Discussion

The present study was designed to compare ketoprofen 150 mg daily with ibuprofen 1,200 mg daily in the treatment of rheumatoid arthritis.

Cromie (1963) pointed out that gross alterations in formulations of trial drugs could possibly alter bioavailability, and theoretically the change in presentation of ibuprofen in the present study might have affected its bioavailability and reduced its effectiveness. However, the manufacturers (Boots) thought that the 200 mg capsules of ibuprofen used in this study were suitable for clinical trial purposes.

The results suggest that ketoprofen has analgesic and anti-inflammatory activity superior to ibuprofen. It is noted particularly that statistically significant differences in activity, favouring ketoprofen, were obtained even with the comparatively small number of patients used in this study. These results are consistent with those of Owen-Smith and Burry (1972) and Gyory *et al.* (1972), who showed, respectively, indomethacin 75 mg to have greater activity than ibuprofen 1,200 mg, and ketoprofen 100 mg to have comparable activity with indomethacin 100 mg.

Cardoe (1969) and Goldberg *et al.* (1971) reported an overall reduction in E.S.R. in patients with rheumatoid arthritis treated with ibuprofen. The reduction in E.S.R. in the present study favoured ibuprofen ($P < 0.05$), despite the reverse finding for joint circumference.

A factor influencing the therapeutic efficacy of drugs, both in clinical trials and in other clinical situations, is drug interaction. Ketoprofen has been shown to have no effect on hepatic drug-metabolizing enzymes, based on a study of plasma-clearance of antipyrine (Cathcart *et al.*, 1973), and is unlikely therefore to interact with drugs metabolized by the liver.

An important consideration in assessing the value of a new drug for treatment of rheumatoid arthritis is incidence of adverse reactions. A drawback to the use of indomethacin, a powerful analgesic and anti-inflammatory agent, is a relatively high incidence of side effects. Ibuprofen has been found to be better tolerated, but its therapeutic efficacy has been questioned (Hart, 1972; Owen-Smith and Burry, 1972). Previous long-term studies of ketoprofen 150 mg daily have shown that this dose is well tolerated by patients, and is not associated with serious adverse reactions or with significant changes in biological values monitored at monthly intervals for up to 12 months (G. Gomez, personal communication, 1973). These findings are consistent with the present results in which side effects of ketoprofen and ibuprofen were found to be comparable and not serious.

In conclusion, the present study has shown that analgesic and anti-inflammatory activity of ketoprofen is significantly superior to that of ibuprofen, while adverse reactions of the two drugs are comparable and not serious. This is further evidence that ketoprofen may be a useful drug in the clinical management of rheumatoid arthritis.

Requests for reprints should be sent to Dr. F. E. Bruckner.

Ketoprofen will be available in the United Kingdom from next month.

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Tetracycline-resistant Beta-haemolytic Streptococci in South-west Essex: Decline and Fall

M. H. ROBERTSON

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Summary

The prevalence of tetracycline-resistant beta-haemolytic streptococci in South-west Essex has been recorded over the past 10 years. It has fallen from a peak of 35% in 1965 to a level of 9·2% in 1972. Ear infections no longer provide the highest incidence of these organisms; vaginal, perineal, and skin infections now seem to be of greater relative importance but throat swabs still provide the greatest actual number of isolations. Erythromycin-resistant strains are still rare.

St. Margaret's Hospital, Epping, Essex
M. H. ROBERTSON, M.B., M.R.C.PATH., Consultant Bacteriologist

Introduction

Tetracycline-resistant beta-haemolytic streptococci have often been recorded since 1960 and their incidence in South-west Essex has been monitored since 1963 (Robertson, 1965, 1968). The incidence rose to a peak of 35% in 1965, remained at 33·5% in 1966, and fell slightly to 27% in 1967, when it was speculated that the figures might have begun to decline.

Recent reports indicate that the incidence of tetracycline-resistant beta-haemolytic streptococci is indeed falling. A survey of these organisms causing ear, nose, and throat infections in London shows their incidence declining from 42% in 1967 to 27% in early 1971 (Rees, 1971). A level of 6% is recorded in Sweden (Kahlmeter and Kamme, 1972), though no previous figures for Scandinavia were found by these authors.

We present the figures for South-West Essex from 1968 to 1972. The methods of isolation and sensitivity testing were as previously used—that is, organisms were grown on blood agar base No. 2 (Oxoid) or sensitivity test agar (Oxoid) both containing 7% added horse blood. Antibiotic discs containing 10 μg of tetracycline, 10 μg of erythromycin, and 1·5 units of penicillin were applied, and the organism was regarded as resistant if it grew right to the edge of the disc on overnight incubation.

TABLE I—*Sources of Isolation of Beta-haemolytic Streptococci and No. of Tetracycline-resistant (T.R.) Strains 1963-7*

	Tetracycline-resistant Streptococci														
	1963			1964			1965			1966			1967		
	Total	T.R.		Total	T.R.		Total	T.R.		Total	T.R.		Total	T.R.	
		No.	%		No.	%		No.	%		No.	%		No.	%
Throat	159	39	24·5	176	55	31	252	89	35	258	78	30	235	57	24
Sputum	78	15	19	77	10	13	44	12	27	59	12	20	74	19	26
Ear	21	14	—	27	20	—	38	18	—	29	19	—	35	14	—
Nose and sinuses	7	4	—	12	5	—	18	8	—	11	6	—	10	5	—
Wounds and skin infections	36	17	—	63	27	43	59	26	44	57	27	47	89	27	30
Perineum	5	—	—	8	6	—	2	1	—	5	3	—	7	2	—
Vulva	19	3	—	27	9	—	60	16	27	57	17	30	56	16	28
Miscellaneous	9	2	—	5	2	—	21	5	—	22	5	—	22	5	—
Total	334	94	28	395	134	34	494	175	35	498	167	33·5	528	145	27

TABLE II—*Sources of Isolation of Beta-haemolytic Streptococci and No. of Tetracycline-resistant (T.R.) Strains 1968-72*

	Tetracycline-resistant Streptococci														
	1968			1969			1970			1971			1972		
	Total	T.R.		Total	T.R.		Total	T.R.		Total	T.R.		Total	T.R.	
		No.	%		No.	%		No.	%		No.	%		No.	%
Throat	335	58	17	364	59	16	460	73	16	339	16	5	444	25	6
Sputum	105	22	21	149	38	25·5	97	29	30	65	7	11	99	6	6
Ear	18	6	—	28	9	—	18	1	—	18	3	—	27	3	—
Nose and sinuses	14	1	—	53	10	19	73	13	18	13	1	—	7	1	—
Wounds and skin infections	95	36	38	99	20	20	100	24	24	110	7	6	119	23	19
Perineum	4	nil	—	6	4	—	8	3	—	16	2	—	22	2	—
Vulva	72	19	26	75	25	33	62	20	32	73	17	23	80	14	17·5
Miscellaneous	22	3	—	13	7	—	18	2	—	16	2	—	27	2	—
Total	665	145	22	787	172	22	836	165	20	650	55	8·5	825	76	9

Lancefield grouping was carried out by the acid extraction method (Cruickshank, 1969).

Results

The results are shown in table II for the five years 1968 to 1972 and in table I, already published, for the five years 1963 to 1967. Percentages (rounded to the nearest whole number) are recorded where the number of isolations exceeds 50. The frequency of tetracycline-resistant strains declined over 1966 to 1970 and then fell sharply in 1971 to a level of 8·5%, though this rose slightly to 9% in 1972. No penicillin-resistant strains were found, apart from two Lancefield group D strains which produced reduced zones and were not fully sensitive but did not grow on MacConkey medium. Nine similar strains were encountered in 1965-7. Erythromycin-resistant strains continue to be rare, only four being seen in the second five years of the survey. These came from a leg ulcer in a geriatric patient, a vaginal swab and a throat swab in hospital patients, and an ear swab from general practice. Two of these were also resistant to clindamycin (2 μg disc) and one to lincomycin (2 μg disc) before clindamycin was routinely tested in this laboratory. Four other strains were reported in the earlier part of this survey, making eight in 10 years from a total of 6,012 isolations. In addition, three others regarded as partially sensitive were seen in the period 1965-7. Lancefield grouping of 44 strains from the last five years show 48% to belong to group A, 11% to group B, 2% to C, 4·5% to D, 14% to G, and 20% to none of these groups. These figures again show a slight fall in the proportion of group A strains but the numbers tested are too small to be of significance.

Discussion

The final two years of this survey, 1971 and 1972, show a much lower incidence of tetracycline-resistant beta-haemolytic streptococci than the previous eight years. The incidence for the first five-year period 1963-7 was 31·8%, and for the second five years 1968-72 16·2%. The period 1971-2 shows an incidence of only 8·8%.

Ear infections, which previously carried the highest percentage of tetracycline-resistant streptococci in this area (70% in 1963-4), no longer yield the highest proportion of these organisms. The figures for 1971-2 being only 13·3%—equal to that shown by wound infections and below the level of 20% found for vaginal swabs, which now have the highest rate.

Though throat swabs at 5·2% yield a low percentage of these organisms they are still the site of the greatest number of isolations followed by vaginal swabs and wound and skin infections. The vulva, perineum, and skin infections seem to have become major sources of these streptococci.

The material for the last two years when broken down into the sources of referral of the specimens—general practice (499 specimens), inpatients (573), outpatients (333), and nurses (70)—shows pronounced falls from the figures for all these groups in 1965-7—that is, general practice 7·6% (35·3%), inpatients 7·85% (33·5%), outpatients 13·2% (29%), and nurses 5·7% (16%) (earlier figures are shown in parentheses). It is to be hoped that this decline of the tetracycline-resistant streptococcus is due to greater selectivity in the prescribing of tetracycline, and that this situation will be maintained. Penicillin remains the drug of choice for beta-haemolytic streptococcal infections, with erythromycin and clindamycin as alternatives for patients allergic to penicillin.

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