Comparison of the Nephrotoxicity of Oral Neomycin and Ampicillin in Rats

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ABSTRACT

Neomycin is widely used in the treatment of patients with porto-systemic encephalopathy. Because of its nephrotoxicity ampicillin has been tried as a substitute. Recently there has been some reports of nephrotoxicity with ampicillin. So the relative nephrotoxicity of the two antibiotics were studied. 18 albino rats were divided into three groups of six each. One group received neomycin, the second ampicillin and the third acted as control. At the end of two weeks it was found that there was histological evidence of interstitial nephritis in two rats receiving neomycin. The blood urea and creatinine values were high (significant at 0.05 level) in the neomycin group when compared with the other groups. So we conclude that because of its nephrotoxicity neomycin should be used with caution in the treatment of patients with porto-systemic encephalopathy especially in the presence of azotemia. Ampicillin appears to be a satisfactory substitute.

Key Indexing terms: Nephrotoxicity, Ampicillin, Neomycin.

The use of oral antibiotics forms an integral part of the management of patients with porto-systemic encephalopathy (PSE). The antibiotics act by reducing the bacterial flora in the gut and this reduce the absorption of toxic products produced by bacterial metabolism. Neomycin is the most widely used antibiotic in the management of PSE(1). The obvious disadvantage in the use of neomycin is its nephrotoxicity(2,3,4). Antibiotic nephropathy may account for some of the cases of renal failure seen in advanced liver disease. Ampicillin has been suggested as a satisfactory substitute in the management of patients with PSE(5,6). There are some reports on the nephrotoxicity of penicillins including ampicillin(7,8), and as very high doses (4-6 g/day) of ampicillin are used in the management of PSE we felt that its nephrotoxicity should be studied. There are no studies comparing the nephrotoxicities of the ampicillin and neomycin. So this study was undertaken to compare the relative nephrotoxicity of neomycin and ampicillin in experimental animals.

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MATERIAL AND METHODS

Eighteen albino rats (Holtzman strain 150-200 g) were divided into three groups of six each. They were matched for age, sex and weight and were given food and water ad libitum. One group was given neomycin, the second group received ampicillin and the third group acted as control. The drugs were administered by gavage with 1% gum acacia as vehicle. The control group received only the vehicle. The rat dose (Neomycin 47 mg/100 g, Ampicillin 70 mg/100 g) was calculated from the human dose (neomycin 4 g/day(9) and ampicillin 6 g/day(5)) by the formula described by Freirich et al.(10). The rats were sacrificed at the end of fourteen days. Haemoglobin, blood urea and blood creatinine were estimated from heart blood. The kidney was removed for pathological examination. The specimens were coded and examined by a pathologist who was not aware of the drugs administered. The Wilcoxon rank sum test was used for statistical analysis.

RESULTS

The results of the haemoglobin, blood urea and creatinine estimations are given in the table. There was no significant difference in the haemoglobin values. All the values were within the normal limits(11). The blood urea and creatinine values did not show any significant difference between the ampicillin and control groups. The neomycin treated rats showed a significant increase in the blood urea values when compared with the controls (P = 0.05) and with the ampicillin group (P < 0.05). The creatinine values were also high in the neomycin group when compared with the controls (P < 0.05) and the ampicillin group (P = 0.05). The blood urea values were above the upper limit of normal(11) in two rats in the neomycin group.

On gross examination the kidneys were normal. The histology of the kidneys did not reveal any abnormality in the controls, the ampicillin group and in four rats receiving Neomycin. Histological evidence of interstitial nephritis (Fig) was present in two rats which received neomycin.

DISCUSSION

The results show that oral Neomycin is nephrotoxic. It produces elevation of blood urea and creatinine and interstitial nephritis. Ampicillin did not appear to be nephrotoxic to the rats in the doses employed. Even though only a small number of rats have been studied here the nephrotoxicity of neomycin is significant.

We feel that because of the nephrotoxicity neomycin should be used with caution in the management of patients.
with PSE in advanced liver disease especially in the presence of azotemia. As the effectiveness of ampicillin has been established(6,6). Ampicillin should be preferred in the presence of azotemia. In one in vitro study(12) it was observed that 88% of urease producing organisms in the stool samples were sensitive to neomycin, whereas only 40% were sensitive to ampicillin. This was possibly because the concentration of ampicillin used in the discs, to study sensitivity, was small (1/5 of neomycin). High doses of ampicillin are recommended for the treatment of patients with portal-systemic encephalopathy(5).

Table. Mean Values of Haemoglobin, Blood Urea and Creatinine in the three groups

<table>
<thead>
<tr>
<th></th>
<th>Haemoglobin (g%)</th>
<th>Urea (mg%)</th>
<th>Creatinine (mg%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>13.6 ± 0.74</td>
<td>42 ± 3.92</td>
<td>4.11 ± 0.47</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>13.4 ± 1.55</td>
<td>36.4 ± 3.05</td>
<td>4.52 ± 0.37</td>
</tr>
<tr>
<td>Neomycin</td>
<td>13.4 ± 1.52</td>
<td>55.5 ± 3.04</td>
<td>5.84 ± 1.79</td>
</tr>
</tbody>
</table>

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REFERENCES