TREATMENT OF ANORECTAL GONORRHOEA INFECTION IN MALES AND FEMALES WITH ORAL AMPICILLIN

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SYNOPSIS

Anorectal Gonococcal infections are more difficult to cure than genital infections in both males and females but more so in the males. An evaluation was done to establish the efficacy of extended oral ampicillin therapy for anorectal infection. The regimen consisted of a single oral dose of 3.5g ampicillin trihydrate and lgm probenecid on day one of treatment followed by 0.5g of ampicillin trihydrate four times a day on days two and three. One follow up culture was taken 7—28 days after completing therapy. Out of a total of 194 patients who were treated with this regimen, there were 3 treatment failures. The over all failure rate of 1.5% compares favourably with the current preferred modes of treatment.

MEDICATION USED IN THIS STUDY:

Ampicillin trihydrate (generic name) 0.5g capsules produced by E.R. Squibb & Sons of Princeton, NJ. The proprietary name is Principen.

Probenecid (generic name) 500mgs tablets produced by Merck Sharp & Dhome of West Point, PA. The proprietary name is Benemid.

Both drugs were purchased by the Health Department of Santa Clara County, San Jose, California.

INTRODUCTION

Most authors (1, 2, 3, 4, 5, 6) report that anorectal gonococcal infections in both men and women are more difficult to cure than genital infection i.e., urethral infections in the men or urethral, vaginal or cervical infections in women. In addition it has been reported (7) that anorectal infections in men are more difficult to cure than comparable infections in women.

Washington (7) has published an excellent review of various therapeutic regimens for the treatment of anorectal gonorrhoea in both men and women. Published reports (8) related to oral ampicillin therapy describe the efficacy of either single dose ampicillin or one dose followed by a repeat dose in 8-14 hours. This report describes the result obtained with both single dose ampicillin therapy and 'extended' ampicillin therapy. The latter approach was applied to the treatment of pharyngeal gonorrhoea by Dr Mary Riggs, the former director of The Central Veneral Disease Clinic of the Santa Clara County Public Health Department San Jose, California, and other staff members. (8)

The two kinds of treatment regimens were used in this study.

The extended regimen (Regimen # 1) consisted of ampicillin trihydrate given in a loading dose of 3.5 gm with 1 gm of probenecid. This is followed on day two and day three with 0.5 gm of ampicillin given 4 times a day for a total of 7.5 gm.

The single dose (Regimen # 2) consisted of ampicillin trihydrate given in a single dose of 3.5 gm with 1 gm probenecid. No further medication is given. The latter regimen was introduced, when high failure rates with single dose ampicillin therapy were reported by clinic staff. Since staff were skeptical that such high failure rates prevailed in our clinic, the clinicians were given the option to use either regimen, and then both regimens were in use concomitantly. However, regimen # 2 was used only in patients who had no oral sexual contact which eliminated the possibility of inadequate treatment for possible pharyngeal gonorrhoea. Regimen # 1 was used for patients with concomitant pharyngeal infections proved by positive throat cultures or who gave a history of anogenital contact.

PATIENTS & METHODS

Selection of patients was done as following: The laboratory log book was used to obtain the names of all patients who had presumptive positive rectal cultures with N. gonorrhoea within the one year period between Jan — Dec 1981. The charts of all these patients were reviewed. Only those patients were included in the study who fulfilled the following criteria. Patients who has culture positive gonococcal infection of the rectum, had received regimen under study and had at least one test of cure culture within two weeks of being treated, but no sooner than seven days before completing therapy.

Rectal cultures were taken routinely on all females. Rectal cultures were done only on males who gave a history of rectal exposure. All the cultures were taken in the recommended manner (9) and plated immediately on modified Thayer-Martin medium. Then incubated in 10% carbon dioxide at 35° C in a humid atmosphere. All isolates obtained in males were identified by colony morphology and oxidase reaction and finally confirmed by sugar fermentation. Isolates obtained in females were not confirmed by sugar fermentation since most of the rectal infections were associated with genital infection. The latter were confirmed by morphology and sugar fermentation. The following categories of patients were treated for anorectal gonorrhoea: Those with diagnosed anorectal gonorrhoea, those who were diagnosed as having gonorrhoea at another site and had rectal exposure, and those wno were treated on epidemiological grounds because of rectal exposures to a diagnosed case of gonorrnoea. Only those individuals whose cultures were positive or presumptive positive for anorectal gonorrhoea were included in the study.

If the follow-up examination revealed persistant infection, a PPNG (Penicillinase Producing Neisseria Gonorrhoea) screen was done by the penicillin disc method, (9) and the zone size used as criteria for resistant infection. Only those patients were included in the final selection who had received either of the two treatment regimens under study beside fulfilling the selection criteria given above. This left us with a total of 247 patients. 194 of these, 147 males and 47 females were treated with regimen # 1 (Extended therapy), and 53 patients 32 males, 21 females were treated with regimen # 2 (single dose therapy). The age range of male patients was 14 to 62 years with a median of 27 years. 73.4% of the patients were infected at two or more sites, 60% of these being oral and rectal infections. The age range of female patients was 15 to 51 years with median of 22 years. 81% of the patients were infected at two or more sites, 90% of these being combination of rectal and genital infections.

RESULTS

Women

Regimen #1:

Out of a total of 47 women treated with the regimen #1 (Extended therapy) there were 3 with positive test of cure culture on a follow up examination within two weeks.

Patient #1 was a 33 year old female, who also had positive cervical cultures on initial examination. Follow up examination after one week of completing therapy revealed persisting rectal infection, although cervical infection had cleared. There was no history of re-exposure. PPNG screen with the pencillin disc method was negative. This patient was retreated with spectinomycin 2gm intramuscular, and her infection cleared. Patient #2 was 35 year old female. Her sexual contact was from Malaysia; PPNG screen, however, was negative, again done by the disc diffusion technique. Rectum was the only site of infection. The test of cure culture done 10 days after completing therapy was positive. She too, was retreated with spectinomycin (2 gm intra muscular) and was cured.

Patient #3, a 21 year old female, also positive genital cultures. Follow-up one week after completing therapy revealed persistent genital and rectal infections. On clinical examination she demonstrated signs and symptoms of salpingitis which were absent when she was first seen. She also gave history of sexual contact on the sixth day following medication (one day before reculture). PPNG screen was negative. She was retreated with ten days of medication with ampicillin, dosage: 3.5 gm of ampicillin plus 1 gm probenecid as loading dose with 0.5 gm ampicillin four times a day for 10 days and was cured. This patient, therefore may not represent a true failure but a case of reinfection. No information was available on the sexual contact of this person. Including all the above, the failure rate for women who were treated with extended therapy (regimen #1) was calculated to be 6.3% (3 out of 47). If the person with re-exposure is excluded, the failure rate is reduced to 4.2%.

Regimen 2

21 women were treated with regimen 2 (single dose therapy). All of them had test of cure cultures within 7 —

14 days of their visit to the clinic. All were cured of their infections.

Men

Regimen # 1

A total of 147 males were treated with extended ampicillin therapy. Out of these there was one treatment failure.

Patient #1 was a 23 year old male who, after taking the loading dose, took a total of 5 tablets over the next two days. He had only rectal infection, was retreated with the same regimen and cured. A PPNG screen done on the isolate with the penicillin disc method was negative.

In this series of male patients the failure rate was calculated to be 0.6% (1 out of 147).

Regimen # 2

31 patients were treated with the regimen #2 (single dose therapy). Out of these one patient was a treatment failure. This person was a 20 year old male, who had a positive test of cure, rectal culture after 10 days of taking the medication. PPNG screen was negative. He was retreated with aqueous procaine penicillin G 4.8 million units with 1 gm of probenecid. His subsequent test of cure culture was negative. This person did not give any history of sexual exposure after treatment. With this regimen the failure rate was calculated to be 3.2% (1 out of 31).

If the two groups (female and males) are combined, the overall failure rates calculated with each regimen, are 1.5% with regimen #1, and 1.9% with regimen #2. Both of these regimens were found to be effective in eradicating infection from all infected sites. The failure rates for this regimen vis a vis pharyngeal gonorrhea have been evaluated in a separate report. (Unpublished). Although there was an overlap of patients in both studies, there was no overlap of treatment failures.

DISCUSSION

Since patients with rectal gonorrhoea are not very reliable as far as follow up is concerned, it is important to treat initially with an effective regimen. This is more significant since the recent reports of emerging B — Lactamase producing strains. (3, 5, 7) The drugs routinely used for urogenital infections have been less effective in treating rectal infections. The failure rates in men have ranged from zero to 28.6% (A.A Zaidi and G.H. Reynolds — unpublished observation) (7) with ampicillin plus probenecid. Washington (7) has compiled the studies done in the last decade very comprehensively in which he compares the failure rates with different drug regimens used by various authors. Klein et al (10) after a review of the subject conclude that there is not enough published data to recommend optimal therapy. Fiumara (5) and Sands (2) have used Aqueous procaine Penicillin G with fairly good success rates (96.6%). (2) Sands (2) was not able to get such good results with oral ampicillin, the failure rate in this instance was 14.8%, using 3.5 gm of ampicillin as a single dose. Klein (6) and Fiumara (5) have also reported single dose treatment failures.

John and Jefferis (4) treated 103 cases with oral ampicillin 250 mg four times a day for five days and had a failure rate of 6%. Our study has shown a much lower rate than this in males (0.6% and 3.2%) and as well as in females (4.2%). Sands-Seller (11) in another trial have shown that ampicillin probenecid therapy in two doses has a failure rate of 1.6% as opposed to 10.7% with single dose. Spectinomycin HCl has consistently shown virtually 100% success rates (2) which was also our experience. Since no significant differences have been found in 2 gm and 4 gm dose of spectinomycin, CDC recommends using the former. When spectinomycin is indicated there is no biological explanation for the observation of the high failure rate of 4.2% to 6.3% higher in women treated with regimen #1 (extended treatment) than in women treated with regimen #2, (single dose therapy) in whom the failure rate was 0%. Thus it is reasonable to calculate the failure rate for both regimens #1 and #2, to be 3 or 4 of 68 (47 + 21) or 4.4% to 5.8%. The cure rates for Regimen #1 (extended therapy) were higher for men than for women which is at variance with the findings of most other investigators. (6, 7, 12) However, higher failure rates, have been reported in women than in men when spectinomycin was employed.

Using tetracycline hydrochloride researchers have found a fairly high failure rate, 14.4% in men although nation wide there seems to be an increased sensitivity of the gonococcus to tetracycline. (6) It is possible that the regimen is inadequate as far as dosage, or there is poor patient compliance.

Rectal gonorrhoea associated with urogenital gonorrhoea in women is common in the USA. (13, 14) Stansfield (15) found an overall incidence of 46% in her study. Four of her patients had only rectal infection diagnosed by proctoscopy. We diagnosed single site GC infection of the rectum in a total of five patients in our series by rectal cultures alone. The route of infection of rectum in women who deny rectal contact is uncertain but King (16) has suggested that the spread is via the contaminated vaginal secretions. Washington (7) has done an excellent review of therapeutic regimens used in anorectal infections in women. Most of the regimens recommended by United States Public Health Service have failure rates of 1.8 — 7.9%. (1) The National Gonorrhoea Therapy Monitoring Study (6) used a large sample of people and found a failure rate of 3.2% with APPG 4.8 × 10 units intramuscularly, and 1 gm probenecid. For an oral 3.5 gm ampicillin and 1 gm probenecid dose they reported the rate of 3.0%. Zaidi (7) A A. (unpublished data) reported much higher failure rates in men than in women. 28.6% vs 7.9%. John and Jefferis (4) have found rates of 5.8% in women using oral ampicillin.

The highest failure rates have again been observed with tetracycline hydrochloride by different authors (7) and as reported by CDC. These results suggest that tetracycline should not be used as the drug of choice in these infections.

Among drugs which have given high success rates is spectinomycin (2 gm or 4 gm) given intramuscularly. We did not see any failure in our study sample although failure rate of 1.8% has been reported. (2, 12) Generally the results seem to be encouraging.

From the observations of this study it is concluded that the treatment regimen #1 (extended ampicillin therapy) is an effective first line treatment of uncomplicated anorectal gonorrhoea. The low failure rates with a single dose therapy are also quite encouraging, specially if one is concerned about patient compliance. Amongst the advantages of oral ampicillin therapy, over parenteral injectable penicillin therapy are the much lower risk of anaphylaxis and the absence of procaine reactions. The success rate obtained is higher than that obtained with other recommended regimen. (1, 4, 7)

The extended regimen in exactly similar dosage has been evaluated for oropharyngeal gonorrhoea and has given an overall failure rate of 3%. (unpublished data) Since the patient population presenting with gonococcal infections has involvement of multiple sites, we feel

TABLE I TREATMENT OF ANORECTAL GONORRHOEA FAILURE RATES IN MEN

	Regimen # 1*	Regimen # 2**
No. treated	147	32
No. failed treatment	1	1
Failure rate (%)	0.6%	3.2%

* Ampicillin 3.5G + 1 gm Probenecid + Ampicillin 500 mgs 4 × day for 2 days
** Ampicillin 3.5G + 1.gm Probenecid

TABLE II TREATMENT OF ANORECTAL GONORRHOEA FAILURE RATES IN WOMEN

	Regimen # 1	Regimen # 2
No. Treated	47	21
No. Failed treatment	3	0
Failure rate	4.2% — 6.3%	0%

TABLE III TREATMENT OF ANORECTAL GONORRHOEA MALES & FEMALES COMBINED

	Males	Females	Total	No. Failed treatment	Failure Rates
Regimen #1	147	47	194	3	1.5%
Regimen #2	32	21	53	1	1.9%

this is an effective initial regimen to use in patients who have history of contact in multiple sites.

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