SUMMARY

INTRODUCTION: Diagnosis of Gilbert's disease often involves unnecessary testing and patient anxiety. Rifampin test can support the diagnosis; it has been described in short series and lacks standardization in dose, collection times, result presentation and interpretation. Our objective was to compare the response to oral rifampin in a series of patients with Gilbert's disease, 2 and 4 h after drug administration.

PATIENTS AND METHODS: Eighty-nine patients with Gilbert's disease (elevated total bilirubin with no hepatopathy or hemolysis) were recruited. After a basal blood collection, 900 mg rifampin were administered per os and new samples were drawn 2 and 4 h later. Total and esterified bilirubin were measured in every sample. Haptoglobin concentration was also analyzed.

RESULTS: When expressed as relative increase with respect to basal values, variations observed 2 h after rifampin intake were all above 15%. A significant correlation (r = 0.902; p = 0.000) was found between relative increases 2 and 4 h after drug administration. No significant variations were found in haptoglobin concentrations.

CONCLUSION: Rifampin test is useful in diagnosing Gilbert's disease, but variations in total bilirubin concentrations (basal and post-rifampin) make that no absolute cut-off value can be used. Correlation between 2- and 4-h relative increases suggests that a shortened version could simplify the test.

INTRODUCTION

Gilbert's syndrome is a frequent hereditary chronic and benign disorder characterized by unconjugated hyperbilirubinemia in the absence of structural liver disease or hemolysis.
the most frequently performed in our setting. Pérez et al.

nicotinic acid, phenobarbital or rifampin. The last one is

there are tests based on the bilirubin response to fasting,

of tests that support the initial diagnosis; among them,

tion of the absence of disease explains the use of a variety

reference. However, the need for a follow-up confirma-

ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline

Fig. 1. Relative increase in total bilirubin at 2 and 4 h after rifampin

Rifampin test normally takes 4 h and is considered as po-

Nevertheless important to point out that no consensus exists

About the test procedure and the interpretation of results.

Several authors have proposed the use of a shorter ver-

sible if total bilirubin concentration rises above 32.5

Table I.

Characteristics of the 78 included patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Average ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bilirubin (μmol/l)</td>
<td>30.78 ± 9.23</td>
<td>13.68-53.35</td>
</tr>
<tr>
<td>LDH (IU/l)</td>
<td>293.46 ± 57.37</td>
<td>126-462</td>
</tr>
<tr>
<td>GGT (IU/l)</td>
<td>15.60 ± 8.30</td>
<td>6-42</td>
</tr>
<tr>
<td>ALP (IU/l)</td>
<td>176.01 ± 74.13</td>
<td>83-600</td>
</tr>
<tr>
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<td>20.93 ± 4.66</td>
<td>13-34</td>
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</table>

Bilirubin increase above basal value (%)

<table>
<thead>
<tr>
<th>Time</th>
<th>0%</th>
<th>20%</th>
<th>40%</th>
<th>60%</th>
<th>80%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 h</td>
<td>100</td>
<td>120</td>
<td>140</td>
<td>160</td>
<td>180</td>
<td>200</td>
</tr>
<tr>
<td>4 h</td>
<td>80</td>
<td>100</td>
<td>120</td>
<td>140</td>
<td>160</td>
<td>180</td>
</tr>
</tbody>
</table>

BT2-BT0/BT0 BT4-BT0/BT0

HALLAL H, ET AL. A SHORTENED, 2-HOUR RIFAMPIN TEST: A USEFUL TOOL IN GILBERT’S SYNDROME

After administration of 900 mg rifampin, concentrations

and 95% confidence interval [95% CI] were, respecti-

6.5) μmol/l at 2 h and 55.1 (95% CI, 32.8-80.4) and 37.8

-1.5) μmol/l at 2 h and 33.4 (95% CI, 22.1-47.5) and 17.6

μmol/l (95% CI, 1.9 mg/dl). On calculating relative incre-

ODU-1) μmol/l at 4 h and 3.4 (95% CI, 1.1-6.5) and 1.9

ODU-1) μmol/l at 2 h and 11.1 (95% CI, 5.1-16.8) and 16.1

In order to standardize results, and to avoid the effects of intra- and in-

Mathematical and statistical methods

were within the acceptable criteria according to external quality assu-

other patient sample. Variations due to analytical bias or random error

In vitro

Procedure used for total bilirubin measurement. Characteristics of the sub-

After a 12-h fasting, a basal blood sample was collected, and immedia-

Procedure for rifampin test

After ultrasound examination, patients were admitted to the digestive dis-

Pregnancy, lactation or allergy to rifampin were established as criteria

were made at 2 and 4 h after rifampin intake. A catheter was inserted to

Before and after the test, the following laboratory parameters were eval-

No patient had alcoholic liver disease. In the previous 6 months, the pa-

Table II.

Characteristics of the 78 included patients (25 women, and 53 men)

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In conclusion, according to our results:

- There were no change in haptoglobin levels, 2 h after rifampin administration.
- Increases at 2 and 4 h are correlated and thus can give significant information, and similar results have been published by Murthy et al. 3
- In our study, all patients with Gilbert's syndrome showed a relative increase in total bilirubin concentration of at least 0.15 times their basal value at 2 h, and 0.38 at 4 h.
- A positive correlation was found between the haptoglobin levels and the total bilirubin concentration greater than 32.5 μmol/l (1.9 mg/dl) to 4 h. 
- A positive response was considered a 50% increase in unconjugated bilirubin above its basal value. 
- Noguerado et al. 9 gave 900 mg rifampin fasting, with blood drawing at 2, 4 and 6 h, and considering a total bilirubin concentration greater than 32.5 μmol/l (1.9 mg/dl) to 4 h.
- In our study, all patients with Gilbert's syndrome showed at least an increase of 15% at 2 h and 38% at 4 h.

DISCUSSION

- Rifampin is useless in diagnosing Gilbert's syndrome. In contrast, Erdil et al. 8 set no threshold value and concluded that rifampin is useless in diagnosing Gilbert's syndrome on exclusion rather than on a panel of tests.
- Many different tests exist that can support the diagnosis, like those utilized a 300 mg dose and collected samples 3 h post-rifampicin. These 2 latter are comparable.
- Away from our results, many authors have designed their tests. 
- The last one has been published by Atmetlla Andreu J, Más Pujol M, Flor Escriche X. Síndrome de Gilbert: ¿es tan fácil el diagnóstico por exclusión? Aten Primaria. 1993;11:84-6.
- Diagnosis of Gilbert's syndrome is based on exclusion rather than on a panel of tests. Many different tests exist that can support the diagnosis, like those utilized a 300 mg dose and collected samples 3 h post-rifampicin. These 2 latter are comparable.