THERAPEUTIC EFFECT OF ANTIBACTERIAL AGENTS IN URTICARIA

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Summary

Treatment of 64 patients having urticaria of unknown aetiology, with antibacterial drugs for 1 to 2 weeks brought relief in 27. Out of the remaining 37 patients, 6 obtained relief on receiving a second different antibacterial drug. In a control group of 18 patients having urticaria of known aetiology, none obtained any relief with antibacterial agents. A double blind comparison between tetracycline and a placebo in another group of 18 patients having urticaria of unknown aetiology showed tetracycline to be superior. It seems worth-while trying a course of antibacterial agents in patients having urticaria of unknown aetiology.

In a significant proportion of patients having urticaria, a detailed history does not provide any clue to the aetiological agent. Most of these patients suffer for long periods with several daily attacks which do not correlate with meals, environment, emotional stimuli, physical exertion, or physical agents such as sunlight, heat, cold, friction or pressure. The possibility of drug intake can also be excluded with reasonable certainty. These patients are usually lumped together as the unclassified group and constitute nearly 60 per cent of the urticaria patients seen by us.[1]

Hypersensitivity to bacteria as a cause of urticaria has been mentioned in the literature[2] but the matter is quite controversial[3,4]. Most patients have no obvious septic focus; and even if a tooth or the tonsil is discovered to be septic, eradication of the infection does not necessarily lead to disappearance of urticaria. Since bacterial foci can be located at many sites in the body such as teeth, tonsils, kidneys, gall bladder, intestines or paranasal sinuses, it is often impossible to locate the bacterial focus, particularly when it is not producing any clinical signs or symptoms. However, such a focus may still discharge the bacterial antigen into the circulation and lead to allergic symptoms. If such a patient was treated with an antibacterial agent, it is likely to act on the bacterial focus wherever it is, provided that the bacteria are susceptible to the drug. Improvement in such a case would indirectly suggest that the allergic symptoms in such a case depended on the bacterial focus. The present therapeutic trial was undertaken to evaluate this hypothesis.

Materials and Methods

Every patient having urticaria was thoroughly interviewed to enlist the circumstances noticed to precipitate the attacks. Patients in whom the attacks were occurring all round the day or at irregular intervals were asked to take only sugar, salt and water (complete diet elimination) for 2 days to see if

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some food item was responsible. If there was no improvement, the patient was asked to breathe through a cloth mask, made of a double layer of handkerchief, for the next 2 days to exclude inhalants as a cause. Concurrently, 3 consecutive stool specimens were also examined by the formol-ether concentration method[5]. When parasite(s) were found, the patient was given appropriate treatment and eradication of the parasite(s) was confirmed by repeating examination of 3 more specimens of stools[6]. If no improvement followed any of the above procedures, the patient was given an antibacterial agent in its usual therapeutic dose for 7 days. A patient was considered to have improved if the number of daily attacks and their severity were reduced by at least half compared to that before the treatment. If the patient improved during this period the same treatment was continued for another 7 days, but in case there was no improvement, the patient was given 7-day course of a different antibacterial agent to cover the possibility that the bacteria may not be susceptible to the first antibacterial agent used.

During these procedures, the patients were not allowed to take antihistamines. Thus, the patients were not on any drugs for at least 4 days before starting the antibacterial treatment.

Controls

To confirm that the antibacterial agents are not having a merely psychotherapeutic role in controlling urticaria, two types of controls were also included in this study.

Control Group 1 : Effect of antibacterial agents was assessed in 18 patients with urticaria of known aetiology (cold, 10 ; cholinergic, 3 ; dermographism, 2 ; inhalants, 2 and pressure, 1). These patients were given 500 mg tetracycline twice a day for 7 days.

Control Group 2 : A double blind comparison was made between a placebo and tetracycline in 18 urticaria cases of the unclassified group in whom the known causes of urticaria had been excluded by history and investigations as outlined earlier. Some patients received a combination of tetracycline 500 mg and ascorbic acid 500 mg twice a day orally for 7 days, while others were treated with placebo capsules containing glucose, in a comparable manner. If a patient improved, the same treatment was continued for the second week; otherwise the patient was given another known antibacterial agent.

Results

Out of 64 patients included in the first part of this study, 3 patients were in

TABLE 1

Response to antibacterial agents in patients having urticaria due to an unknown cause.

Antibacterial agent	Dose	Number of patients		
		Improved	No relief	Total
Tetracycline	500 mg B.D.	21	28 (3)*	49
Sulphamethoxazole-trimethoprim	800 mg + 160 mg B.D.	5	3 (1)	8
Sulphaphenazole	500 mg B.D.	0	2	2
Ampicillin	500 gm B.D.	0	2 (1)	2
Sulphadiazine	1.0 gm TDS	0	1	1
Erythromycin	500 mg B.D.	1	0	1
Streptomycin (oral)	1.0 gm O.D.	0	1 (1)	1
Total		27	37 (6)	64

* Figures in parenthesis indicate the number of cases who improved following treatment with a second antibacterial agent given during the second week.

the first decade, 12 patients in the second decade, 26 patients in the third, 14 patients in the fourth, 5 patients in the fifth and 4 patients in the sixth decades of life. The duration of urticaria was less than 1 month in 2 cases, 1 to 3 months in 10 cases, 3 to 6 months in 10 cases, 6 to 12 months in 10 cases, 1 to 3 years in 15 cases and more than 3 years in 17 cases. Following treatment with an antibacterial agent, 27 patients showed improvement, while 37 patients were not relieved. However, 6 patients in the latter group improved on using a second antibacterial agent during the second week (Table 1). Continuation of antibacterial therapy during the next week maintained the improvement in most of these cases. Ten cases were relieved completely while others had 50–90% relief.

In control group 1, none of the patients having urticaria due to known causes showed any improvement following treatment with antibacterial agents.

In control group 2, nine patients received tetracycline–ascorbic acid for the first week, of which 6 patients improved by more than 50 per cent. Of the 6 patients who improved, the tetracycline–ascorbic acid combination was continued for the second week in 4 patients and 3 of these improved further, while the fourth patient did not show any further improvement, though he did not get worse either. Of the 3 patients who had no relief following tetracycline –ascorbic acid during the first week, one patient was changed over to sulphamethoxazole – trimethoprim during the second week with which he showed complete relief.

Of 9 patients on placebo during the first week, only 2 patients showed relief, but continued placebo therapy during the second week caused worsening of the disease in both of them. Of the remaining 7 cases who showed no relief from placebo during the first week, tetracycline–ascorbic acid was given to 6 patients during the second week, and it showed relief in one case which was maintained during the next week of treatment with tetracycline-ascorbic acid as well (Table 2).

TABLE 2

Double blind comparison between tetracycline-ascorbic acid and a placebo (glucose) in patients having urticaria due to an unknown cause.

Antibacterial agent	Number of cases		
	Improved	No relief	Total
Tetracycline-ascorbic acid	6	3 (1)*	9
Placebo	2**	7 (1)*	9

* Figures in parenthesis indicate the number of cases who responded to another antibacterial agent during the second week.

** Both these patients worsened during the second week of treatment with placebo.

Discussion

Relief of urticaria following treatment with antibacterial agents in a significant proportion of cases of the unclassified group suggests that the urticaria in these patients was dependant upon some bacterial focus in the body. The possibility of a psychotherapeutic effect of the medicine was ruled out by the almost total lack of response in cases of urticaria due to known aetiology or when comparison was made with the placebo in a double blind manner. The bacterial aetiology of urticaria in these cases is further supported by the observation that the therapeutic effect was not limited to just one antibacterial agent but several of them produced similar effects and in some cases there was indication of resistance to one antibacterial agent and susceptibility to another. The relief obtained with antibacterial therapy was complete in some cases, while in others, the disease had become insignificant. This relief was maintained for variable periods following which there was recurrence of symptoms in some cases. This is con-

sistent with the fact that the bacterial focus can form again. Some of the cases who reported with recurrence of symptoms were again treated with antibacterial agents resulting in relief of the symptoms.

With these findings it seems worthwhile to try treatment with antibacterial agents in every case of urticaria where a detailed history does not point out any cause and tests like complete diet elimination and the mask test are also negative. Nearly 50% of such cases are likely to be relieved and this relief is more long lasting compared to that obtained with antihistamines. Such a therapeutic trial is far economical and easier than the elaborate laboratory tests required to locate the bacterial focus.

Acknowledgements

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LETTER TO THE EDITOR

Madame,

'Insect Bite Allergy'

I have been observing a change in the behaviour pattern of insect bite allergy since six years. Prior to this period the reaction was dominantly seen in infants beyond 4 months of age, but is now apparent in younger infants. A history of small pox vaccination few weeks prior to onset of the first attack was noticed in many patients. As B. C. G. and small pox vaccination are now carried out in neonates, this seems to be the reason for the shift in the age group involved. Many children start suffering from papular urticaria immediately after attacks of chicken pox or measles. It seems vaccination and infectious diseases result in production of antibodies which are specific as well as nonspecific, and the latter act as triggers for setting off attacks of papular urticaria.

I shall be grateful for information on the above associations.

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