METHACYCLINE IN NON-GONOCOCCAL URETHRITIS*

BY

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Methacycline (6 methylene-5-hydroxytetracycline) is a wide-spectrum antibiotic which belongs to the
class of 6 methylenetetracyclines first described by
Blackwood, Beereboom, Rennhard, von Wittenhau,
and Stephens (1961). It has been reported to be
effective against a wide range of organisms (Te-Wen
Chang and Weinstein, 1962; English, McBride, and
Riggio, 1962), including the gonococcus (Marmell,
Sills, and Prigot, 1962). A dose of 150 mg. thought
to be the equivalent of 250 mg. tetracycline or oxytetra-
cycline induces serum levels of 0·39–3·12 μg./ml.
serum, reaching double these levels in the occasional
patient (Limson and Guevara, 1963). Higher levels of
plasma binding (in vitro though probably not in vivo)
have been described with methacycline than with
tetracycline (Remington and Finland, 1962); these
writers also reported a higher incidence of side-effects,
particularly nausea, vomiting, and diarrhoea, with
methacycline than with tetracycline.

Taking these facts into account, it was decided
to make use of methacycline in a small series of
cases of non-gonococcal urethritis (NGU), though
the search for an ideal treatment for NGU is
unlikely to be successful until the aetiology is more
fully understood.

Patients Studied

The series consisted of fifty men with non-gonococcal
urethritis, the only basis of selection being the proba-
bility of return for surveillance. One case of Reiter's
disease was included. 37 were born in the United
Kingdom, four in Pakistan, three in Jamaica, three in
Aden, one in West Africa, one in Somaliland, and one
in Italy. The average age was 30 years (range 16–51).
Nine of the 29 married men denied an extra-marital risk.
A history of urethritis was given in 23 cases: five had had
both gonorrhoea and NGU, six gonorrhoea only, and
twelve NGU only. The estimated incubation period
ranged from 3 days to 6 months and was thought to be
less than 10 days in twelve, more than 10 days in 33,
and unknown in five. In five cases the duration of the
discharge was longer than 10 days. The discharge was
mucoid in five, purulent in twelve, and muco-purulent
in 29, whilst no discharge was detected in four though the
history, leucocytic urethral scrape, and hazy urine bore
out the diagnosis. The first urine in the two-glass urine
tests was hazy with flocculations or contained floccu-
lations alone in 47 cases, in eight cases the specimen
in the second glass also showed a haze of pus, whilst in
eleven cases no second glass specimen was passed.

Management

Gonorrhoea was excluded by Gram-stained smears and
by culture, and trichomoniasis either by wet film and
methyl violet-stained film or by wet film and culture.
Blood was taken for a Wassermann reaction, Kahn test,
and Reiter protein complement-fixation test from
all patients at their initial visit.

The treatment given was methacycline 150 mg. 6-hrly
for sixteen doses.

The patients were asked to return for examination on
the 3rd, 7th, 14th, 21st, 35th, 60th, and 90th days. In
fact four cases never attended again, five re-attended
once only on the 3rd or 4th day, and only 21 for 2 months
or longer. Prostatic massage and examination of pros-
tatic fluid was advised between the 2nd and 4th week
after treatment and was completed in twenty cases.

Results

Successful treatment is defined as the absence of
urethral discharge and a clear urine. One patient
was excluded from the series: he had a recurrence
9 weeks after treatment when a culture of urethral
discharge grew Trichomonas vaginalis and further
sexual risk was denied. His prostatic fluid was the
only one of the twenty examined which contained an
excessive number of pus cells. 39 of the remaining
49 patients responded to treatment, giving a success
rate of 79·6 per cent.

Four patients did not return after treatment and
by definition are not classed as successes.

Two men had slight mucoid urethral discharge
and hazy urine on the 3rd and 4th post-treatment
day respectively, but did not return and are included
with the failures.

The case of Reiter's disease still had a muco-
purulent urethral discharge on the 2nd and 3rd days
of treatment, though the eye and joint manifes-
tations were subsiding. There was no previous
history of NGU or Reiter's disease.

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The only other immediate failure still had a mucopurulent urethral discharge on the 4th post-treatment day. He had NGU three times previously and a prostatic bar had been detected on cystoscopic examination.

Two other cases are counted as failures since no note was made of a new exposure to risk: one had a recurrence of signs and symptoms 4 weeks after treatment and one after 6 weeks. Both had had NGU previously.

Four of the successfully-treated cases had recurrences at 13 days, 14 days, 5 weeks, and 10 weeks respectively—all admitted a new risk.

Side-effects of the Drug.—Nausea, vomiting, and diarrhoea were complained of by four men; in no case were the symptoms so distressing that the drug had to be discontinued.

Discussion

Assessment of treatment schedules in NGU is never easy. The absence of a recognizable cause of the condition, its variable clinical presentation, its recurrent nature, and no less the absence of double-blind trials all contribute to this. There is little doubt, however, that some antibiotics do favourably modify the disease both strikingly and promptly. It is widely agreed that the tetracycline group falls into this category (Willcox, 1953, 1955; Morton and Read, 1957; Doyle, Gill, and Laird, 1957; Csonka and Rosedale, 1962). In these circumstances we have felt it permissible to dispense with a comparable number of untreated controls.

A response rate of 79·6 per cent. compares well with the response to other antibiotics and is in keeping with those resulting from administration of other members of the tetracycline group.

One of our failures showed the features noted as common in those failing to respond (Csonka and Rosedale, 1962), i.e. previous history of NGU and previous failure to respond to treatment.

Side-effects of methacycline were few, and did not necessitate withdrawal of the antibiotic.

Summary

(1) Fifty cases of NGU were treated with methacycline 150 mg. 6-hrly for 4 days. One case was excluded from the series when Trichomonas vaginalis was found later.

(2) The type of urethritis and duration of discharge are noted.

(3) Successful treatment as defined occurred in 39 (79·6 per cent.).

(4) The results compare favourably with those obtained with other tetracyclines.

We are pleased to acknowledge the help of the clinic staff and the gift of methacycline from Pfizer Limited.

REFERENCES


Le traitement de l'urérite non-gonococcique par la méthacycline

RÉSUMÉ

(1) Cinquante cas d'urérite non-gonococcique ont été traités par la méthacycline à la dose de 150 mg. toutes les six heures pendant 4 jours. Un cas a été exclu de la série quand des Trichomonas vaginalis ont été découverts plus tard.

(2) Le genre d'urérite et la durée de l'écoulement ont été notés.

(3) La cure radicale comme décrite a eu lieu chez 39 malades (79,6 pour cent).

(4) Les résultats se comparant favorablement à ceux obtenus avec d'autres tetracyclines.
Methacycline in non-gonococcal urethritis.

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