TREATMENT WITH METHENAMINE HIPPURATE IN THE PATIENT WITH A CATHETER

BY

K NORRMAN, MD and L WIBELL, MD
Tunåsen Hospital, Uppsala and the Department of Medicine, University Hospital, Uppsala, Sweden

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Treatment with Methenamine Hippurate† in the Patient with a Catheter

K Norrman, MD, and L Wibell*, MD, *Tunåsen Hospital, Uppsala and the Department of Medicine, University Hospital, Uppsala, Sweden*

Methenamine hippurate, 1 g twice daily, was given for four months to twenty-two elderly female subjects with an indwelling catheter. The incidence of catheter blockage was significantly reduced when compared with the control period of similar duration, although bacteriuria persisted throughout treatment. The incidence of symptomatic urinary tract infection also decreased during treatment with methenamine hippurate.

Introduction

Elderly patients with chronic disease often suffer from bladder incontinence. During treatment with an indwelling catheter a chronic urinary tract infection is likely to develop rapidly. In the care of such patients additional work and cost is caused by frequent problems with catheter incrustation, which manifests itself as an obstruction of the urinary flow through the catheter, urinary leakage into the bed linen, or both. The use of long-term antibiotic treatment to reduce these problems is usually condemned as it appears to have little beneficial effect but may instead contribute to the development of multi-resistant bacterial strains within a hospital. Still, these patients often receive antibiotic treatment when fever and impairment of their physical or mental condition is judged to depend on the urinary tract infection.

Methenamine hippurate has for many years been considered to be a drug of value for the treatment of chronic urinary tract infections (Andelman 1968, Gerstein *et al* 1968, Seneca, Zinsser & Peer 1967). Though not considered a powerful chemotherapeutic agent it has the advantage of not being likely to induce the development of resistant bacterial strains. Our own experience with methenamine hippurate in patients with indwelling catheters was that while it had little effect on the presence of bacteriuria, it did seem to reduce the incidence of blocked catheters due to incrustation. We therefore set out to see if this clinical impression could be verified under controlled conditions.

Design of the trial

Twenty-nine elderly female patients, in the age range 70 to 80 years, entered the trial. All were in-patients in a hospital for chronic diseases. Only twenty-two of them are included in this report for the following reasons. One patient no longer needs catheterization, two patients died and in four patients the scheduled treatments and observations were not adequately performed.

†Methenamine hippurate was supplied by 3M Riker Laboratories, United Kingdom and is known as 'Hiprex' in Europe and as 'Urex' in the United States of America

*Request reprints from: L Wibell, MD, Department of Medicine, University Hospital, S-750 14 Uppsala 14, Sweden

All twenty-two patients had an indwelling Foley catheter and significant bacteriuria ($> 10^5$/ml) according to a dip slide culture of fresh urine. Each patient was observed during four months of treatment with methenamine hippurate (Hiprex, supplied by 3M Riker Laboratories, UK), 1 g twice daily, and during a control period without such treatment, also amounting to about four months. The length of the treatment periods (mean value ± SD) was 120 ± 10 days and for the control periods 131 ± 21 days. Nine patients started with a treatment period and the other thirteen patients first passed through the control observation period. Episodes of symptomatic infection were treated in the same way during the methenamine hippurate and the control periods. When an antibiotic was prescribed during the treatment periods methenamine hippurate was usually not withdrawn.

During the eight months of the study the catheters were as a rule only changed when the responsible nurse considered it necessary. The reason for changing the catheter was recorded on each occasion. Episodes of clinical infection and other drug treatments were also recorded. Dip slide urine cultures were performed once monthly.

Results

General observations

No adverse reactions to methenamine hippurate were noted. According to the monthly dip slide cultures significant bacteriuria persisted in all subjects during the control period and during treatment with methenamine hippurate. It was felt by the nursing staff that there were less problems with the catheter during the treatment periods and it was noticed that the urine usually became less cloudy during the course of treatment.

Change of indwelling catheters

As shown in Table 1 there was less need to change the catheter during the treatment periods. The difference was mainly accounted for by a decreased incidence of incrustation. During methenamine hippurate treatment the mean rate of catheter replacement, because of incrustation, was 0·0256 per patient per day and during the control period 0·0398 per patient per day. Thus the mean difference was 0·0142. The standard deviation for the differences in all paired observations was 0·0196. The mean difference was significant ($p < 0·01$).

Table 1

Frequency of changing indwelling catheters in twenty-two patients during 2650 days of treatment with methenamine hippurate and 2880 days of control observation

Reason for catheter change	*Treatment period*	*Control period*
Incrustation with leakage or obstruction	69	117
Patient removed the catheter	10	14
Routine change	6	6
Haematuria	0	1
Total	85	138

Table 2

Incidence of treated episodes of clinical infection. Patients and material as in Table 1

Diagnosis	*Treatment period*	*Control period*
Urinary tract infection	4	17
Fever of unknown origin	4	2
Pneumonia	0	2
Skin infection	0	1
Total	8	22

Clinical infection episodes and antibacterial treatment

Episodes of clinical infection occurred more often during control periods than during treatment with methenamine hippurate. This is shown in Table 2. The difference was mainly accounted for by the frequencies of urinary tract infection with clinical signs or symptoms. It is shown in Table 3 that antibacterial treatment was prescribed for almost three times as many days during the control periods as in the treatment periods.

Table 3

Drug treatment during episodes of clinical infection. Patients and material as in Tables 1 and 2

Drug prescribed	*Treatment period*		*Control period*	
	episodes	*days*	*episodes*	*days*
Ampicillin	5	78	8	109
Nitrofurantoin	1	21	6	133
Sulphonamide	1	24	2	88
Trimethoprim/sulpha	–	–	2	28
Doxycycline	–	–	2	24
Erythromycin	–	–	2	24
Penicillin	1	14	–	–
Total	8	137	22	406

Discussion

It has previously been shown (Gerstein *et al* 1968) that treatment with methenamine hippurate is not likely to eliminate bacteriuria in patients with an indwelling catheter. In the present study bacteriuria persisted during treatment in spite of a significantly reduced incidence of catheter change due to incrustation (Table 1). Although the present study was not designed to investigate the reasons for reduced incrustation, a few comments are warranted.

The decrease in the number of clinical infections during the treatment periods (Table 2) makes it likely that the antibacterial properties of methenamine hippurate played a part. The semi-quantitative dip slide technique does not allow a good quantitative estimation of bacteriuria and was here used only to establish the presence of infection. It is thus possible that a considerable reduction of the bacterial count was achieved in some patients without having been discovered. Such a decrease, if present, could have relevance for the incrustation process as well as for symptoms of infection.

It is conceivable that methenamine hippurate could also reduce the rate of incrustation by mechanisms other than its antibacterial action. In the urine the drug dissociates to form hippuric acid and methenamine, and the latter substance at a pH-dependent rate releases acidic formaldehyde. The presence of these substances in the urine may affect the precipitation of, for example, magnesium and ammonium phosphates. Also, in patients with a sufficiently low pH the concentration of acidic formaldehyde in the urine might be sufficient to influence the inflammatory process in the bladder wall and the formation of debris.

It was not the aim of the present study to find the most suitable dose schedule for treatment with methenamine hippurate. However, the use of a higher dose or acidifying agents might be expected to improve the therapeutic results in some patients at the possible expense of side-effects.

It appears that the use of methenamine hippurate in patients with an indwelling catheter might save nursing time and, in the present study, about one Foley catheter for each 100 tablets of methenamine hippurate given to the patients. Further, patients in the control group were found to require treatment with other antibacterial agents more frequently (Table 3). The results thus suggest that treatment with methenamine hippurate might be worthwhile in the chronically ill patient with a catheter.

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