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ADVERSE PHYSICAL EFFECTS OF ANTIRETROVIRAL THERAPY AND METHADONE ON PEOPLE LIVING WITH HIV/AIDS (PLWHA) USING INJECTION DRUGS (IDUS)

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ABSTRACT

Background: People with HIV who use injecting drugs besides taking ARVs also use methadone. With these conditions, of course there will be a risk of causing various side effects. Based on this, researchers are interested in exploring the physical side effects experienced by PLWHA IDUs while using ARV therapy and Methadone. **Method**: This qualitative research uses a phenomenological study approach. Participants were taken based on criteria referring to the purposive sampling technique (snowball sampling). Participants were PLWHA with a history of injecting drug users (IDU) aged 20 years and over and had undergone ARV therapy and Methadone maintenance therapy for at least 6 months. Researchers conducted semi-structured in-depth interviews and used Colaizzi's data analysis stages. **Results**: HIV AIDS sufferers who inject drug users experience physical side effects on the digestive system, namely tooth decay, constipation, anorexia. Side effects on the musculoskeletal system include muscle pain and weakness and insomnia. Side effects of the covering system are the appearance of itching and rashes. Side effect on the reproductive system is a decrease in sexual function. **Recommendation**: The results of this study need to be followed up with studies with a larger number of participants so that they can represent other problems experienced by PLWHA while using ARV therapy and methadone together.

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1. INTRODUCTION

The prevalence of people living with HIV continues to increase. United Nations Program on HIV/AIDS (UNAIDS), reports that until 2020 the total number of people living with HIV reaches 37.7 million and as many as 16 million are adults, as many as 1.5 million are new sufferers, with deaths reaching 680,000 people (UNAIDS, 2021).

From 2010 to 2020, Indonesia is the top 3 countries that have experienced a very rapid increase in the number of PLWHA (UNAIDS, 2021). There are 144,000,000 people living with HIV and as many as 34,500 are people who inject drugs, while only 26% of people living with HIV on treatment (UNAIDS, 2021).

The therapy received by PLWHA is Anti-retroviral therapy (ARV). ARVs function to inhibit HIV replication. ART treatment could be safely used for patients with HIV to reduce the viral load (Hirofumi Fukda et al, 2022). Currently there are 3 classes of ARVs namely nucleoside reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRT), protease inhibitors (PI).

People living with HIV who inject drugs, apart from using ARVs, they also use methadone. The use of methadone as an opioid agonist has been carried out since 1950 (L. Nicholls, L. Bragaw, Ch. Ruetsc, 2010). Methadone is an opioid agonist replacement (PAO) treatment (Emmanuel Krebs., et al., 2022). To minimize the effect of using a substitute for an opioid agonist, restrictions on the type, dose, and duration of drug administration are carried out (Jin et al., 2020).

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Injecting PLWHA who use ARV therapy and Methadone simultaneously will certainly be at risk of causing various side effects. Based on this, the researchers were interested in exploring the physical side effects experienced by IDU PLWHA while using ARV therapy and Methadone

2. RESEARCH METHODE

Research Design

This qualitative research uses a phenomenological study approach. Researchers describe, interpret, and analyze the adverse physical reactions of antiretroviral therapy and methadone used simultaneously in people living with HIV AIDS, especially injecting drug users. This phenomenological approach includes four stages, namely bracketing, intuitive, analyzing, and describing.

Partisipant

Participants in this study were taken based on criteria that referred to purposive sampling to be precise with the snowball sampling technique. The research was conducted at 2 satellite methadone maintenance therapy programs (MMTP) in Bogor City, namely the Kedung Badak Health Center, and the East Bogor Health Center, Bogor City, West Java, facilitated by the Bogor City Health Office.

Participants are PLHIV with a history of injecting drug users (IDU) aged 20 years and over and have undergone ARV therapy and Methadone maintenance therapy for at least 6 months, are able to communicate well, and are willing to become participants. The exclusion criteria were PLHIV IDUs who were still active using other narcotics.

The process of identifying criteria for potential participants was assisted by the MMTP coordinator at the Kedung Badak Health Center and East Bogor Health Center. The total recommended number of potential participants was 13 people, two participants were used for the interview guideline trial, one participant was not analyzed because he met the exclusion criteria, namely using methadone with other types of injectable opiates that were known during the interview process. So that there were 10 participants who were involved as actual research subjects.

Data Collection Method and Procedure

Data in this study were collected by the following methods: interviews with field notes, participant observation. Researchers conducted semi-structured in-depth interviews. The researcher has created an interview guide (interview script) which contains several research topics. The interview guideline has been tested on 2 participants and has been revised. Development of questions adapted to the process and participants' answers. Interviews were conducted 1-2 times for 30-60 minutes for each participant.

The role of the researcher is only to help participants express experiences without providing assumptions, opinions, and criticism. To improve the accuracy of data collection, researchers used open-ended questions, recorded interviews, and made verbatim transcripts. Data Analysis Information in this study was analyzed simultaneously with the data collection process. Data obtained from interviews, participant observation, and documentation studies were copied in the form of transcripts. Researchers used the Colaizzi data analysis stage. Each transcript of the interview results is analyzed separately so that an understanding can be obtained that relates to the whole essence of the phenomenon under study.

Ethical considerations

Ethical considerations that refer to the principle of respecting the dignity of participants, the principle of paying attention to welfare, justice for all participants, approval after explanation (informed consent).

3. RESULT

Participant characteristics

Participants in this study were recruited voluntarily and agreed to take part in interviews that were conducted in closed rooms. Demographic characteristics of the 10 participants live in several different cities, namely Jakarta, Bogor, and Tangerang with the sexes of 3 women and 7 men. The age of the participants ranged from 30 to 40 years.

The characteristics of the educational background were high school, bachelor (S1) and master (S2) masters. The participants' religions varied, namely Islam, Christianity, Protestantism with various ethnic groups, namely Sundanese, Javanese, Batak, Betawi, Ambonese, Bugis and Chinese, as well as Arabic. Participants told that they started experiencing drug addiction when they were still in junior high and high school or before marriage. The duration of ARV therapy ranges from 1 to 14 years.

Some of the participants were married and had children, and some were widows and widowers. Participants who are currently undergoing ARV therapy in a different place, namely in the hospital. Marzoeki Mahdi Bogor, Tangerang Municipality Hospital, and Jakarta Jatinegara Health Center, and Jakarta Cilandak Health Center.

The type of ARV used by the participants according to the first-line recommendations, namely: 2 NRTIs + 1 NNRTI. The names of the drug combinations currently used are duviral and neviral, duviral and efavirenz, tenofavir + hiviral + neviral. Participants also underwent methadone therapy at different methadone satellites, namely the

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Kedung Badak Health Center and East Bogor Health Center. The lowest dose of methadone the participant lived was 10 mg and the highest was 260 mg.

Disorders of the Digestive, Integumentary, Musculoskeletal, and Reproductive Systems.

People with HIV AIDS who use needles experience physical side effects on the digestive system, namely tooth decay, constipation, anorexia. Side effects on the musculoskeletal system include feeling of pain and weakness in the muscles and insomnia. Side effects on the integumentary system are the appearance of itching and rashes. Side effects on the reproductive system are decreased sexual function.

Tooth Damage

Tooth decay was revealed based on the experience of participants who claimed they could not stand the bitter taste so if they drank methadone, they always asked for more sweetening syrup. Following are the participant's expressions:

"Teeth become porous, break, and wear out after a while, all of my teeth have been used up" (P1)
"Maybe, the chemicals in methadone damaged my teeth, because the medicine was taken, so it stuck to the teeth, ... what is clear is that the teeth are gone, the average methadone drinker has incomplete teeth" (P3)
"My teeth are turning black" (P4)
"I have 4 broken teeth, it's hard to eat" (P6)

Constipation

Participants revealed that since starting methadone and ARVs they often had difficulty defecating (BAB). Following are the participant's expressions:

"The effect of methadone makes it difficult for me to defecate"...
"I feel it is difficult to defecate, for 2 weeks at most I only defecate 2 times 3 times, that effect makes hemorrhoids. Because it's hard, we don't want to force it, if it doesn't it won't be pleasant for the stomach"...(P3)
"This week I defecate 2 times"

Anorexia

Participants expressed their experience of experiencing a decrease in appetite while using ARVs and Metahadone together. This was revealed from the following patient statements:

"I feel my appetite dropping"
"I don't eat as much as before"
"as long as you take ARVs and Methadon you don't eat much"

Muscle pain and Weakness

Participants expressed complaints of muscle pain and weakness, this can be seen from the following participant expressions:

"I now feel my muscles are weak"
"My muscles are often sore and weak"
"Now I am no longer able to lift heavy objects, what I feel now I am weaker"

Insomnia

Participants revealed that they experienced sleep pattern disturbances while using ARVs and methadone. Following are the participant's expressions:

"I find it hard to sleep, sometimes before dawn I can sleep"...
"I don't sleep well, I often wake up"
"Waking up I don't feel refreshed"
"At least I only sleep 4 hours at night"

Rashes and Itching of the Skin

The experience of the participants expressed was that they experienced dermatitis in which itchy reddish nodules were accompanied by rashes and later blackened on the skin of the hands and back of the back. Following are the participant's expressions:

"Now, my skin is itching (while showing problematic skin) for almost two months".... (P1).
"For a time his body was red-red, he had a rash too" ... (shape?)..
"It's round like that... it's red like a swollen one but it's red.... Some are as big as coins, some are small, some are big"... (P4).

Sexual Function Disorder

Disorders of Sexual Function Participants expressed problems related to sex drive (libido) and the ability to ejaculate and have orgasms while using methadone and ARVs. Following are the participant's expressions:

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"It has an effect, yes, it reduces (libido) yes... lowers (libido)... I think methadone tends to be them too... the effect of methadone"...
"The ejaculation is normal, right... maybe there's a bit of a problem, ehhh…. Fast… it tends to be faster"… (P3).
"It's just not like it used to be... in the past it was tight and now you have to rest first. Ejaculation, if it used to be long, now it's fast"... (P7).
"That's methadone… His libido is dropping"… (What about ejaculation?) "No…. I don't even ejaculate"… (P8).

4. DISCUSSION

ARV therapy is indicated for people living with HIV with CD4 less than 200 cell/mm^3 or if there are symptoms of opportunistic infections. The goal of this therapy is to control the spread of HIV and reduce CD4 damage. In PLHIV who come from injecting needle users sometimes also run methadone therapy to control addiction to narcotics. As long as you use ARVs and methadone together, of course there will be some drug reactions that cause various physical complaints.

Methadone maintenance therapy is recommended for someone who has been addicted to narcotics for a long time. The use of methadone can cause physical side effects on the body system. In the digestive system, methadone can give side effects such as nausea, vomiting, anorexia, constipation, stomach cramps, and diarrhea (L. Nicholls, L. Bragaw, Ch. Ruetsc, 2010). However, in the results of this study, the only physical complaints of the digestive system that patients complained about were anorexia, constipation, and tooth decay.

The anorexia that participants complained about could occur as a side effect of using ARVs or methadone. There are several ARV drugs that have been proven to cause side effects of decreasing appetite in users, such as ARV types Abacavir, Saquinavir, Lopinavir, Atazanavir, Darunavir and Raltegravir.

Mitochondrial toxicity as a reaction from zidovudine gives the side effect of anorexia at the start of therapy (Andrew Carr, David A Cooper, 2000). Methadone also causes a decrease in appetite (Piotr Łój et al, 2014). Complaints of decreased appetite were conveyed by 6 out of 10 participants.

In addition to complaints of anorexia, residents also complain of constipation. Constipation is a condition of difficulty in removing feces. Methadone often causes constipation in users (Piotr Łój et al, 2014). Constipation complaints were submitted by 7 out of 10 participants. It is possible that this constipation occurs due to the effects of methadone use because there is no literature that explains that ARVs can cause constipation. Nevertheless, physiologically the effect of methadone on innervation causes a decrease in intestinal motility performance which results in constipation.

Participants also complained about pain and weakness in the muscles. This condition can arise as a reaction from ARVs and methadone. high concentrations of zidovudine in the blood can cause pain and a feeling of weakness in the muscles (Andrew Carr, David A Cooper, 2000). Most of the respondents who complained of muscle pain and weakness were users of Zidovudine and Methadone. An increase in zidovudine concentrations may occur as a reaction to methadone. Methadone can increase zidovidone concentrations by 40% in users (Piotr Łój et al, 2014). Weakness in the muscles can be reaction from Efavirenz and lopinavir exposure was associated with significantly lower glucose accumulation (Bethany J. Heaton, et al., 2022).

Methadone is an opioid agonist whose use has an impact on nerve activity. Methadone users complain about insomnia while using it. Efavirenz or nevirapine increased R-methadone (Gavin Bart, 2021). The sleep disturbances complained of by PLHIV IDUs can occur as a result of methadone (Piotr Łój et al, 2014). Methadone can change CNS activity, causing methadone users to experience insomnia (Bracken. B., George Trksak. 2012).

Insomnia can also occur as a result of ARV users. ARV types Lamivudine, Emtrycitabina, Saquinavir, Lopinavir, Darunavir and Raltegravir have also been shown to cause insomnia (Piotr Łój et al, 2014). Common reactions of evafirenz, nevirapine, delavirdine cause side effects on the central nervous system (CNS) such as dizziness and insomnia, as well as impaired concentration and nightmares (Andrew Carr, David A Cooper, 2000)

Erectile dysfunction and decreased libido were complained by several participants. This condition is predicted as an effect of using ARVs and metahadone together. Methadone and ARV users of saquinavir, lopinavir, darunavir and raltegravir generally experience erectile dysfunction and libido disorders (Piotr Łój et al, 2014).

5. CONCLUSION

People with HIV AIDS who use needles experience physical side effects, namely tooth decay, constipation, anorexia, feeling of pain and weakness in the muscles and insomnia, itching and rashes, decreased sexual function. This condition needs attention in order to increase PLWHA compliance to undergo both therapies consistently without many disturbing physical complaints. It is advisable to also conduct research with a larger sample or participant scale in order to explore all PLWHA complaints while using both therapies simultaneously.

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