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RESEARCH ARTICLE SUPPLEMENT

SURVEYFORM

Demographic & General Information

1. Birthyear:

2. Gender:

☐ Woman
☐ Male
☐ Other……..

3. Branch:

☐ Psychiatry
☐ Infection

4. Academictitle:

☐ Specialist(Yearof specialization:)
☐ Research assistant (Year you started your specialization education:)

5. Have you examined an HIV positive patientwith mental problems within the last 6months?Ifso,howmanypeopleperweekonaverage?

6. Typeof hospital:

☐ Education–Research
☐ University
☐ Public Hospital
Other……

Approaches About Drug-Drug Interactions(DDIs)

1. Who do you use when you want to know more about potential DDI s? (You can choose more than one)

☐ Prospectus ☐ Written material (book, brochure, monograph)
☐ Pharmacist ☐ Internet
☐ Smart device applications ☐ senior physician
☐ Other …… ……. ☐ medical pharmacologist

2. How often does a potential DDI affect your decision when prescribing medication?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

3. How often do you inform patients about potential DDI s?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always

4. How sufficient do you think your DDI knowledge is to intervene in medical treatment?

☐ None ☐ Little ☐ Middle ☐ A lot ☐ Full

5. Please choose the appropriate one(s) for you regarding DDI s between antiretroviral and psychiatric drugs for your patients. (You can choose more than one)

☐ I check it at every meeting.
☐ I only check when starting a new psychiatric medication.
☐ I check when an antiretroviral drug is added to psychiatric medication.
☐ I never check.
☐ Other ……

6. Have you ever had a patient who was adversely affected by the combined use of antiretroviral and psychiatric drugs?

☐ Yes
☐ No

7. What approach do you take when you encounter a DDI?

☐ Changing all medications,
☐ Changing all antiretroviral medications
☐ interacting antiretroviral medications
☐ Changing all psychiatric medications
☐ Changing interacting psychiatric medications
☐ None
☐ Other ……

CASES

CASE 1

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patient history

OA 48 years old, male

Height: 166 cm, Weight: 75 kg.

Cigarettes: 52 packs/year; No alcohol or substance use.

He was diagnosed with schizophrenia at the age of 28. He was started on paliperidone 3 years ago and his delusions and hallucinations improved subsequently. The patient does not describe any side effects. He complains of difficulty falling asleep.

HIV infection was detected in tests performed 2 years ago due to oral thrush and weight loss, and treatment was started. After ART, the thrush lesions in his mouth resolved and he gained weight.

Laboratory findings

CD4 cell count: 215/mm 3, HIV viral load: negative.

ALT:8 U/L (<35 U/L), AST:18 U/L (<35 U/L), GGT:26 U/L (<35 U/L)

BUN: 8.5 mg/dl (6-20 mg/dl), Uric acid: 5.67 mg/dl (2.6-6 mg/dl), Creatinine: 0.81 mg/dl (0.5-0.95 mg/dl) LDH:188 U/L (<248 U/L), CK:134 U/L (<171 U/L)

Medicines

Antiretroviral Drugs:

- Tenofovir / Emtricitabine (245/200 mg)
- Darunavir / ritonavir (800/100 mg)

Psychiatric Drugs:

- Quetiapine (100 mg)
- Paliperidone (6 mg)

1st question;

In this patient Who do you use when you want to know more about potential DDIs? (You can choose more than one)

☐ Prospectus
☐ Written material (book, brochure, monograph)
☐ Pharmacist
☐ Internet
☐ Smart device applications
☐ senior physician
☐ Other …… …….
☐ medical pharmacologist

2nd question;

If you think there is a DDI, which of the following would you do? Circle the drug(s) you intend to intervene with.

- ☐ Dose change of interacting drug(s)
- ☐ Change in interacting drug(s)
- ☐ Discontinuation of interacting drug(s)
- ☐ Extra monitoring regarding interaction (ECG, plasma level)
- ☐ Clinical monitoring (continue routine monitoring)
- ☐ I don't think there is a DDI

a. Tenofovir / Emtricitabine (245/200 mg)
b. Darunavir / ritonavir (800/100 mg)
c. Quetiapine (100 mg)
d. Paliperidone (6 mg)

_____

DDI databases (1st case, 1st interaction)

- ritonavir + quetiapine
  - Using quetiapine and ritonavir simultaneously quetiapine may result in increased exposure; There is an increased risk of QT prolongation.
  - Ritonavir It will increase the level and effect of quetiapine by affecting CYP3A4, one of the hepatic/intestinal enzymes.

3rd question;

In light of the information given above, if you think there is a DDI, which of the following would you do? Tick the box(es). Write the code of the drug(s) you want to intervene in parentheses.

- ☐ Dose change of interacting drug/drugs ( )
- ☐ Change of interacting drug(s) ( )
- ☐ Discontinuation of interacting drug/drugs ( )
- ☐ Extra monitoring related to interaction (ECG, plasma level)
- ☐ Clinical monitoring (continue the same routine monitoring)
- ☐ I don't think there is a DDI

a. Tenofovir / Emtricitabine (245/200 mg)
b. Darunavir / ritonavir (800/100 mg)
c. Quetiapine (100 mg)
d. Paliperidone (6 mg)

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CASE 2

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patient history

AE 23 years old, male

Height: 175 cm, Weight: 55 kg.

Cigarettes: 5 packs/year, Alcohol: 2 double raki per week; Substance: marijuana, bonsai, heroin (last 1 year ago)

Bipolar for 5 years due to substance abuse He has been followed for 3 years due to Affective Disorder Type 1, and while it was stable, escitalopram was added for depression after the diagnosis was made.

He presented with withdrawal symptoms 1 year ago and was started on buprenorphine / naloxone. He has been followed up with HIV infection for 3 months and is receiving antiretroviral treatment.

Laboratory findings

CD4 cell count: 199, HIV viral load 800 copies/ml.

ALT:40 U/L (<35 U/L), AST:71 U/L (<35 U/L), ALP:91 U/L (30-120 U/L), GGT:24 U/L (<35 U/L),

BUN: 49.66 mg/dl (6-20 mg/dl), Uric acid: 9.02 mg/dl (2.6-6 mg/dl), Creatinine: 0.84 mg/dl (0.5-0.95 mg/dl)

LDH:199 U/L (<248 U/L), CK:80 U/L (<171 U/L)

Li plasma level: 0.85 mEq /L (0.6-1 mEq /L)

Medicines

Antiretroviral Drugs:

- Tenofovir / emtricitabine / elvitegravir / cobicistat (245/200/150/100 mg)

Psychiatric Drugs:

- Lithium (900 mg)
- Buprenorphine / naloxone (4/1 mg)
- Escitalopram (10 mg)

1st question;

In this patient Who do you use when you want to know more about potential DDI s? (You can choose more than one)

☐ Prospectus
☐ Pharmacist
☐ Smart device applications
☐ Other …… …….
☐ Written material (book, brochure, monograph)
☐ Internet
☐ senior physician
☐ medical pharmacologist

2nd question;

If you think there is a DDI, which of the following would you do? Write the drug (s) you intend to intervene with in parentheses.

☐ Dose change of interacting drug/drugs ( )
☐ Change in interacting drug (s) ( )
☐ Discontinuation of interacting drug (s) ( )
☐ Extra monitoring related to interaction (ECG, plasma level)
☐ Clinical monitoring (continue the same routine monitoring)
☐ I don't think there is a DDI

a. Tenofovir / emtricitabine / elvitegravir / cobicistat (245/200/150/100 mg)
b. Lithium (900 mg)
c. Buprenorphine / naloxone (4/1 mg)
d. Escitalopram (10 mg)

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Interaction information according to DDI databases;

- ***elvitegravir / cobicistat / emtricitabine / tenofovir + buprenorphine (2nd case, 1st interaction)***
  - Cobicistat will increase the level and effect of buprenorphine by affecting CYP3A4, one of the hepatic/intestinal enzymes.
  - Cobicistat is a CYP3A4 inhibitor, therefore concomitant use with CYP3A4 substrates is contraindicated because serious and life-threatening events may occur due to increased plasma concentration.

3rd question;

In light of the information given above, if you think there is a DDI, which of the following would you do?

☐ Dose change of interacting drug/drugs ( )
☐ Change in interacting drug (s) ( )
☐ Discontinuation of interacting drug (s) ( )
☐ Extra monitoring related to interaction (ECG, plasma level)
☐ Clinical monitoring (continue routine monitoring)
☐ I don't think there is a DDI

a. Tenofovir / emtricitabine / elvitegravir / cobicistat (245/200/150/100 mg)
b. Lithium (900 mg)
c. Buprenorphine / naloxone (4/1 mg)
d. Escitalopram (10 mg)

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DDI databases (2nd case 2nd interaction);

- ***elvitegravir / cobicistat / emtricitabine / tenofovir + escitalopram***
  - Cobicistat will increase the level and effect of escitalopram by affecting CYP3A4, one of the hepatic/intestinal enzymes.
  - Cobicistat is a CYP3A4 inhibitor, therefore concomitant use with CYP3A4 substrates is contraindicated because serious and life- threatening events may occur due to increased plasma concentration.

4th question;

In light of the information given above, if you think there is a DDI, which of the following would you do?

☐ Dose change of interacting drug/drugs ( )

☐ Change in interacting drug (s) ( )

☐ Discontinuation of interacting drug (s) ( )

☐ Extra monitoring related to interaction (ECG, plasma level)

☐ Clinical monitoring (continue routine monitoring)

☐ I don't think there is a DDI

a. Tenofovir / emtricitabine / elvitegravir / cobicistat (245/200/150/100 mg)

b. Lithium (900 mg)

c. Buprenorphine / naloxone (4/1 mg)

d. Escitalopram (10 mg)

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CASE 3

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patient history

NY 68 years old, female Height: 155 cm, Weight: 76 kg.

No smoking, alcohol or substance use.

He has been followed up for HIV infection since the age of 48 and has been receiving antiretroviral treatment since the age of 52.

He lost his wife 6 months ago and was diagnosed with depression.

Laboratory findings

CD4 cell count: 392/mm 3, HIV viral load: negative

ALT:21 U/L (<35 U/L), AST:35 U/L (<35 U/L), ALP:44 U/L (30-120 U/L), GGT:28 U/L (<35 U/L)

BUN: 25.46 mg/dl (6-20 mg/dl), Uric acid: 4.42 mg/dl (2.6-6 mg/dl), Creatinine: 0.65 mg/dl (0.5-0.95 mg/dl)

LDH:140 U/L (<248 U/L), CK:95 U/L (<171 U/L)

Medicines

Antiretroviral Drugs:

- Tenofovir / emtricitabine (245/200 mg)
- Rilpivirine (25 mg)

Psychiatric Drugs:

- Venlafaxine (150 mg)
- Trazodone (50 mg)

1st question;

In this patient Who do you use when you want to know more about potential DDI s? (You can choose more than one)

☐ Prospectus
☐ Pharmacist
☐ Smart device applications
☐ Other …… …….
☐ Written material (book, brochure, monograph)
☐ Internet
☐ senior physician
☐ medical pharmacologist

2nd question;

If you think there is a DDI, which of the following would you do?

☐ Dose change of interacting drug/drugs ( )
☐ Change in interacting drug (s) ( )
☐ Discontinuation of interacting drug (s) ( )
☐ Extra monitoring related to interaction (ECG, plasma level)
☐ Clinical monitoring (continue the same routine monitoring)
☐ I don't think there is a DDI

a. Tenofovir / emtricitabine (245/200 mg)
b. Rilpivirine (25 mg)
c. Venlafaxine (150 mg)
d. Trazodone (50 mg)

DDI databases (3rd case, 1st interaction)

- efavirenz + trazodone
  - o Efairenz affects the CYP3A4 enzyme, causing trazadone to reduces its effectiveness. It should be used with caution and clinical monitoring.
- rilpivirine + trazodone
  - o Potential weak interaction. There are not enough studies. However, the possibility of interaction is low based on metabolism and excretion. Rilpivirine Its interaction with trazodone at therapeutic doses (25 mg/day) does not appear to be clinically significant. However, it is known that at supratherapeutic doses (75-300 mg/day), there is an increase in the risk of Torsades de Pointes by prolonging the QTc interval.

3rd question;

In light of the information given above, which of the following would you do if you think there is a DDI?

☐ Dose change of interacting drug/drugs ( )
☐ Change in interacting drug (s) ( )
☐ Discontinuation of interacting drug (s) ( )
☐ Extra monitoring related to interaction (ECG, plasma level)
☐ Clinical monitoring (continue the same routine monitoring)
☐ I don't think there is a DDI

e. Tenofovir / emtricitabine (245/200 mg)
f. Rilpivirine (25 mg)
g. Venlafaxine (150 mg)
h. Trazodone (50 mg)

CASE 4

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patient history

KO is 41 years old. Male Height: 185 cm, Weight: 63 kg.

Smoking 32 packs/year, alcohol social drinker, no substance use.

He has been under follow-up for HIV infection for 9 months and has been receiving ART for 8 months. There is no resistance transferred.

Posttraumatic stress disorder was diagnosed 7 months ago and fluoxetine 40 mg was started. Carbamazepine 500 mg was prescribed to regulate mood , and lorazepam 1 mg was prescribed if necessary for anxiety accompanied by sleep disturbance .

Laboratory findings

CD4 cell count: 342/mm 3 , HIV viral load: negative

ALT:17 U/L (<35 U/L), AST:19 U/L (<35 U/L), ALP:117 U/L (30-120 U/L), GGT:13 U/L (<35 U/L)

BUN: 13.11 mg/dl (6-20 mg/dl), Uric acid: 5.44 mg/dl (2.6-6 mg/dl), Creatinine: 0.74 mg/dl (0.5-0.95 mg/dl)

LDH:194 U/L (<248 U/L), CK:84 U/L (<171 U/L)

Medicines

Antiretroviral Drugs:

- Tenofovir / emtricitabine (245/200 mg)
- Darunavir / ritonavir (800/100 mg)

Psychiatric Drugs:

- Lorazepam (1mg)
- Fluoxetine (40 mg)
- Carbamazepine (500 mg)

1st question;

In this patient Who do you use when you want to know more about potential DDI s? (You can choose more than one)

☐ Prospectus
☐ Pharmacist
☐ Smart device applications
☐ Other …… …….
☐ Written material (book, brochure, monograph)
☐ Internet
☐ senior physician
☐ medical pharmacologist

2nd question;

If you think there is a DDI, which of the following would you do?

☐ Dose change of interacting drug(s)
☐ Change in interacting drug(s)
☐ Discontinuation of interacting drug(s)
☐ Extra monitoring related to interaction (ECG, plasma level)
☐ Clinical monitoring (continue routine monitoring)
☐ I don't think there is a DDI.

a. Tenofovir / emtricitabine (245/200 mg)
b. Darunavir / ritonavir (800/100 mg)
c. Lorazepam (1mg)
d. Fluoxetine (40 mg)
e. Carbamazepine (500 mg)

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DDI databases (4th case 1st interaction)

- carbamazepine – darunavir
  - o Concurrent use of CARBAMAZEPINE and DARUNAVIR may result in potential for reduced darunavir concentrations, loss of therapeutic effect, and development of resistance.
  - o carbamazepine decreases levels of darunavir by increasing metabolism contraindicated.
  - o carbamazepine will decrease the level or effect of darunavir by affecting hepatic / intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug.
  - o darunavir will increase the level or effect of carbamazepine by affecting hepatic / intestinal enzyme CYP3A4 metabolism. Use Caution / Monitor plasma levels when used concomitantly
- carbamazepine – ritonavir
  - o Concurrent use of CARBAMAZEPINE and RITONAVIR may result increased carbamazepine exposure; decreased ritonavir exposure.
  - o carbamazepine will decrease the level or effect of ritonavir by affecting hepatic / intestinal enzyme CYP3A4 metabolism. Avoid or Use Alternate Drug.

3rd question;

In light of the information given above, if you think there is a DDI, which of the following would you do?

□ Dose change of interacting drug/drugs ( )
□ Change in interacting drug (s) ( )
□ Discontinuation of interacting drug (s) ( )
□ I make extra monitoring regarding the interaction (ECG, plasma level)
□ Clinical monitoring (continue the same routine monitoring)
□ I don't think there is a DDI

a. Tenofovir / emtricitabine (245/200 mg)
b. Darunavir / ritonavir (800/100 mg)
c. Lorazepam (1mg)
d. Fluoxetine (40 mg)
e. Carbamazepine (500 mg)

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drug-DDI databases (4th case 2nd interaction)

- fluoxetine - ritonavir
  - o Concurrent use of FLUOXETINE and RITONAVIR may result increased fluoxetine exposure; increased risk of QT- interval prolongation
  - o Ritonavir will increase the level or effect of fluoxetine by affecting hepatic enzyme CYP2D6 metabolism. Minor / Significance Unknown.

4th question;

In light of the information given above, which of the following would you do if you think there is a DDI?

- ☐ Dose change of interacting drug/drugs ( )
- ☐ Change in interacting drug (s) ( )
- ☐ Discontinuation of interacting drug (s) ( )
- ☐ I make extra monitoring regarding the interaction (ECG, plasma level, etc.)
- ☐ Clinical monitoring (continue the same routine monitoring)
- ☐ I don't think there is a DDI

a. Tenofovir / emtricitabine (245/200 mg)
b. Darunavir / ritonavir (800/100 mg)
c. Lorazepam (1mg)
d. Fluoxetine (40 mg)
e. Carbamazepine (500 mg)

_____

*****The survey was completed. Thank you for your participation*****