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Dr. E. L. López is a consultant of Sanofi Pasteur, Argentina
OFFICIAL CONFIRMED HEPATITIS A CASES IN ARGENTINA*

* DIEPI MINISTRY OF HEALTH
HEPATITIS A CASES BY AGE – 2002/07
MINISTERY OF HEALTH DATA

No. of cases

- <1 yr
- 1 yr
- 2-4 yrs
- 5-9 yrs
- 10-14 yrs
- 15-49 yrs
- 50 and more

2002 2003 2004 2005 2006 2007
NATIONWIDE SEROPREVALENCE STUDY IN DIFFERENT ARGENTINEAN AREAS

No: 1890 (children and adolescents)
Period of study: Oct/04 to Mar/05

* Severe Outbreak occurred in Mendoza, during the Study – 2004-2005

Lopez EL et al: Abstract presented at SLIPE Congress
Veracruz, Mexico 2005
Argentina Anti-HVA-Antibodies Seroprevalence by Age

N=1890

- Buenos Aires
- Suburban Area
- Chaco
- Córdoba
- Jujuy
- Neuquén
- Santa Cruz

% in 1 to 4: 24.3%
% in 5 to 9: 47.3%
% in 10 to 15: 52%
OBJECTIVE OF THE STUDY

To evaluate the long-term immunity following two doses schedule with an inactivated HAV (Avaxim 80U™) in children vaccinated at 1 to 4 years old, ten years ago.
HEPATITIS A 80 U VACCINE: INITIAL DATA OF IMMUNOGENICITY

* López EL, et al. PIDJ, 2001;20:48-52
HAV Vaccine (80U) Study
Geometric Mean Titres in Initially Seronegative Subjects after Vaccination*

<table>
<thead>
<tr>
<th>Day 0</th>
<th>Day 14</th>
<th>Week 24</th>
<th>Week 27</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6.25</td>
<td>98.5</td>
<td>190</td>
</tr>
<tr>
<td></td>
<td>190</td>
<td>190</td>
<td>6743</td>
</tr>
</tbody>
</table>

No. of children= 111

* López EL, et al. PIDJ, 2001;20:48-52
HAV Vaccine (80U) Study
seroconversion Rates (SC) and GMT in mIU/mL in all Initially Seronegative Children

<table>
<thead>
<tr>
<th></th>
<th>Day 0 (n=111)</th>
<th>Day 14 (n=111)</th>
<th>Week 24 (n=107)</th>
<th>Week 27 (N=103)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GMT</strong></td>
<td>6.25</td>
<td>98.5</td>
<td>190</td>
<td>6743</td>
</tr>
<tr>
<td><strong>95% CI</strong></td>
<td>5.8-6.8</td>
<td>86.9-112</td>
<td>162-224</td>
<td>5805-7833</td>
</tr>
<tr>
<td><strong>% SC</strong></td>
<td>0</td>
<td>99.1</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td><strong>95% CI</strong></td>
<td>0.0-3.3</td>
<td>95.1-100</td>
<td>96.6-100</td>
<td>96.5-100</td>
</tr>
</tbody>
</table>

López EL, et al. PIDJ, 2001;20:48-52
Material and Methods (I)

• **Study Population:** 52/111 children who received under protocol Inactivated HAV Vaccine (80U) were controlled after 10 years of immunization.

• **Inclusion Criteria**
  – To have been enrolled in the former study
  – Have not received any HAV Vaccine after study Immunization
  – Informed Consent signed by parents / Asent by adolescents

• **Exclusion Criteria**
  – Whole blood, red blood cells and/or blood derived products transfusion during the last 6 months
  – Underlying disease that can cause immunosupresion
  – Immunosupresive therapy during the last 6 months
MATERIAL AND METHODS (II)

- Anti-HAV Antibody titres were measured by VIDAS® Anti-HAV Total (HAVT), from BioMerieux®, France.

- **Principle**: the assay principle combine a 2-step enzyme immunoassay competition method with a final fluorescent detection (ELFA).

- The patient Relative Fluorescent Value (RFV) is interpreted by the VIDAS system. Results are expressed in mIU/ml (WHO reference standard 1st Reference Preparation Hepatitis A immunoglobulin) (100 IU/ml).

- The results are interpreted as follows:

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15 mIU/ml</td>
<td>Negative</td>
</tr>
<tr>
<td>≥15 and &lt;20 mIU/ml</td>
<td>Borderline positive</td>
</tr>
<tr>
<td>≥20 mIU/ml</td>
<td>Positive</td>
</tr>
</tbody>
</table>
FOLLOW-UP RESULTS
CHARACTERIZATION OF POPULATION

<table>
<thead>
<tr>
<th></th>
<th>SERONEGATIVE (n=48)*</th>
<th>SEROPOSITIVE (n=4)*</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AGE: mo.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>156.1 (±11.3)</td>
<td>148 (±14.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Range</td>
<td>137 – 176</td>
<td>137 – 170</td>
<td></td>
</tr>
<tr>
<td><strong>SEX</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>26 (96.3%)</td>
<td>1 (3.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>22 (88%)</td>
<td>3 (12%)</td>
<td></td>
</tr>
</tbody>
</table>

*In the initial screening all subjects were seronegative by a qualitative assay before immunization, however 4 subjects were seropositive by a quantitative assay.
17/52 (32.7%) of subjects who had received the vaccine had an known close contact with Hepatitis A cases after vaccination.
• Family: 4/52 (7.7%)  
• School: 11/52 (21.2%)  
• Neighborhood: 7/52 (13.5%)  
• 24% of them had > 1 contact
FOLLOW-UP OF ANTI – HAV ABs LEVELS

- Initially Seronegative*
  - Only 1 Subject (2.1%) who were initially Seroconverted had < 20mIU/mL at ten years follow-up.
<table>
<thead>
<tr>
<th>CONDITION</th>
<th>VALUE</th>
<th>95%CI</th>
<th>( p ) (( M-W ))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Serol. Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative (n: 48)</td>
<td>390.9 (370.1)</td>
<td>282.2- 499.5</td>
<td></td>
</tr>
<tr>
<td><strong>SEX</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>430.6 (433.4)</td>
<td>275.9 - 641.2</td>
<td>0.18</td>
</tr>
<tr>
<td>Male</td>
<td>483.9 (825.3)</td>
<td>65 - 1083</td>
<td></td>
</tr>
<tr>
<td><strong>HAV CONTACT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any contact</td>
<td>445.6 (464.4)</td>
<td>206.8 – 684.4</td>
<td>0.88</td>
</tr>
<tr>
<td>No contact</td>
<td>455.4 (691.2)</td>
<td>214.2 – 696.6</td>
<td></td>
</tr>
</tbody>
</table>
Geometric Mean Titres (GMT) anti-HAV Abs (mIU/ml) Over time by Linear Regression

- Geometric mean titre antihAV Abs (mIU/ml) over time.
- Linear regression analysis with coefficients: $eta = -0.45$ and $R^2 = -0.60$.

- Markers on the graph:
  - 1 month post-booster (7 mo)
  - Pre-booster 6 mo
PREDICTION OF ANTI-HAV AB TITRES OVER TIME BY LINEAR REGRESSION AT YEAR 20

Ant-HAV titres (GMT – mIU/ml)

Period (mo)

7 mo 10 yr 20 yr

5888.44 263.02 209.02
CONCLUSIONS

• Using Inactivated Hepatitis A vaccine (80U) the long-term immunity at 10 years follow-up showed seroprotection levels in 97.9% of children.

• HAV contact after vaccination did not increased the anti-HAV titres ($p=0.88$)

• There were no difference in anti-HAV titres according to gender ($p=0.44$).
CONCLUSIONS (CONT.)

• Linear Regression analysis predict seroprotection level of anti-HAV for at least 20 years after two dose HAV vaccine schedule

• This is the first study with this vaccine in a selected population that shows long term protection in ten years follow-up.

• A close and effective surveillance should be done to evaluate the need of a second dose of Hepatitis A vaccine in Argentina since 50% of children ≥5 ys old are seronegative after an important outbreak in Argentina.
THANK YOU FOR YOUR ATTENTION