# CARBENICILLIN INDANYL SODIUM IN THE TREATMENT OF GONORRHOEA

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**SYNOPSIS**

**50 male patients with acute gonococcal urethritis were treated with 15 gm. of Carbenicillin Indanyl Sodium and 1 gm. of Probenecid. The known minimum failure rate was 4%. One patient developed an erythematous rash. This makes it a safe and satisfactory antibiotic in the treatment of gonorrhoea.**

Carbenicillin a semi synthetic, bactericidal antibiotic, is effective against a variety of gram negative organisms. Its unique activity against pseudomonas aeruginosa and Proteus species is well recognized; but its wide range of activity in urinary tract infections has lent its use in these infections.

The original salt, disodium carboxybenzyl penicillin was administered paranterally because of poor intestinal absorption and acid lability. Recently the indanyl ester of carbenicillin was shown to be acid stable and easily absorbed by the gastro-intestinal tract. The oral formulation now possible, has facilitated the use of the antibiotic to ambulatory patients with infections such as gonococcal urethritis.

Carbenicillin indanyl sodium is a water soluble white crystalline powder. Following absorption, it is hydrolysed in the body to its active component carbenicillin and indanol, which in turn is excreted as glucuronide or sulphate conjugates (Butler *et al*, 1971). In vitro studies have shown, its efficacy in controlling urinary tract infections to be comparable with parenatal carbenicillin (English *et al*, 1972). Following a single oral dose of 1000 mg., peak serum concentrations of 10·2 meg./ml. were reached in one hour. 16% of the administered dose was excreted between 3 to 6 hours in the urine (Butler, 1971). The simultaneous administration of probenecid augments serum levels further (Bran *et al*, 1971).

We report in this paper, our experience using carbenicillin indanyl sodium in the treatment of acute gonococcal urethritis in males.

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## MATERIAL AND METHODS

50 male patients with acute gonococcal urethritis were included in this study. Diagnosis of gonorrhoea was based on (*1*) history of exposure (*2*) compatible incubation period (*3*) urethral discharge and (*4*) the demonstration of intra and extra cellular diplococci on gram stained smears. The diagnosis was confirmed in each instance by isolating the causative organisms on chocolate agar medium and oxidase tests. 1·5 gm. of carbenicillin indanyl sodium and 1 gm. of probenecid was administered orally under supervision in the clinic, after establishing the diagnosis by smear examination.

Those patients in whom cultures failed to confirm the diagnosis were dropped from the study. Patients were requested to report on the 3rd, 7th and 15th post-treatment days and examined for the presence of urethral discharge. Urethral smears and cultures were repeated to detect the presence of gonococci. The V. D. R. L. slide test was done routinely on the day of treatment, 6 weeks and 12 weeks to unmask any concurrent asymptomatic syphilis.

## IN VITRIO ANTIBIOTIC SUSCEPTIBILITY TEST

The minimal inhibitory concentration (M.I.C.) of carbenicillin and seven other antibiotics were determined by serial plate dilution technique for 32 strains of N. gonorrhoeae.

## MEDIUM

Wellcotest (Burroughs-Wellcome) medium containing 6% human blood and heated at 60°C was used. Antibiotics were incorporated into plates of media to give the following final concentrations: penicillin G (0·01, 0·025, 0·05, 0·1, 0·25, 0·5, 1.0 & 2·5 units per ml.); ampicillin and carbenicillin (0·01, 0·025, 0·05, 0·1, 0·25, 0·5, 1·0, 2·5, 5·0 & 10·0 ug. per ml.); erythromycin, streptomycin, kanamycin, tetracycline & chloramphenicol (0·1, 0·25, 0·5, 1·0, 2·5, 5·0 & 10 ug. per ml.).

## METHOD

The strains were subcultured on chocolate agar. A suspension in nutrient broth to give a turbidity corresponding to 1% barium sulphate was made from each. Using a 2 mm. loop, a loopful was streaked on to each plate. It was possible to streak 10 or 11 cultures on each plate. The plates were incubated at 36°C in tins with lighted candles. After 48 hours the lowest concentration of antibiotic which completed inhibited growth was taken as the minimum inhibitory concentration. A strain of S. lutea (ATCC 9341) with a M.I.C. of 0·008 u/ml. penicillin G was used as control.

The criteria for cure were the absence of urethral discharge and bacteriological evidence of infection. Treatment was deemed to have failed if smears and cultures showed the presence of N. gonorrhoea within 14 days of treatment, and if patients denied any further marital or extra marital intercourse.

TABLE I

| No. Admitted to trial | No. followed up | No. defaulted | No. cured | No. reinfected | No. failed | % Failure Rates | |
|---|---|---|---|---|---|---|---|
| | | | | | | Known Minimum | Maximum Theorctical Possibility |
| 50 | 42 | 8 | 37 | 3 | 2 | 4% | 20% |

TABLE II

ANTIBIOTIC SENSITIVITY OF N. GONORRHOEAE

| M.I.C. | Pen G. | Amp | Carb | Ery | Strept | Kana | Tetra | Chlor |
|---|---|---|---|---|---|---|---|---|
| ⩽0·01 | 2 | 0 | 0 | — | — | — | — | — |
| 0·025 | 2 | 0 | 2 | — | — | — | — | — |
| 0·05 | 7 | 6 | 4 | — | — | — | — | — |
| 0·1 | 5 | 9 | 5 | 10(⩽·1) | 0 | 0 | 1(⩽·1) | 0 |
| 0·25 | 6 | 13 | 19 | 8 | 1 | 0 | 1 | 0 |
| 0·5 | 6 | 4 | 1 | 8 | 5 | 0 | 1 | 0 |
| 1·0 | 2 | 0 | 0 | 5 | 7 | 0 | 5 | 0 |
| 2·5 | 1 | 0 | 0 | 1 | 0 | 0 | 8 | 0 |
| 5·0 | 1(>2·5) | 0 | 0 | 0 | 0 | 17 | 5 | 7 |
| 10·0 | — | 0 | 1 | 0 | 2 | 14 | 7 | 10 |
| >10·0 | — | — | — | — | 17 | 1 | 4 | 15 |
| Criteria for less sensitive | >0·05 | >0·1 | >0·1 | >1·0 | >10 | >10 | >1·0 | >10 |
| % less sensitive | 66 | 53 | 66 | 3 | 53 | 3 | 75 | 47 |

M.I.C. of S. lutea: 0.01 u/ml Pen G

## RESULTS

Of 52 patients admitted to the study, 42 returned for regular checkups. Eight defaulted, three on the 3rd day and five on the 7th day. These five were free of infection when examined on the 3rd day. In three reinfection was assumed, because of the recurrence of urethral discharge and history of re-exposure. In two treatment failed (Table I). One patient developed a generalised maculo-papular rash after the 3rd day of treatment. No other side effects were observed, though many patients expressed difficulty swallowing the large tablets.

Table II shows that 66% of the strains were less sensitive to carbenicillin. All but one strain were susceptible to 0·5 ug. per ml. The least sensitive strain had a M.I.C. of 10 ug. per ml.

## DISCUSSION

Past experience has shown that treatment failures develop quickly with the gonococcus. This disturbing quality necessitates the need for constantly searching for newer antibiotics in the treatment of gonorrhoea. Presently penicillin in doses of not less than 2·4 mega units and ampicillin in doses of 1 or 2 grams with probenicid have given good results in Singapore (Rajan, 1972). The day may not be far away when ampicillin, at the present dosage, ceases to be effective against local strains of the gonoccoci.

The M. I. C. results show that carbenicillin was not more effective than ampicillin against the gonococci. In view of this, it is not surprising that some treatment failures were encountered at the dosage used.

Calculations of true failure rates are difficult, because of defaulters in post-treatment follow-ups. Their significance may vary, and interpreted differently by different authors. To reach statistical reality, we have chosen to express failure rates as the known minimum and the theoretically possible maximum failure rates. The method and advantages of this expression have been discussed previously (Rajan 1972).

Calculated thus, the failure rate with 1·5 gm. of carbenicillin indanyl sodium in this study ranged between a minimum of 4% to a theoretical maximum of 20%. Perhaps the true rate is nearer 4%. This makes it a satisfactory and safe antibiotic in the treatment of gonorrhoea.

## ACKNOWLEDGEMENT

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