Viral Hepatitis Prevention Board Meeting

Burden and Prevention of Viral Hepatitis in Portugal

Epidemiology of coinfection (HIV, HCV) in Portugal

Rui Sarmento e Castro

Infectious Diseases Depart., Hosp. Joaquim Urbano
Health Sciences School, University Minho
Portuguese Study Group on Coinfection, President

Lisbon, 19 Nov 2010
PORTUGAL
HIV and AIDS cases reported by year and stage of infection

N = 37793

Number of cases

Year of diagnosis
CVEDT 31-03-2010
PORTUGAL
AIDS cases by gender

3041

13147

81.2%
18.8%

Female
Male

CVEDT
30-09-2010
PORTUGAL
AIDS cases by age

Age

< 1 1 a 4 5 a 14 15 a 24 25 a 34 35 a 44 45 a 54 55 a 64 > 64

52 32 47 1410 6227 4733 2142 996 483

CVEDT
30-09-2010
PORTUGAL
AIDS cases by transmission category

Total = 16 189
PORTUGAL
New AIDS cases: trends by transmission category

Year of diagnosis
CVEDT 31-12-2009
PORTUGAL
AIDS cases: death by transmission category

N = 7475
PORTUGAL
AIDS cases: mortality by opportunistic disease

Graph showing cases and deaths for various opportunistic diseases:
- Tuberculosis: 6809 cases, 3108 deaths
- PPj: 2563 cases, 1210 deaths
- Tub+PPj: 745 cases, 489 deaths
- OI: 4236 cases, 1926 deaths
- SK: 567 cases, 276 deaths
- OI-SK: 139 cases, 94 deaths
- Lymphoma: 372 cases, 217 deaths
- Encephalopathy: 165 cases, 84 deaths
- Wasting S: 198 cases, 115 deaths
- Inter Lymph: 21 cases, 3 deaths
- Cervical cancer: 57 cases, 9 deaths

CVEDT 31-03-2010
Prevalence of hepatitis C in the HIV population
(1960/5957 patients = 33%)

Regions:
South
Central
North
East

North: 359 = 23.2%
Central: 293 = 19.6%
South: 695 = 41.4%
East: 613 = 46.9%

Rockstroh et al. J Inf Dis 2005;192:992–1002
Epidemiology of HCV in Portugal

- Estimated HCV prevalence: 1.0 to 1.4%
  100,000-140,000
  Rui Tato Marinho, DGS

- Number of reported cases of HIV Infection: 38,000
  CNLCS, 2009

- Estimated prevalence in the South of Europe: 41.4%
  Eurosida, 2005

- Estimated number of coinfected patients (HCV/HIV): 15,732
Epidemiology of HCV in Portugal

HCV monoinfected versus HCV /HIV coinfected patients

- **AIM and Methods**
  - Evaluation of differences between HIV negative and HIV positive patients infected with HCV
  - Retrospective, transversal, multicentric survey
  - Participation of 10 hospitals (ID, IM, Gastroenterology)

<table>
<thead>
<tr>
<th>Monoinfected</th>
<th>Coinfected</th>
</tr>
</thead>
<tbody>
<tr>
<td>783 pts</td>
<td>1650 pts</td>
</tr>
</tbody>
</table>

Organized by the Portuguese Study Group on HIV/Hepatitis coinfection

Data were analyzed for statistical significance by student t test or non parametric test
### HCV monoinfected versus HCV/HIV coinfected patients

<table>
<thead>
<tr>
<th></th>
<th>HCV/HIV-</th>
<th>HCV/HIV+</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>627 (80.1%)</td>
<td>1294 (78.4%)</td>
<td>1952 (78.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>156 (19.9%)</td>
<td>356 (21.6%)</td>
<td>512 (21.0%)</td>
</tr>
<tr>
<td>Mean age, ♂</td>
<td>39.8 years</td>
<td>39.3 years</td>
<td>39.5 years</td>
</tr>
<tr>
<td>Mean age, ♀</td>
<td>42.3 years</td>
<td>37.1 years</td>
<td>38.8 years</td>
</tr>
</tbody>
</table>

- **VH negativo**
  - Número: [Diagram](#)
  - Idade: [Histogram](#)
- **VH-1 positivo**
  - Número: [Diagram](#)
  - Idade: [Histogram](#)
HCV monoinfected versus HCV/HIV coinfected patients

Transmission

- 78.8% (1955) IVDU
- 2.3% (58) Sexual
- 7.8% (193) Transfusion
- 9.3% (231) Unknown

HCV monoinfected versus HCV/HIV coinfected patients
HCV monoinfected versus HCV/HIV coinfected patients

Transmission by HIV status

HIV -

HIV +

Risco:
- IVDU
- Unknown
- Transf
- Sexual

5.4%
HCV monoinfected versus HCV/HIV coinfected patients

Genotype distribution

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Frequency</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54,0%</td>
<td>1130</td>
</tr>
<tr>
<td>2</td>
<td>1,5%</td>
<td>32</td>
</tr>
<tr>
<td>3</td>
<td>25,9%</td>
<td>542</td>
</tr>
<tr>
<td>4</td>
<td>18,4%</td>
<td>384</td>
</tr>
<tr>
<td>5</td>
<td>0,2%</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>0,0%</td>
<td>1</td>
</tr>
</tbody>
</table>
HCV monoinfected *versus* HCV/HIV coinfected patients

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>HCV/HIV -</th>
<th>HCV/HIV+</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>384 (52.7%)</td>
<td>728 (54.9%)</td>
<td>1112 (54.0%)</td>
</tr>
<tr>
<td>2</td>
<td>12 (1.6%)</td>
<td>20 (1.5%)</td>
<td>32 (1.5%)</td>
</tr>
<tr>
<td>3</td>
<td>209 (28.7%)</td>
<td>321 (24.2%)</td>
<td>530 (25.9%)</td>
</tr>
<tr>
<td>4</td>
<td>123 (16.9%)</td>
<td>255 (19.3%)</td>
<td>378 (18.4%)</td>
</tr>
</tbody>
</table>
Distribution of genotype by gender and mode of transmission

HCV monoinfected versus HCV/HIV coinfected patients

Gender

Mode of transmission

Graphs showing the distribution of genotypes by gender (male or female) and mode of transmission (IVDU or sexual).
HCV monoinfected versus HCV/HIV coinfected patients

Genotype distribution by HIV status and gender

HIV negative

HIV positive

relative genotype distribution by gender in the HIV negative population

relative genotype distribution by gender in HIV positive patients

P = 0.03
HCV monoinfected versus HCV/HIV coinfected patients

BASELINE ALT BY GENOTYPE, HIV STATUS AND CD4 CELLS

- Baseline ALT by HCV genotype
  - Genotype 1: n=908, p<0.0001
  - Genotype 2-4: n=313

- Baseline ALT by HIV status
  - HIV negative: n=740
  - HIV positive: n=1235
  - HIV discordant: n=444

- Baseline ALT by T-cell CD4+ count
  - T-cell CD4+ count categories: n=274, n=229, n=177, n=63, p=0.05
HCV monoinfected versus HCV/HIV coinfected patients

HCV VIRAL LOAD BY GENOTYPE, HIV STATUS AND CD4 CELLS

- Genotype
  - HIV neg (n=702)
  - HIV + (n=1132)

- CD4 cells
  - >500 (n=422)
  - >300 (n=259)
  - >200 (n=210)
  - >100 (n=152)
  - <100 (n=44)
Main reasons to treat chronic HCV in HIV-infected patients

- HIV patients live longer
- HIV increases viral load of HBV and HCV
- Faster progression to liver cirrhosis\(^1\)
- Increased mortality due to end-stage liver disease (ESLD)\(^2\)
- Higher risk of hepatotoxicity following treatment with antiretroviral therapy (ART) drugs

## Treatment of coinfection in Portugal

### Reasons for non-treatment of chronic hepatitis C in HIV infection

<table>
<thead>
<tr>
<th>Reason</th>
<th>Prevalence</th>
<th>Reasons</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4+ T cells count &lt;200/mm³</td>
<td>26.8% (n=30)</td>
<td>Precarious socioeconomic conditions</td>
<td>3.6% (n=4)</td>
</tr>
<tr>
<td>Severe psychiatric disease*</td>
<td>17.9% (n=20)</td>
<td>Patient refusal</td>
<td>2.7% (n=3)</td>
</tr>
<tr>
<td>Chronic alcohol abuse</td>
<td>16.1% (n=18)</td>
<td>Recent immunological recovery</td>
<td>1.8% (n=2)</td>
</tr>
<tr>
<td>Active intravenous drug use</td>
<td>14.3% (n=16)</td>
<td>Active opportunistic infections / Infectious diseases</td>
<td>2.7% (n=3)</td>
</tr>
<tr>
<td>Previous unsuccessful HCV treatment</td>
<td>10.7% (n=12)</td>
<td>Absence of liver biopsy</td>
<td>3.6% (n=4)</td>
</tr>
<tr>
<td>Nonadherence with medical visits</td>
<td>8.9% (n=10)</td>
<td>Decompensated hepatic cirrhosis</td>
<td>1.8% (n=2)</td>
</tr>
<tr>
<td>Thrombocytopenia &lt;70 000</td>
<td>7.1% (n=8)</td>
<td>Concomitant medication with rifampin/rifabutin, isoniazide, pyrazinamide</td>
<td>2.7% (n=3)</td>
</tr>
<tr>
<td>Serum creatinine level &gt;1.5x ULN</td>
<td>2.7% (n=3)</td>
<td>Anatomic splenectomy</td>
<td>0.9% (n=1)</td>
</tr>
<tr>
<td>Hgb&lt;12(M) ou &lt;11 (F) [mg/dl]</td>
<td>1.8% (n=2)</td>
<td>Pregnancy</td>
<td>0.9% (n=1)</td>
</tr>
<tr>
<td>Age &gt;50 years</td>
<td>2.7% (n=3)</td>
<td>Nonadherence to HAART</td>
<td>3.6% (n=4)</td>
</tr>
<tr>
<td>Severe pulmonary disease</td>
<td>0.9% (n=1)</td>
<td>Unidentified reasons</td>
<td>11.6% (n=13)</td>
</tr>
</tbody>
</table>

Barriers to HCV Antiviral Treatment Among IDUs

Patient desire = fear of therapy and lack of understanding regarding importance of therapy

Zehnter E et al. AASLD 2007. Abstract 276
Barriers to HCV Antiviral Treatment Among IDU

- Concern side effects
- Don’t feel sick
- Other health problems
- Don’t want to make liver biopsy
- Inadequate information
- Length of treatment

- Clinical decision based in probable lower adherence in IDUs
HCV monoinfected versus HCV/HIV coinfected patients

Sustained Virological Response

**HIV NEG**
- n = 296
- 69.3%
- 30.7%

**HIV POS**
- n = 290
- 53.0%
- 47.0%

- 62% Genotype 1
- 84% Genotype 3
- 25.9%
- 78%
Deaths in a cohort of 23,441 HIV patients on antiretrovirals


- Hep B, C, D
- Drug-related toxicity
Causes of Death in 2000 and 2009 in HIV-infected Patients Admitted in ID Service (HJU)

- **2000**
  - N = 52
  - HCV/HIV 71%

- **2009**
  - N = 43
  - HCV/HIV 70%

- Admitted in ID Service (HJU): N = 52
  - HCV/HIV 71%

- N = 43
  - HCV/HIV 70%
CONCLUSIONS

- The prevalence of HCV in the HIV-infected population is higher than 40%.
- The number of new cases of HCV/HIV coinfection is decreasing in recent years.
- Male/female ratio in coinfected patients is ≈ 4:1.
- Mean age of coinfected patients is, at the moment of diagnosis, 38-39 years.
- IVDU is the most important mode of acquisition of both viruses.
CONCLUSIONS

ุม Genotype 1 (55%) and genotype 3 (26%) are the most prevalent genotypes in coinfected patients
ุม Genotype 4 (18.5%) is also relevant in this population

ุม In patients infected with genotype 3 mean baseline ALT values were higher than in patients with other genotypes
ุม Baseline ALT values were lower in coinfected versus monoinfected patients
ุม In coinfected patients ALT levels were directly associated with CD4 cell count
CONCLUSIONS

- Mean baseline HCV viral load was higher in coinfected patients when compared with monoinfected patients.

- In coinfected patients, HCV viral load was inversely associated with CD4 cells count.

- SVR was lower in coinfected patients with genotype 1 (when compared with monoinfected patients) but response to treatment was good in patients with genotype 3.

- All efforts must be done to treat coinfected patients to prevent the rising mortality registered in this population.
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