Relative efficacy of neomycin and ampicillin against urease producing organisms

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In a total of 63 stool samples from 36 patients with portal hypertension studied, urease producing organisms were grown from 33 per cent of the samples. While 88 per cent of the organisms were sensitive to neomycin, only 40 per cent were sensitive to ampicillin \( (P < 0.005) \). It is therefore suggested that neomycin should be preferred to ampicillin in the treatment of hepatic encephalopathy.

Hepatic encephalopathy is the result of metabolic insults occurring in patients with liver disease. The striking improvement with non-absorabe antibiotics\(^1\)\(^-\)\(^4\) suggests a major role for the bacterial degradation of nitrogenous intestinal contents in the etiopathogenesis of hepatic coma.

The efficacy of neomycin in hepatic encephalopathy was highlighted\(^3\) as early as in 1957. The azotemia associated with some forms of severe liver disease\(^5\) militates against the use of neomycin in these circumstances\(^6\)\(^-\)\(^8\). The usefulness of ampicillin has been reported and the antibiotic has been suggested to be a satisfactory substitute\(^9\),\(^10\). However, no study has directly compared the efficacy of ampicillin over neomycin in the treatment of hepatic encephalopathy. Further, no study has been done directly comparing the \textit{in vitro} sensitivity of urease producing organisms isolated from the faeces of patients suffering from portal hypertension. The present study was undertaken to see the relative efficacy of ampicillin and neomycin in the treatment of hepatic encephalopathy cases on the basis of the sensitivity pattern of the urease producing organisms isolated from their gut.

Material and Methods

Thirty six patients prone to develop hepatic encephalopathy and suffering from a variety of hepatic diseases were studied. Five of them were cirrhotic, 9 had non-cirrhotic portal fibrosis, 6 extrahepatic portal obstruction, 5 had hepatic outflow obstruction and 11 had alcoholic liver disease.

One to five stool samples from each patient were collected in buffered glycerol saline and inoculated into MacConkey's agar and desoxycholate citrate agar plates. After incubating overnight
at 37°C, the colonies of lactose and non-lactose fermenters were picked up and subjected to the following tests for identification: indole, methyl red, citrate utilization, urea hydrolysis, Voges-Prausniker reaction, and triple sugar iron slope. The identification of the urease producing organisms was done by routine methods. The antibiotic sensitivity of the urease producing organism was performed by the disc diffusion method, using discs of streptomycin (50 μg) chloramphenicol (50 μg) tetracycline (50 μg) ampicillin (10 μg) gentamycin (10 μg), neomycin (50 μg) and kanamycin (50 μg).

**Results and Discussion**

Total number of patients included in the study were thirty six. Adequate sample for processing was available in only 35 patients. Sixteen of the 35 patients (46%) had urease producing organisms in their stool. In all, 68 samples were received, of which only 63 could be processed. Of the 63 samples processed, 21 (33%) grew urease producing organisms while 3 (5%) showed salmonella species and 39 (62%) were sterile.

A single organism was isolated in 17 samples of which 15 (88%) were klebsiella and 2 (12%) proteus. Both klebsiella and proteus were present in 4 samples. Excluding the three samples showing salmonella, the 25 urease-producing organisms revealed antibiotic sensitivity, as shown in the Table. All the organisms were sensitive to gentamycin although two were only moderately sensitive. Sixty per cent of the organisms were resistant to ampicillin while only 12 per cent were resistant to neomycin.

These results indicate a definite superiority of neomycin over ampicillin.

### Table. The sensitivity of urease producing organisms to ampicillin and neomycin

<table>
<thead>
<tr>
<th>Sensitivity tested against</th>
<th>No. of urease producing organisms</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Sensitive</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>Neomycin</td>
<td>22 (88%)</td>
</tr>
</tbody>
</table>

Resistance to ampicillin*/*neomycin† along with any of following drugs in order of frequency: tetracycline, chloramphenicol, streptomycin, kanamycin. Resistance to both ampicillin and neomycin was found in only one organism (P<0.005 by X² test). It is known that there is considerable resistance amongst intestinal organisms against multiple antibiotics by the acquisition of R-plasmids. However, the short term use of non-absorbable antibiotics in patients with hepatic coma has been shown to produce striking improvement in encephalopathy.

A comparative in vitro study of neomycin and ampicillin against urease producing organisms has not been reported before. The study of Meyers concerns itself only with the effectiveness of ampicillin in reduction of gastric ammonia production and ammonia released from the colon was not studied. The clinical usefulness of ampicillin reported by Tandon and associates utilised a number of other measures along with ampicillin, which were used empirically and no direct comparison with neomycin was made.
We suggest that neomycin may be superior to ampicillin in the treatment of hepatic encephalopathy in the absence of azotemia.

References


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