Conference proceedings

The place of antimalarials in rheumatology*

A conference held in London in November 1980 under the chairmanship of Dr G. R. V. Hughes brought together ophthalmologists and rheumatologists to discuss the present role of antimalarials in rheumatic diseases, as well as to review the optimal ophthalmological screening required in patients taking long-term therapy.

The meeting was prompted by the resurgence of interest in the use of antimalarials, in particular low-dose hydroxychloroquine in systemic lupus, and discussed guidelines for optimal ophthalmological screening, especially in the context of overburdened National Health Service facilities.

The principal speakers were 2 rheumatologists, Dr R. Rynes (Albany, New York State) and Dr J. S. Marks (Manchester), both of whom had contributed to studies on the subject and 2 ophthalmologists, Dr T. Barrie (Western Infirmary, Glasgow) and Mr P. Leaver (Hammersmith Hospital).

Safety of chloroquine

Retinal toxicity has until recently been regarded as a major hazard restricting the use of antimalarials. It followed early administration of the drugs in large doses for long periods without ocular screening. Dr Rynes and 5 colleagues studied the ocular safety of hydroxychloroquine in a daily dose of 400 mg in 99 patients who had taken a median dose of 365 g. His results emphasised the safety of hydroxychloroquine in this dose, as no significant loss of vision was recorded, and minor ocular toxicity was found in 3 patients, only 1 of whom had to stop the drug permanently. He presented further data, collected after the publication of this study, covering these patients for a median 5-year period, and no instances of significant vision loss were recorded.

Dr Marks's study reached similar conclusions about the safety of chloroquine phosphate. He found only 1 patient with loss of vision as a result of the drug in 222 patients on long-term chloroquine therapy. Differences emerged between these 2 studies on the issue of whether retinal toxicity is related to dose. Dr Rynes's findings are in disagreement with those of Dr Marks, who supports the orthodox view of toxicity being dose-related. Dr Marks pointed out that although a few patients have developed mild retinopathy on low doses, the great majority of patients reported in the literature with vision loss and bull's eye pigmentation of the retina had been on high doses of antimalarials. Thus, the crucial issue of whether the retinal toxicity depends on total or daily dose remains unresolved despite the increasing evidence that low daily dosage is safer.

Dr Marks asserted that, if a critical threshold daily dose could be established below which retinal accumulation of the drug did not occur, then the necessity for screening would fall away. Alternatively if toxicity is determined by total dose, then screening should be directed primarily towards those individuals who had consumed the highest total dose. A large study from Sweden suggests that it is only in the older patients that toxicity is dose-related and corroborates Dr Marks's findings that the risks of toxicity increase with age.

Visual testing

In the context of the limited ophthalmological services in the National Health Service discussion centred on the minimum effective ocular screening programme for patients on antimalarials. No single screening test for retinal toxicity is adequate, because there is no uniform sequence in which abnormalities in visual acuity, visual fields, colour vision, or fundal appearance occur. The commonest presenting feature of retinal toxicity is pigmentary stippling of the macula, usually without concomitant loss of visual function. These macular changes do not always reflect retinal toxicity. They are difficult to distinguish from normal senile macular atrophy occurring in 30% of the population over 65. From his study Dr Rynes concluded that ophthalmological screening should comprise visual acuity testing, funduscopic examination, and tangent visual field testing with red and white objects. Dr Barrie, however, believes that further assessment of visual function is necessary, particularly testing of colour vision.

The Glasgow study reports several cases in which abnormal colour discrimination, as assessed by the Farnsworth Munsell 100 hue test, and visual

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field defects presented well before the presence of any change in the appearance of the macula. Indeed visual function may rarely continue to deteriorate even after stopping the antimalarial; this further emphasises the need for identifying antimalarial toxicity at a very early stage. In order to identify the most appropriate screening procedure the Glasgow group are submitting all patients on antimalarials to baseline and 3-monthly assessment of visual acuities, detailed visual fields, and colour vision, and funduscopy with dilated pupils. It is hoped as a result of this study to identify the most appropriate screening procedure for chloroquine retinopathy.

Efficacy of antimalarials

Dr J. T. Scott (Charing Cross Hospital) directed the discussion towards the question of the efficacy of antimalarials and noted that in rheumatoid arthritis in particular the efficacy of these drugs had to be established in comparison with gold and penicillamine. Some centres routinely use antimalarials in preference to gold or penicillamine because of their greater safety, although only 1 controlled trial has been performed comparing their efficacy. In a group of 33 patients studied in Canada over a 6-month period gold, chloroquine, and azathioprine were found to be equally effective. In systemic lupus the impression that antimalarials are mainly useful for skin and joint manifestations is widespread but unproved. Dr G. R. V. Hughes suggested that their effects in SLE might well extend beyond these features. In discoid LE their role is undoubted, a 94% response rate to antimalarials having been reported.

The choice between the various antimalarials was discussed by Dr Marks. Although the majority of reports on retinopathy concern chloroquine phosphate, he felt that might have been due to the earlier use in high dosage. Chloroquine phosphate is still widely used (250 mg daily), although recent years have seen hydroxychloroquine (200 mg daily) being prescribed more frequently. The dose of hydroxychloroquine can be doubled or trebled during disease exacerbations, and if necessary mepacrine can be introduced. The use of mepacrine is limited by its tendency to cause yellow skin discoulouration: it is probably not retinoatopic.

Conclusions

The consensus of opinion was that antimalarials are effective and relatively safe drugs, probably safer than most alternative forms of 'second line' therapy in rheumatic disease. Although the present recommendations for 6-monthly full ophthalmological assessment of all patients on antimalarials are probably overcautionous, it was argued that the expense of this was still considerably less than monthly monitoring of patients on gold or penicillamine.

Because of the continuing interest in antimalarials, it was felt that in addition to the work in progress assessing the ophthalmological side effects, further controlled trials of the therapeutic effects of these drugs were warranted.

References


Note

Essential metals

An international symposium on the role of copper and other essential metals in inflammatory diseases will be held at the College of Pharmacy, University of Arkansas, during 10-13 August, 1981. Details from Professor John R. J. Sorenson, College of Pharmacy, UAMS, Slot 522, 4301 West Markham, Little Rock, AR 72205, USA.
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