MANDELIC ACID IN THE TREATMENT OF URINARY INFECTIONS

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Since the introduction of the ketogenic diet treatment of urinary infections by Clark¹ and Helmholtz² in 1931 there has been ample proof of its efficacy. While many workers have been convinced of its remarkable bacteriostatic power they have, however, been hardly less impressed by the practical difficulty of carrying out the treatment.

Report on Sixteen Cases

The following is a report on sixteen cases of urinary infection treated with mandelic acid. The drug was given, as advised by Rosenheim, in the form of the sodium salt in a neutral mixture, according to the following prescription:

R. Mandelic acid gr. 45
Sod. bicarb. gr. 21
Syr. aurantii 5 j
Aq. to 3 j

Sig.: 3 j ex. aq. four times a day.

Appropriate doses of ammonium chloride were given to maintain a urinary pH below 5.5. This drug was given in cachets containing 10 grains. Six cachets in the day were usually sufficient to secure the desired acidity, though larger doses were sometimes necessary. The fluid intake was limited to between two and three pints a day, to ensure a strong concentration of the mandelic acid in the urine.

The varying types of case treated and the results obtained are shown in the accompanying table.

Case	Sex	Age	Infection	Duration of Infection	Diagnosis	Days Till Urine Sterile	Minimum pH Attained	Side Effects	Remarks
1	F	37	B. coli	8 years	Chronic pyelitis	8	—	Nil	Cure
2	F	43	"	7 years	"	8	—	A few casts; trace albumin	Cure
3	F	58	B. coli; Strep. faecalis	5 years	Chronic cystitis	Not sterile	5.0	Nil	Left hospital after 8 days treatment. Much improved
4	F	14	B. coli	1 year	Chronic pyelitis	12	5.4	Nil	Cure
5	M	67	B. coli; streps; staphs	1 year	Chronic cystitis	Not sterile	5.3	Nausea; vomiting; dysuria	Failure. Treatment stopped after 12 days, owing to side effects
6	F	60	B. coli; Strep. faecalis; diphtheroids	4 months	"	6	4.8	Trace albumin; a few casts	Cure
7	M	66	B. proteus; staphs; streps	4 months	"	Not sterile	7.8	Acidosis; nausea; vomiting	Failure to produce an acid urine. Not improved
8	M	72	B. coli	3 months	"	8	4.9	Buzzing in ears	Cure
9	M	28	T.B.; B. coli; staphs	3 months	Tb. bladder	8	5.4	R.B.Cs.; indigestion; buzzing in ears	Cure of secondary infection only
10	F	39	Staphs; T.B.; B. coli	3 months	"	10	—	R.B.Cs.	Cure of secondary infection only
11	M	22	B. coli; staphs; diphtheroids	3 months	Subacute cystitis	10	5.2	Giddiness; a few casts	Cure. Relapse in a week.
12	M	47	B. coli	7 months	"	6	5.0	Nil	Cure of relapse in a week
13	F	63	"	4 weeks	"	8	5.2	Giddiness; buzzing in ears	Cure. Relapse in 3 months
14	F	56	"	16 days	Acute cystitis	10	5.1	Nil	Cure of relapse in 5 days
15	F	53	"	7 days	Acute pyelitis	5	5.0	Nil	Cure. Relapse in 1 month
16	F	73	"	7 days	"	5	5.4	Nil	Cure. Relapse in 2 days

The ketogenic diet lacks universality of application, owing to the necessity for rigid and skilled dietetic supervision, and owing to its nauseating and expensive character.

The bacteriostatic agent in the urine of patients under ketogenic treatment has been shown by Fuller³ to be β -hydroxybutyric acid. Little or no effect, however, is produced on urinary infection by the oral administration of this acid, since when given in this way it is completely oxidized before reaching the urine. Attempts have therefore been made to find a related non-toxic acid which would exert a similar bacteriostatic effect, but which would not be oxidized when given by the mouth, and which would be excreted unchanged in the urine. It has recently been claimed by Rosenheim⁴ that mandelic acid ($C_6H_5 \cdot CHOH \cdot COOH$) fulfils these requirements, and that when 12 grams are given daily in divided doses and the urine rendered strongly acid by ammonium chloride, it forms an effective substitute for the more cumbersome ketogenic diet treatment.

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Cases 1 to 5 comprised very chronic types of urinary infection, in which the condition had been present for from one to eight years. They had all been previously subjected to a great variety of medicinal, and in some cases, local treatment, to which they had proved entirely recalcitrant, with the exception of Case 4, who had responded satisfactorily to the ketogenic diet but had relapsed shortly after it was discontinued. Cases 6 to 10 were also chronic cases, though giving a somewhat shorter history, which had also proved recalcitrant to treatment. In this group Cases 9 and 10 were suffering from genito-urinary tuberculosis, complicated by a secondary infection. The treatment was directed to the eradication of this latter, without, of course, any expectation of influencing the underlying tuberculous disease. Cases 11 to 16 were more acute types of disease, which had failed to clear up under ordinary massive alkali therapy. It is true that in the last two cases this had only been given a short, and possibly inadequate, trial, but Case 16 was getting rapidly worse in spite of thorough alkalization, and was desperately ill when mandelic acid treatment was started.

Cases 1, 3, 5, 7, 9, 10, 11, and 12 had the diagnosis confirmed by cystoscopic examination.

The type of infection found in each case is shown in the table. As was to be expected, the coliform bacillus was predominant, but in seven of the cases a mixed infection was present. Repeated bacteriological examinations of catheter specimens by cultural methods were made in all cases.

The initial pH of the urine before treatment is omitted from the table, as it was very frequently artificially raised owing to the fact that the patient had been taking alkalis previously. It will be seen that, with the exception of one case, a minimum urinary pH of below 5.5 was always procured, and this effect was usually obtained by the daily administration of as little as 60 grains of ammonium chloride. Less than this was never given, and in a few cases a larger dose was necessary. Case 7, however, resisted all efforts to acidify the urine. This patient, after prostatectomy, developed a mixed infection of the prostatic bed, with *B. proteus*, streptococci, and staphylococci. He had suffered from marked frequency, dysuria, and slight incontinence for a year, and had resisted all local and medicinal treatment. His urine was found to be highly alkaline (pH 8.4) owing to ammoniacal decomposition in the bladder. As much as 360 grains a day of ammonium chloride was given to this patient, and when this failed to acidify the urine a similar quantity of calcium chloride, combined with bladder wash-outs, was tried. These measures produced a true acidosis, as indicated by a CO₂-combining power of the blood of 45 volumes per cent., and some nausea and vomiting, but in spite of this the urine remained persistently alkaline, the pH never falling below 7.8.

General Commentary

It will be seen that, with three exceptions, the treatment was successful in sterilizing the urine. This result was brought about with remarkable rapidity, when the chronic and intractable nature of many of the cases is considered. The effects produced in this series of patients were even more rapid than those recorded by Rosenheim,⁴ who quotes ten to twenty-one days as being the usual time to elapse before sterilization of the urine is complete. It is true that four of the cases relapsed, two almost immediately after treatment was discontinued, one within a month, and one within three months. In Cases 11, 13, and 16, however, the relapse was successfully treated with mandelic acid, the urine again becoming sterile within a few days. In Case 15 it was not possible to treat the relapse, the patient having left the district. Since no patient has been under observation for longer than five months it is probably too early to regard the successful results as complete cures. In view of the relapses it would seem wiser not to discontinue the treatment immediately the urine has become sterile, and possibly to give further courses to prevent recurrence.

The treatment failed in Case 7. As has been said, it was found impossible to render this patient's urine even mildly acid, and the failure can probably be ascribed to this fact, since mandelic acid is only effective in a strongly acid urine. It was also completely ineffective, after twelve days' trial, in Case 5. This patient suffered from dyspepsia, and nausea and vomiting resulted from the treatment. He also complained of increased dysuria. These symptoms necessitated the abandonment of the treatment. Case 3 had to leave hospital owing to domestic difficulties after she had taken mandelic acid for only eight days. Though the infection was greatly improved, complete sterilization of the urine had not been obtained by this time. In spite of this her symptoms of frequency

and dysuria had completely disappeared for the first time for five years, and she felt very much better. On her last day in hospital she passed urine only four times in twenty-four hours. Previous to treatment the average daily frequency, even while at rest in hospital, had been twelve.

A striking feature of the treatment, indeed, was its effect in diminishing the frequency of micturition and the dysuria from which the majority of the patients suffered. The amelioration of symptoms was usually manifest in the first few days of treatment, before the urine had become sterile. This effect was not observed in Case 5, where the dysuria actually increased, nor in Cases 9 and 10, who suffered from tuberculous ulceration of the bladder, and whose symptoms remained very much the same in spite of the disappearance of the secondary infection. In these two latter cases, however, it was surprising that no increased dysuria resulted from the highly acid urine.

With the exception of Case 5, already referred to, and Case 7, where massive doses of ammonium and calcium chloride caused an acidosis, only trivial side effects were observed. Four of the cases, while being treated, complained of very slight giddiness, lightness in the head, and buzzing in the ears. A slightly increased albumin excretion and a few granular casts made their appearance during the period of acid therapy in two of the cases, and a definitely increased haematuria occurred in both cases of tuberculous ulceration of the bladder, one of whom also complained of mild indigestion. These effects, which are similar to those noted by Rosenheim,⁴ all rapidly subsided on withdrawal of the drugs.

The nauseating effects of ammonium chloride are well known, and it is not surprising that even in doses of 60 to 120 grains a day it should sometimes produce mild digestive disturbances, especially in those already dyspeptic. We^{5, 6} have already drawn attention to the deleterious effects of acids and acid ash diets on the kidney function of patients suffering from chronic interstitial nephritis. It would appear wise, therefore, not to persevere with this treatment for a long period of time, especially in patients suffering from renal impairment, or in those in whom albumin and casts make their appearance while under treatment.

The CO₂-combining power of the blood was noted before and after treatment in a number of cases in this series, but apart from Case 7, where it fell from 63 to 46 volumes per cent., no very significant changes occurred, a mild reduction of the alkali reserve, within the limits of normal, being all that took place.

Conclusion

The treatment of severe chronic urinary infections has hitherto been notoriously unsuccessful in spite of the large number of antiseptics available. The very multiplicity of such preparations on the market, indeed, speaks for their inefficacy. Our results would seem to suggest that in mandelic acid a really efficient urinary antiseptic has been found, confirming the original claims made for the drug by Rosenheim. If this is so, this simple and practical treatment forms a really important therapeutic advance in the attack on a very common and disabling condition.

REFERENCES

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- 6 *Idem*: *Lancet*, 1931, ii, 1009.