First experiences with single-dose treatment of vaginal trichomoniasis with carnidazole (R 25831)

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SUMMARY This paper reports the results of treating 152 women with carnidazole, a new trichomonocidal drug. They were divided into two groups. The first comprised 91 patients who were treated with 2 g, while the second group comprised 61 patients who were treated with 1.5 g carnidazole in a single oral dose. Defaulter rates were 6.6% for the first group and 13.1% for the second. Of the remaining 85 patients in the first group, 76 (89.5%) were negative at the first follow-up one to three weeks after treatment, three (3.5%) were considered to be treatment failures, and six (7.0%) were considered to be reinfected. Of 53 women treated with 1.5 g, 39 (73.6%) were negative at first follow-up, eight (15.1%) were considered to be treatment failures, and six (11.3%) were considered to be reinfected. The difference between the number of patients cured in both groups is statistically significant. Fourteen patients experienced side-effects, but these were of little significance. Carnidazole given in a single oral dose of 2 g in 16 women did not cause consistent changes in any of the haematological and biochemical parameters studied.

Introduction

Carnidazole (0-methyl [2-(2-methyl-5-nitro-1 H-imidazol-1-yl) ethyl] carbamothioate) is a new derivative related to nitroimidazole. The structural formula is as follows:

It has been shown to be highly effective against different species of trichomonads as Thiénpont (1973) demonstrated in animals. Animal toxicity of carnidazole is insignificant (Niemegeers, 1974).

Carnidazole has been used in Belgium since December 1974 in veterinary medicine, mainly in pigeons.

Because of the good results obtained in animals, the drug was tried in human trichomoniasis. The first clinical studies in Brazil (Nogueira, 1975) showed a very high percentage of gastrointestinal

side-effects when given in tablets which disintegrated in the stomach. After enteric-coating of the tablets these side-effects became insignificant. To find out the ideal dosage, treatment schedules were established, based on the posology of metronidazole and tinidazole. In these limited clinical studies high cure rates were found with a single dose treatment of 2 g carnidazole. As single doses of the drug can be taken under supervision, this is the ideal regimen for use in a sexually transmitted diseases department. We therefore decided to evaluate the efficacy of single doses of carnidazole. Two dosages, namely 2 g and 1.5 g, were tested. In 16 patients who were treated with 2 g, haematological and biochemical parameters were also studied.

Material and methods

The efficacy of a single oral dose of either 2 g or 1.5 g of carnidazole (R 25831) was studied in 152 non-pregnant women with a trichomonas-positive wet film of vaginal secretion who visited the outpatient department for venereal diseases at Rotterdam University Hospital in the summer of 1975. Treatment with either 2 g or 1.5 g was given alternately for periods of four weeks. Thirty patients were prostitutes; 49 also had gonorrhoea and one had primary syphilis.

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Patients were only selected on the presence of *Trichomonas vaginalis* in the wet film, absence of pregnancy, and the expectation of return for follow-up examination. Ages ranged from 16 to 67 years (median: 24). A preparation of vaginal mucus (collected from the posterior fornix) was made by diluting it with physiological saline on a slide and examining it microscopically for *T. vaginalis* within five minutes of collection. Another sample, taken with a sterile swab, was immediately inoculated on a specific growth medium (containing Ringer solution, cysteine, liver, and glucose—RCLG). The patients were also investigated for gonorrhoea by Gram stain and culture. Syphilis serology was done at the start, and again at the end of the study or three months after the first visit. Patients were treated with a single oral dose of either 4 (group 1) or 3 (group 2) enteric-coated tablets, each containing 500 mg of carnidazole, which was taken in the presence of a nurse. Whenever possible the sexual partner was given the same treatment, but in most cases it was impossible to do this in the presence of a nurse. Concomitant medication was given to 49 patients for gonorrhoea. This treatment consisted of 1 g ampicillin intramuscularly, four hours later 2 g orally (Stolz and Kerkkamp, 1974), and in one case 2 g tetracycline daily for five days. In one case of primary syphilis 10·8 iu PAM intramuscularly divided into three doses of 600·000 iu each week for six weeks was given. Fourteen patients did not return for follow-up, giving a defaulter rate of 9·2% overall. The defaulter rate for the first group was 6·6% (six out of 91 patients) and for the second group 13·1% (eight out of 61 patients). Details of these patients have not been included in this report.

Patients were re-examined in the same way as at their first visit three weeks after treatment, most patients within eight days of treatment, and many were re-examined one week later. Side-effects were noted. At the follow-up visits they were questioned regarding possible reinfection. Reinfection was presumed when patients admitted to unshielded sexual contact with untreated partner(s) before the first follow-up examination. Most prostitutes continued to work. Condoms were seldom used.

In 22 consecutive patients who were treated with 2 g carnidazole blood and urine samples were collected once before and once 4 to 19 (median eight) days after treatment. The blood investigations included: ESR, haemoglobin, haematocrit, total and differential white cell counts, platelet count, sodium, potassium, chloride, cholesterol, creatinine, urea, alkaline phosphatase, bilirubin, transaminases, lactic dehydrogenase, glucose, total protein, albumin, alpha-1, alpha-2, beta and gamma-globulin, IgA, IgG, and IgM. The urine analysis included:

specific gravity, pH, albumin, and sediment. Six patients who had haemolysed blood samples were withdrawn from the analysis. Six patients received concomitant therapy: five were given ampicillin, and one received tetracycline.

Results

GROUP 1 (2 g)

Of a total of 85 patients who returned, 76 were negative for trichomonads (direct preparation and culture) at their first follow-up examination. Six patients were considered to be reinfected; these were all prostitutes who had had multiple unprotected sexual contacts with untreated partners. Three patients (3·5%), not prostitutes, were considered to be genuine treatment failures, but two of them were negative after retreatment, leaving only one real treatment failure and thus lowering the overall failure rate even more. In the six patients considered to be reinfected, four were retreated and only one has become negative.

GROUP 2 (1·5 g)

Of a total of 53 patients who returned 39 were negative at their first follow-up examination. Six patients were considered to be reinfected, eight (15·1%) were considered as treatment failures. From this last group of patients only one was treated again with the same dose and her investigations remained positive for trichomonads.

Side-effects of low significance were noted by 14 patients among whom were six patients who concomitantly received ampicillin in the dosage mentioned. Side-effects were mainly gastrointestinal (nausea, vomiting, diarrhoea, and gastric discomfort) dizziness and dark yellow urine were mentioned by one patient. Statistical analysis showed that the frequency of side-effects was not significantly (Fisher's Exact Test $P > 0·1$) higher in the group of patients who had also received ampicillin. There was no statistically significant difference ($P > 0·1$) in frequency of side-effects between the 1·5 g and 2 g dosage-group.

No consistent changes could be seen in the laboratory investigation when comparing the values before and after treatment.

Discussion

A single oral dose of 2 g carnidazole in the treatment of vaginal trichomoniasis gave a failure rate of 8·8%, which means a minimum cure rate of 91·2%. Taking into account the six patients who were

considered to be reinfected and the results of retreatment there was a cumulative cure rate of 96.5%.

With a single oral dose of 1.5 g carnidazole the failure rate was 26.4%, giving a minimum cure rate of 73.6%. If deduction of the number of patients considered to be reinfected gives a cure rate of 84.9%, the difference between the results in both groups is statistically significant ($P < 0.1$).

When comparing the two dosage groups there was no significant difference ($P > 0.1$) in the number of prostitutes cured in both groups, whereas the results were significantly ($P < 0.1$) better in the non-prostitutes for the group of patients treated with 2 g. This shows the importance of recording promiscuity when evaluating a trichomonocide.

As there is no previous published experience in the use of this drug these results can only be compared with other drugs used in treating trichomoniasis in single doses. With 2 g of metronidazole cure rates of 82% (Csonka, 1971), 85% (Woodcock, 1972), and 90% (Morton, 1972) have been reported. With a 2 g dose of nimorazol, Jones (1972) reported a cure rate of 93.7%. With tinidazole, which is a relatively new drug, reported cure rates range between 93% (Weidenbach and Leix, 1974; Milek and Nedělková, 1974) and 97% (Dellenbach and Muller, 1974).

The incidence of side-effects was low. Extensive blood and urine laboratory analysis in 16 patients treated with 2 g carnidazole did not reveal signs of toxicity.

Conclusion

Carnidazole, used in a single oral dose of 2 g in vaginal trichomoniasis gives a high cure rate with a low incidence of side-effects. When using a 1.5 g dosage a significantly lower cure rate results.

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