100 milligrams twice a day, so that’s two pills of darunavir. Her regimen was simplified down to the once a day because I guess they found out there was no darunavir mutations, but the ritonavir dose was never reduced. So she just combined two pills of ritonavir into one dose and took it with the 800 milligrams of darunavir. What’s strange was that both her former provider and pharmacy never caught that error for three years and continued doubling the dose of ritonavir, hence the GI side effects. So I told her, let’s fix this first. Let’s remove the one ritonavir, continue the medication, and then we’ll talk about switching regimens as needed. Sure enough her GI side effects subsided. She was very happy with the correct regimen, and she is still to this day on the same regimen without having to switch.

So here’s an example of an inappropriate dosing. So this was a patient of mine back in San Francisco before I moved here. He is a 59 year old male on a stabilized regimen of raltegravir 400 milligrams BID plus TDF/FTC once daily. He at that time lived in San Francisco. His provider promised him that if he was adherent and his viral load remained uncontrolled, she would simplify his regimen down to once a day. So she was kind of dangling a carrot in front of his face so he could get his viral load down to undetectable and take his meds every day. And he was being really good at it, too. So he moved to Boston five years ago and before he moved she kept her word and simplified his regimen down to once a day. After a year in Boston, he moved back to San Francisco and became a patient again. When I looked at his regimen, he was taking raltegravir 400 milligrams one tablet once a day plus TDF/FTC once daily for the past year. So he was taking once a day. Unfortunately there was some miscommunication or lost in translation somewhere where she told him to take both pills of the raltegravir once a day to simplify, he heard that he could just disregard the second dose of raltegravir. So for an entire year he was taking half the dose of the raltegravir. So I called the Boston pharmacy and the Boston provider prescribed that regimen but continued that regimen thinking it was what was being done in San Francisco and both the provider and the pharmacy continued to give it to him for an entire year. There is no instance where raltegravir can be halved down to 400 milligram once a day. Right now they’re working on a long-acting formulation of raltegravir where it can be dosed once a day, but that’s not out yet. There are studies including the one I just put in there, the Efficacy of Raltegravir once a day in switching strategies, still there are studies looking at simplifying raltegravir from twice a day down to two pills once a day, so 800 milligrams once a day. Once the patient is suppressed and suppressed for at least six months, that is off-label but it is done and there are studies for it and that’s what the provider did and unfortunately he misunderstood and was on half a dose of raltegravir for an entire year.
Okay, incorrect drug dispensed. This is where I'm going to reference ISMP's list again. A handwritten prescription was given to the pharmacy for a patient SL with the following. Forgive me, because I wanted to demonstrate this error. Truvada once daily, Prezista 600 milligrams twice a day, ritonavir 100 milligrams BID, Selzentry 150 milligrams BID. So instead of ritonavir, the pharmacy dispensed Retrovir 100 milligrams. Ritonavir and Retrovir you can see down in the list is one of the most common confused drug names. So factors leading to the error, one, it was handwritten. So her handwriting was a bit illegible. She was also mixing brand names and generic names. So the pharmacy going by the brand names thought well, that should also be a brand name since she was doing Truvada, Prezista, Selzentry, so they picked Retrovir because ritonavir was not a brand name. To top it all off, the patient used to be on Retrovir. So they saw Retrovir in the patient's profile, thinking it must be Retrovir since they used to be on it. So that was what created the error.

So incorrect dosing adjustment. TM is a 43 year old male on a regimen of darunavir 600 milligrams BID, ritonavir 100 milligrams BID, maraviroc 300 milligrams BID, and etravirine 200 milligrams BID. The provider disagreed with me on the maraviroc dosing. I told him it should be 150 milligrams BID, and his reasoning was that because both a CYP3A4 inhibitor in this case the booster darunavir, and a CYP3A4 inducer, in this case, etravirine, are both on board that they cancel each other out so the dose is in the middle, the 300 milligrams BID. However, if you look at maraviroc when dosed with etravirine, you see the maraviroc dose going down by 53 percent, so the recommendation is doubling the maraviroc dose to 600 milligrams BID when you have an inducer without an inhibitor on board. When you have an inhibitor on board like darunavir, you see that the maraviroc AUC goes up by over 300 percent. When you add on etravirine, the maraviroc AUC still goes up, it still more than doubles. So even with a potent inducer, it doesn't balance out or it doesn't override the inhibitor. So in general when you have both, the inhibitor generally wins. So you have to dose it based on the inhibitor dosing. So in this case it needs to be 150 milligrams twice a day.

And the reason that it's important is that maraviroc is associated with a dose-limiting side effect, specifically symptomatic postural hypotension. And this is a warning that is in the package insert. So the patient can feel very dizzy standing up and just fall down. And that is dose-limiting. So I've seen maraviroc dosed just once a day and still be effective because of this side effect. So you want to make sure that you are adjusting the maraviroc dose correctly.

Okay. So let's look at a second case of incorrect dosing adjustment. So RO is a 64 year old male on an STR of efavirenz/TDF/FTC plus boosted atazanavir 300 milligrams with 100 milligrams of ritonavir. So first of all, this is a treatment-experienced patient. I rarely see efavirenz being combined with boosted atazanavir with TDF on board as well, but this was what the patient was on. So his provider decided to switch him to a Nuc-sparing regimen and sends prescriptions to the pharmacy for efavirenz 600 milligrams, boosted atazanavir 300/100 milligrams, and dolutegravir 50 milligrams all once daily. So no
Nucs at all. So first of all there's a few issues. The first issue is that dolutegravir when dosed, and this was covered before, when dosed with any potent UGT or 3A4 inducer, that you have to increase the dose to twice a day. So efavirenz is one of those. So you have to increase the dolutegravir dose to 50 milligrams twice a day. Secondly, when you are dosing and this was the regimen before the switch, when you are combining— Actually even after the switch. When you are combining efavirenz with atazanavir, boosted atazanavir, the boosted dose should be 400 milligrams, 100 milligrams instead of the 300, 100. Efavirenz decreases atazanavir levels by quite a lot and the ritonavir only overcomes it by so much, so the recommendation is to shoot it up to 400 milligrams boosted.

This is an inappropriately written prescription example. So this patient JM is a 32 year old male presenting prescriptions to the pharmacy for treatment of gonorrhea/chlamydia plus a new prescription for PrEP. So he comes in, gives the pharmacist this prescription and I happen to be there in the pharmacy that day. I look at the prescription, it just says PREP, one tab PO, QD, number 30, with five refills. So this patient proactively went to his provider who is not an HIV specialist and requested PrEP. Now the provider without PrEP experience or HIV experience did not know what that was. So he just wrote PREP, one tab, PO QD. And you can see this can be interpreted by pharmacists who are not HIV specialists. They can interpret this to be a medication name. They might try to find a medication that sounds similar to PrEP. MoviPrep would be the worst. But the patient just got the prescription, brings it to the pharmacy, so now you have a provider that does not know PrEP prescribing PrEP. PrEP is something that you have to do baseline tests for and also regular tests for. Specifically follow-up in labs every three months. So even his prescription should have said TDF/FTC, tenofovir disoproxil fumarate and emtricitabine, which is the medication for PrEP, the refills should only be two. Because every three months the patient is supposed to go back to the provider to draw labs to make sure they're still HIV negative, make sure their kidney function is still fine, and do STI screenings and all that good stuff. So there's one error there and there's another error there.

And then these are some non-recommended ARV dosings, and these were done on purpose which very much surprised me. So the first patient SP is a 50 year old male presenting to the pharmacy with prescriptions for raltegravir 400 BID, fosamprenavir 1400 BID, ritonavir 100 BID and TDF/FTC once a day. On consultation with provider, he said that the reason that he gave fosamprenavir 1400 BID because the patient is complicated and has PI resistance. So as you know the 1400 milligram dose of fosamprenavir is the QD dose. Twice a day should be 700 twice a day. So what he did pretty much was doubled the fosamprenavir dose to hopefully overcome some protease mutation resistance. And that is something that is not done. You don't double a dose of something to hopefully overcome a mutation. This is where a switch to a different protease that would be able to overcome that, for instance, darunavir would be the way to go instead of doubling the fosamprenavir. So you actually created more side effects for this patient. Patient number two. AR is a 46 year old male virologically controlled with a new regimen for darunavir 1200 milligrams BID. No ritonavir. Plus TDF/FTC once a day. And this was one where I went back and forth, back and forth with the provider. The provider chose the regimen because the patient could not tolerate ritonavir. And he had gone through multiple providers who refused to take out the
ritonavir, so what this provider did was doubling up the darunavir and then crossed fingers. Because her reason was that if she would have said no, I have to give you ritonavir, that he would have just leave her and find another one and the next one may not know what they’re doing, so that was her regimen. So this is not done off-label. Even the PK for the non-boosted darunavir for 1200 milligrams is not good. So this is not something that should be done at all and this was done on purpose. Thankfully the patient stayed undetectable because he was already virologically controlled, but this is something that was more than just off-label. And then the last patient, MJ, is a 39 year old male switching to a new provider. He presented with a regimen containing zidovudine/lamivudine, two tabs BID, given by his previous provider to overcome an M184V mutation. So zidovudine/lamivudine is dosed one tab twice a day, that's one of the combination Nucs. The M184V mutation knocks out lamivudine. So this provider not knowing resistance, doubled the dose in the hopes of overcoming that mutation. That is not something you do. You can triple it and you still would not overcome that mutation. So when you have that mutation, pretty much you've lost most of the lamivudine activity, so you would have to switch.

Okay, so let's look at ways to prevent medication errors. And these are some strategies to minimize errors. The very first thing is education. So more clinical HIV education for prescribers, pharmacists, and nursing staff. Cutting technology. Have a clinical pharmacist-led medication reconciliation. Especially in hospitals. Look at hospital formulary interventions. They can help remove errors or even cause errors. You can have prospective audit with feedback and then internal error reporting when you are a large organization.

So let's look at the education of staff. At the center of it is the AAHIVM, the American Academy of HIV Medicine, and they have a credentialing process where HIV specialists can get very good training there. But all of this, what it is saying is that there is room for improvement from all sides, from prescribers, from pharmacists. The article on the top right that you see which looks at pharmacists in New York, it was a survey of pharmacies in New York, show there's a huge room for improvement. The pharmacist survey, the majority of them were hospital-based. Only about 60 percent of them identified efavirenz CNS toxicity and abacavir hypersensitivity. So those are two very very well known toxicities, and only 60 percent identified that. And less than half of them identified drug interactions of atazanavir with a PPI and only 37 percent identified a drug interaction between simvastatin and a protease inhibitor, which is a contraindication. On the bottom it was a different survey, this time physicians regarding ARVs, and in the survey of physicians, residents and non-ID specialists scored in the 30 percentage when it comes to HIV associated questions. So the questions were like, which one of the following statins has an interaction with this ARV? So those were the type of questions. And the residents and non-ID physicians only scored in the 30 percentage. So it shows that a lot of us have a lot to learn and there's a lot of room to learn and grow and improve. There's resources available to you including CEI, there's a line that you can call to ask an expert if you're not sure, there's AUTC, there's Clinical Care Options, there's a guideline, so the HHS. So there's a lot of resources out there to educate yourself and your staff.
Technology. CPOE, a Computerized Physician Order Entry. This eliminates three letter abbreviations and inconsistent brand and generic names. Studies in CPOE error reduction are conflicting, however. Some show that it really helps in reducing errors, others really don't show that. These systems can also be the sources of errors as well. So for instance, they can pre-populate a drug frequency. So if they pre-populate the wrong frequency like BID and the drug is only supposed to be QD, that is a source of error. E-prescribing, and this is great now in New York. Most are e-prescribing. This eliminates pharmacists trying to decipher the handwriting by the physician. Automated dispensing machines. So this helps eliminate human errors in some large pharmacies using machines or robots to dispense medication. Electronic Medical Record, bar coding which puts in a second safety line to make sure that the correct medication is given to the patient. And then there's the Clinical Decision Support Software, like TheraDoc. These are the ones that gives you the pop-ups whether it's for pharmacists or physicians to warn you of drug interactions, duplications, stuff like that. However, this can also be a source of error. If you don't update your software the outdated stuff can lead to errors and then also those warnings as I mentioned before can be ignored if you have something called alert fatigue. You just kind of override all of those warnings that pop up.

00:47:08

Clinical pharmacist intervention. There are many studies out there that show a positive impact when an HIV clinical pharmacist intervenes in the outcome of a patient. And this study was also done by the same former UCSF colleagues and this was a review of 32 publications published in about a decade looking at the involvement of an HIV clinical pharmacist and the impact on outcomes. The studies were primarily in the US, they were mainly observational cohorts, and before and after comparison, those were the main study designs. The majority of studies were done in Amcare or in-patient settings, again there's a lack of community pharmacies as a setting in this analysis. So what they saw was the majority of studies showed a clinically and statistically significant improvement in adherence and viral suppression. They saw a reduction in hospitalization, reduction in physician office visits, lower number of hospital days, reduction of visits to the ER, lower pill burden, and a reduction in the inappropriate discontinuing of outpatient medications. A high percentage of their recommendations, the clinical pharmacists, were accepted by the physician or the health care team. And lastly, those are the things that the pharmacies did in these studies. So they dose ARVs, they looked for drug interactions or adverse drug reactions, provision of drug information, they did adherence counseling and instruction on the use of adherence-enhancing tools.

00:49:01

Now hospital formulary interventions obviously, they always add, delete drugs, and many things go into it. Is it cost issues, are there generics, so this requires frequent evaluations. And hospital formulary because it is restricted sometimes is good because you don't have that many drugs to choose from, so there's less errors to make, but then sometimes there's that. There is a lack of co-formulated products in many hospital formularies and having co-formulated products can decrease errors because they're all in there for you already. There's also drug interactions with non-formulary drugs that a patient may be taking. That is not detected in the hospital. And also formularies restriction can lead to delayed access to the anti-retroviral. If you have to go through the PA process it takes a long time.
Prospective audit with feedback and this is the cornerstone of the IDSA antimicrobial stewardship guidelines. This is a multidisciplinary stewardship to maximize the clinical outcomes and minimize unintended consequences of antimicrobial use. And this is kind of time-consuming. It involves the collaboration of both medicine and pharmacy, ideally ID and HIV trained, requires a lot of resource and time. Because daily audit is ideal, but most of the time there's no manpower to do the daily audit and the feedback and the recommended intervention by the pharmacy team goes directly to the prescriber.

And lastly, internal error reporting is something that all pharmacies should have and the big chain pharmacies do. The error reporting system helps the pharmacy organization gain new information about preventable adverse events and then they would analyze the data, they would see what the root cause of the error is, and then communicate that internally and do some internal fixes to prevent those type of errors from happening in the future. They can provide the organization with information on adverse effects. Medication errors. Close calls before it gets to the patient, and then other safety risks and hazards. So it's a very good tool. So all the information gathered allow the organizations to analyze any failures in their system, and again this is system and not a specific person. Failures in the system and to fix them, to prevent the errors before they get to the patient.

So in summary, we know that HIV therapy is complex. It involves multiple drugs to create a regimen and it evolves, things change all the time. Guidelines change all the time and that can lead to medication errors. And errors happen. No matter how careful we are, they happen, we're human. So just stay vigilant. If something looks off or if you're unsure, then investigate. Recognize the contributing factors that we went over and minimize them. Utilize HIV clinical pharmacists if you have them. And again, keep that communication channel open between provider, pharmacist, patient.

And this is the CEI Ask an Expert line that I referred to, if you have any questions on HIV, HCV, PEP or PrEP, feel free to call this line. And if there's any questions I can take them.
- [Chris] You know, that was a one off. And when I saw that error, I was quite surprised. It shows a few things. It shows that patients are aware of PrEP and they’re asking for PrEP, which is good. It shows that providers are willing to prescribe PrEP, which is good. What it shows is providers still need to be trained on how to prescribe PrEP. And that’s what the example I gave showed and that was the only one, crossing fingers, that I've seen for pre-exposure prophylaxis errors. Most of them are in the HIV positive population.

- [Naomi] So in your case if you were to see that in your setting, what would be your first thing? Would you call the provider right away? Because obviously you don't want to delay that patient getting PrEP if they really want it, but how would you adjust that?

- [Chris] So for that patient what I did, obviously I knew what medication it was and so did the patient. I talked to him about his provider. He admitted the provider is not an HIV specialist but was willing to prescribe PrEP so he asked for it. So I did call the provider and told the provider what the medication was and also recommended the Q3 month guidelines and where to go for the labs and where to go for the guidelines just so that hopefully continuing in the future that he wouldn't give that many refills. Because you kind of want to see the patients back and that’s how you see them back, is to limit the refill.

- [Naomi] Great. And I guess my only other main question, you talked about reconciliation of how you double check on the back end or some other end so maybe could you talk about how you do that within like Duane Reade Walgreens? Do you review prescriptions on a monthly basis to see if you can catch anything? I’m just kind of curious of your process in terms of catching these errors maybe on the back end.

- [Chris] So Walgreens as an organization has an internal error reporting system that I mentioned in my last slide and it is called the STARS Event System, and every time any pharmacist catches an error that was done, regardless of whether the error got to the patient or not, they’re supposed to log in the system. So the system goes to ask them a whole bunch of questions about the error, like which one of the following contributed to the error? Please pick two or three. Or what type of error is it? And in the future, how would you go about to minimize this in the future? So the pharmacist has to fill out this form and then that error no matter how minute or lame if it's not correct it's supposed to be documented and then it gets logged in the system. So the whole point is, as I mentioned on that slide, is to use all of these internal reports on these errors to look at what are the patterns. What is the most common error? How can we prevent those errors from happening in the future using the technology instead of telling the pharmacist, oh be more careful. So that’s how the STARS system at Walgreens would work. It can be anything from the prescription says 30 pills but the pharmacist dispensed only 25.
So that's just a minor error. It needs to be logged. So if somewhere there is a breakdown in the process, the dispensing process at Walgreens is quite... There are many steps. So it's many steps redundancy so that it can create that safety net so that you don't get the wrong medications. You don't get the wrong quantities. You don't have the wrong strength. So there's redundancies. However, errors still happen. You know, you still have humans and things happen. And that's where that internal reporting comes in just so that we can prevent the error before it gets to the patient.

00:58:13

- [Naomi] Thank you so much. That was my only other question that I happened to have, but once again I just wanted to thank you for giving this great presentation on HIV medication errors and all the resources that you gave. But with that, I will end the webinar and hope to see everyone at the next CEI training. Thanks again.

00:58:34

[Video End]