DRUGS ABUSE AND CHEMSEX: A NEW CHALLENGE FOR ANTIRETROVIRAL DRUG-DRUG INTERACTION

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No disclosure to declare
INTRODUCTION – Chemsex

- **Use of illicit/recreational drugs**: Cannabis, Cocaine, Ketamine, MDMA, GHB/GBL, methamphetamine derivatives…

- **Emergence of new psychoactive substances (NPS) in the last decades**

  In a sexualized context: CHEMSEX

- Chemsex has become a major and growing concern in the MSM population…
  
  ➢ Pubmed references: 2015 (n = 6) to 2018 (n = 58)
  
  ➢ Several national monitoring studies in United Kingdom 2014-2016
  
  ➢ **Prevalence** reported in Prep studies ranging from 30%\(^2\) to 44%\(^3\)

\(^2\)Trial Roux P1,2, 1ls on-Demand HIV Pre-exposure Prophylaxis a Suitable Tool for Men Who Have Sex With Men Who Practice Chemsex? Results From a Substudy of the ANRS-IPERGAY - J Acquir Immune Defic Syndr. 2018 Oct 1

\(^3\)Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial Prof Sheena McCormack - Lancet. 2016 Jan 2;387(10013):53-60
INTRODUCTION – Chemsex & HIV

… But not well known enough in the HIV-infected population!

- **Prevalence** among HIV-infected subjects?
  - <5% to 28% according to the drugs in Astra study (MSM cohort)

- **High potential of DDI** between antiretrovirals and illicit drugs?
  - No DDI pharmacokinetic study or dose-effect relationships between drugs and ARV
  - Potentials severe interactions reported from case reports

- Theoretical knowledge about the **metabolic pathways of drugs**
  - Increasing use of ‘party drugs’ in people living with HIV on antiretrovirals: a concern for patient safety - Bracchi M. AIDS. 2015
INTRODUCTION – Chemsex & Drug-Drug Interactions

- **Pharmacokinetic DDI : role of the CYP 450 family**
  - Ritonavir and cobicistat : used as “booster” are strong inhibitors for CYP 3A4 / CY2D6
  - Several drugs are metabolized by CYP450 family :
    - Ketamine, Benzodiazepines, Erectile dysfunction agents (EDA): CYP3A4++
    - MDMA, Cathinones, Methamphetamines: CYP2D6++
    - Cannabis, synthetic cannabinoids… : CYP2C9/1A2
    - GHB/GBL : non-cyp450 pathways but CYP450 unclear ??

- **Pharmacodynamic DDI :**
  - Cocaine and rilpivirine : both induce QT prolongation
STUDY OBJECTIVES

- Describe illicit drugs consumption
- Evaluate the risk of DDI with ARV treatment

Monocentric study: APHM Sainte-Marguerite, Clinical Immuno-Hematological Unit, Marseille, France

In a cohort of HIV-infected patients
PATIENTS AND METHODS

- Prospective survey initiated in March 2018 (still ongoing)

- HIV-infected patients who attended the unit for a follow-up visit

- Self-administered questionnaires as part of the Therapeutic Patient Education Program (TPEP):
  - Number of illicit drugs
  - Type of illicit drugs
  - Frequency of drugs consumption: once in a while, ≥ once a month, ≥ once a week, ≥ once a day, non reporting

- Demographical characteristics and therapeutic data from the electronical database NADIS: age, sex, ARV regimen, HIV transmission mode, HCV co-infection

- DDI evaluation:
  - Online Expert Database of Liverpool
  - Knowledge on the drugs and ARV pharmacokinetics
RESULTS – Population Characteristics

- Descriptive study including **286 HIV-infected patients on ART**
  - 315 questionnaires collected from March 2017 to January 2019
    (1 patient responded to the questionnaire 3 times, 27 patients twice)
  - 75% male; median age: 52 years (range: 19-83)

<table>
<thead>
<tr>
<th>ART Regimen in the cohort</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple therapy</td>
<td>62%</td>
</tr>
<tr>
<td>Single-Tablet Regimen (STR)</td>
<td>60%</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>34%</td>
</tr>
<tr>
<td>Booster (ritonavir or cobicistat)</td>
<td>33%</td>
</tr>
</tbody>
</table>
RESULTS – Prevalence of Drugs Consumption

33% of drug users (93 / 286 patients)

Multiple drugs use: 41% of patients use > 1 drug

Mode of HIV transmission

- MSM: 52%
- IVDU: 28%
- Heterosexual: 13%

Chemsex Context

- Sexual context: 47%
- Non sexual context: 35%
- Non reporting: 18%
RESULTS – Type and Proportion of Drugs Use

Chemsex drugs

Cannabis: Cohort: 42%, Sexual context: 10%
Poppers: Cohort: 37%, Sexual context: 17%
Cocaine: Cohort: 16%, Sexual context: 16%
Ecstasy/MDMA: Cohort: 12%, Sexual context: 7%
GHB/GBL: Cohort: 10%, Sexual context: 5%
Cathinones: Cohort: 4%, Sexual context: 10%
Amphetamines derivatives: Cohort: 2%, Sexual context: 2%
Others (Kamagra): Cohort: 1%, Sexual context: 0%
Ketamine: Cohort: 6%, Sexual context: 2%
Synthetic cannabinoids: Cohort: 1%, Sexual context: 0%
LSD: Cohort: 1%, Sexual context: 4%
Other psychostimulants: Cohort: 1%, Sexual context: 1%
Non prescribed Benzodiazepines: Cohort: 2%
RESULTS – Frequency of Drugs Use

- Non prescribed Benzodiazepines
  - ≥ once a day: 55%
  - ≥ once a week: 38%
  - ≥ once a month: 69%
  - Once in a while: 44%
  - Non reporting

- Cannabis
  - ≥ once a day

- Cathinones
  - ≥ once a day

- Cocaine
  - ≥ once a day

- Ecstasy/MDMA
  - ≥ once a day

- GHB/GBL
  - ≥ once a day

- Ketamine
  - ≥ once a day

- LSD
  - ≥ once a day

- Methamphetamine derivatives
  - ≥ once a day

- Others (Kanaatra)
  - ≥ once a day

- Poppers
  - ≥ once a day

- Other psychostimulants
  - ≥ once a day

- Synthetic cannabinoids
  - ≥ once a day
# RESULTS – Drug-Drug Interaction Evaluation

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ARV REGIMEN</th>
<th>INTERACTION</th>
<th>EFFECT</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketamine</td>
<td></td>
<td>Inhibition CYP3A4</td>
<td>➔ drug exposure</td>
<td>2</td>
</tr>
<tr>
<td>MDMA, Cathinones, Methamphetamines</td>
<td>Ritonavir Cobicistat</td>
<td>Inhibition CYP2D6</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>GHB/GBL</td>
<td></td>
<td>GHB DH CYP?</td>
<td>Unknown ? Narrow therapeutic index</td>
<td>1</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Efavirenz Etravirine</td>
<td>Inhibition CYP2C9</td>
<td>➔ drug exposure</td>
<td>5</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Rilpivirine</td>
<td>QT prolongation</td>
<td>Torsade de pointes</td>
<td>9</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Ritonavir Cobicistat</td>
<td>Inhibition CYP3A4</td>
<td>➔ drug exposure</td>
<td>6</td>
</tr>
<tr>
<td>Poppers</td>
<td></td>
<td>Non CYP mediated</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Nevirapine</td>
<td>Induction CYP3A4</td>
<td>➔ drug exposure</td>
<td>1</td>
</tr>
</tbody>
</table>

DDI in 38 cases (13.3%) ➔ Moderate to Severe in 24 cases (8.4%)
CONCLUSION

- More than 1/3 of patients (33%) reported illicit drugs consumption
- 18% in a “Chemsex” context
  - Probably under-estimated as reported in the Ipergay study where 30% of pts who did not self-reported consuming drugs were positive to the hair screening
  - Poppers, cathinones, MDMA and « G » were the most frequent drugs used in Chemsex
- The risk of consuming Illicit Drugs and ARV should not be under-estimated:
  - IDENTIFY illicit drugs consumption in HIV-infected patients
  - WARN the patient about risk of drug interaction and signs of toxicity
  - ADJUST the antiretroviral regimen
  - AVOID high risk of potential life-threatening toxicities
Aknowledgments

- Dr Caroline Solas
- Dr Isabelle Poizot-Martin

- **APHM Sainte-Marguerite, Clinical Immuno-Hematological Unit, Marseille, France**
  C Lions, Dr H Laroche, Dr O Faucher-Zaegel, Dr S Bregigeon, Dr A Ivanova, V Obry-Roguet, MA Pieve

- **APHM La Timone ; Pharmacokinetics and Toxicology, Marseille, France**
  Pr B Lacarelle, Dr S Quaranta, Dr N Néant, Dr E Sampol-Manos

- Patients