PAPERS AND ORIGINALS

Treatment of optic neuritis by retrobulbar injection of triamcinolone

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Summary

In a single-blind controlled clinical trial patients with optic neuritis caused by demyelination were given a single retrobulbar injection of triamcinolone. Though the treated group showed a trend towards more rapid recovery of vision than the controls, there was no significant difference in visual acuity, colour vision, or visual fields during the first six months after treatment. We conclude that routine use of corticosteroids is not justified in unilateral optic neuritis when vision in the other eye is good. Shortening the period of visual disability in bilateral disease or unilateral disease when vision in the other eye is poor, however, may be justifiable.

Introduction

Opinion on the need to treat acute optic neuritis remains divided. Although more than three-quarters of patients make an excellent spontaneous recovery (to a visual acuity of 6/9 or better), some have a lasting visual deficit.[1 2] A safe treatment that would prevent such an outcome is therefore desirable.

In recent years the most widely used form of treatment has been with steroids. Two controlled trials of corticotrophin treatment have been carried out, but with conflicting results. Rawson *et al*[3 4] reported a shorter time to recovery with treatment but were unable to establish whether there was lasting benefit. They had 25 patients in both the treated and untreated groups. After a follow-up period of a year four patients in the untreated group and one in the treated group had severe persistent visual defects. The difference between the two groups was not significant but it was concluded that this was attributable to the small numbers, and the authors recommended that corticotrophin should be given to patients with optic neuritis. Bowden *et al*[5] reached the opposite conclusion after a controlled trial on 54 patients. In their series three patients had lasting visual impairment, but in contrast to the findings of Rawson *et al* these three patients were in the treated group.

In some respects neither trial was entirely satisfactory. In the first only near visual acuity was assessed, a non-standard type (Jaeger) being used and neither reading distance nor spectacle correction noted. Results of visual field examination and colour vision testing were not reported. In the second trial visual function was carefully documented but fewer than half of the patients entered the trial within the first two weeks of visual loss and were followed up for six months or more.

We describe the results of a controlled single-blind trial of treatment of optic neuritis with a single orbital injection of triamcinolone, which produces a high concentration of steroids within the optic nerve and eye.[6 7] Although the procedure has been recommended for treating acute optic neuritis,[8] this is the first controlled investigation to be reported.

Patients and methods

All patients aged 16-50 years presenting to the casualty department at Moorfields Eye Hospital were considered for the trial if they had (*a*) rapid onset of visual loss that was datable to within 24 hours and had shown no improvement and a history of less than 10 days' visual loss or pain; and (*b*) a best corrected visual acuity of worse than 6/9, recordable central visual field loss and defective colour vision in the affected eye, and a relative afferent pupillary defect. Patients were excluded if they had a retinal lesion or if there was evidence of a condition other than multiple sclerosis likely to cause an optic nerve lesion—for example, gross paranasal sinus disease, blood pressure over 180/110 mm Hg or hypertensive retinal vascular disease, diabetes, a history of amaurosis fugax, rheumatic valvular heart disease, a family history of optic nerve disease, heavy tobacco or alcohol consumption, dietary deficiency, vitamin B_{12} deficiency, regular use of drugs known to cause optic atrophy, hypercholesterolaemia, syphilis, or long-

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standing visual loss from other causes. Patients with a clinical picture suggestive of ischaemic optic neuropathy[9] were also excluded. We concluded that all patients admitted to the trial were likely to be suffering from acute demyelinating optic neuritis.

On admission to the trial the patients were grouped according to visual acuity (6/36 or worse, and better than 6/36), age (under 35, and 35 or over), and time of onset of symptoms before presentation (0-5 days, and 6-10 days). The purpose and implications of the study were explained, and each patient could enter the trial if he or she so wished. Those wishing to take part were allocated to a treatment or control group by means of randomised cards. Treatment consisted of a single injection of triamcinolone 40 mg (1 ml) into the orbit, every effort being made to ensure intraconal deposition.

Visual function was tested on entry to the trial, at weekly intervals for a month, and then at two, three, and six months after entry by one of us (ESG), who did not know to which group the patients belonged. The following four assessments were made. (1) Best corrected visual acuity at 6 m using Snellen's type. Each step on the chart was given a numerical value for statistical analysis. (2) Goldmann kinetic visual fields using IV/4, I/4, and I/1 white targets. Visual field loss was calculated as an error score by measuring the length of radial lines on the chart within the area of field loss and multiplying it by the product of the numerical designation of the target size and brightness. (3) Friedmann visual fields run initially at 0·2 log unit below the peripheral threshold. From these fields an error score was calculated by adding together the log unit deficit recorded for each target. (4) Colour vision using the Farnsworth Munsell 100-hue test under an illuminance "C" source. Errors were calculated. (Tests (3) and (4) were carried out only when visual acuity was 6/18 or better.) For statistical comparison of the two groups χ^2 tests were used.

Results

Out of 74 patients admitted to the trial (15 male, 59 female), eight were withdrawn within the first week because of failure to attend or because other manifestations of multiple sclerosis required inpatient treatment. Seven other patients were withdrawn during the first six months for the same reasons or owing to severe recurrent optic neuritis or because variations in visual function with exercise or temperature (Uthoff's symptom) precluded reliable measurement of acuity. Altogether 61 patients were followed up for one month (31 treated, 30 controls), 56 for three months (27 treated, 29 controls), and 54 for six months (26 treated, 28 controls).

VISUAL ACUITY

Table I shows that there was no significant difference in visual acuities between the treatment and control groups. A trend towards better visual acuity in the first month in the treated group was not significant ($P = 0·1$ at one week, and $0·2 > P > 0·1$ at two, three, and four weeks).

Out of 19 controls with a vision of 6/60 or worse initially, one regained 6/9 visual acuity during the first two weeks, two a vision of 6/18 at one week, and four a vision of 6/18 at two weeks. Out of 18 treated patients with such poor initial visual acuity, three regained 6/9 at one week and five 6/9 at two weeks, and seven 6/18 at one week and nine 6/18 at two weeks. The only significant difference was in recovery to 6/18 during the first week ($P = 0·05$). After one month there was no difference between the two groups in the numbers of patients regaining 6/9 vision.

Table II shows the numbers of patients in each group with visual acuities worse than 6/12 one to six months after onset.

Patients aged over 35 fared no worse than younger patients ($P = 0·4$).

TABLE II—*Patients with acuity worse than 6/12*

Interval after onset (months):	1	2	3	6
No of controls	10	4	1	1
No in treated group	5	3	2	1

Patients who entered the trial within the first five days of visual loss had worse acuity than those who entered later ($P < 0·001$); we suspect that profound visual loss caused more rapid referral to hospital. By one month those treated within the first five days fared no better than those treated later ($P = 0·3$). There was no relation between the severity of the presenting deficit and the persistence of visual impairment (acuity 6/9 or worse in either group), although, as expected, those with a severe lasting deficit had a low acuity when first seen.

GOLDMANN KINETIC FIELDS

There was no significant difference in Goldmann kinetic fields between the two groups at any time (table I).

FRIEDMANN VISUAL FIELDS AND 100-HUE TESTS

These tests were analysed one month after entry to the trial since only then could large numbers of patients be assessed by these techniques (table I). No significant difference was shown between the two groups.

The visual function of those patients who were withdrawn at any time was analysed separately and did not differ significantly from that of the remaining patients.

SIDE EFFECTS

There were no serious side effects of treatment. Local bruising occasionally occurred. Although a few patients reported some discomfort immediately after the injection, more commented that the existing pain in the affected eye was relieved within 24 hours.

Discussion

Our results show a trend towards more rapid recovery of vision in patients with acute demyelinating optic neuritis who are treated with retrobulbar depot corticosteroids. In particular, significantly more treated patients had a notable recovery of vision during the first week after the attack. By contrast, treatment conferred no long-term benefit, and there was no evidence that withholding treatment caused increased visual impairment in any patient. These findings accord with the results of the two previous trials of corticotrophin treatment.[1 2]

Should acute optic neuritis be treated routinely? If corticotrophin or corticosteroids are to be used to treat the disease, the marginally shortened recovery period must be the justification. In unilateral cases with good vision in the other eye (by far the most common clinical presentation) the return of visual acuity

TABLE I—*Visual outcome in treated and control patients (mean values)*

Interval after entry to trial	Visual acuity			Goldmann field			Friedmann field			100-hue		
	Controls	Treated	P	Controls	Treated	P	Controls	Treated	P	Controls	Treated	P
On entry	3/60	6/60	0·21	211	346	0·43						
1 week	6/60	6/24	0·10	120	118	0·95						
2 weeks	6/24	6/18	0·11	133	79	0·37						
3 weeks	6/18	6/12	0·17	88	56	0·13						
4 weeks	6/12	6/9	0·18	68	55	0·50	132	117	0·73	150	135	0·64
2 months	6/9	6/9	0·76	47	37	0·42	95	81	0·67	137	125	0·70
3 months	6/7·5	6/7·5	0·85	25	22	0·64	46	41	0·73	119	113	0·83
6 months	6/6	6/6	0·92	20	18	0·67	27	36	0·51	92	123	0·32

in two weeks instead of three or four does not justify the use of corticosteroids with their inherent risk of side effects. A shortening of the period of severe visual disability in bilateral cases (or in patients with unilateral optic neuritis and poor vision in the other eye), however, would be worth while. We now reserve treatment for this small group.

We are grateful to the physicians and surgeons of Moorfields Eye Hospital, City Road, for agreeing that all patients presenting to the casualty department with optic neuritis during the period of our study should be referred to our clinics. We also thank Mr H Donovan for statistical analysis of the results. A contribution from the Monnell Foundation towards the expenses of the investigation is much appreciated.

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Changing pattern of alcoholic liver disease in Great Britain: relation to sex and signs of autoimmunity

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Summary

A survey of 293 patients with alcoholic liver disease showed that women, particularly those aged under 45, had a significantly higher incidence of alcoholic hepatitis, with or without superimposed cirrhosis, than men. The long-term prognosis for both women who continued to drink and those who stopped drinking was worse than that for men. Autoantibodies were more common in women, which suggested that immune mechanisms may play a part in the pathogenesis and progression of alcoholic liver disease in women.

Introduction

The steady increase in alcohol consumption in Britain over the past 20 years, and particularly in the last decade, has been reflected by a rise in the number of offences associated with alcohol abuse.[1] There has been a parallel rise in the frequency of alcoholic cirrhosis. Thus a survey from Birmingham in 1959-64 attributed 33% of cases of cirrhosis to excessive drinking,[2] whereas the figure for 1964-9 was 51%.[3] In a recent survey in South London the proportion of alcoholics among cirrhotics had risen still further to 65%[4]; the increased incidence was particularly conspicuous among women. We reviewed the records of 293 patients who presented to a specialist referral unit for liver diseases in 1967-75. Possible changes in the pattern of alcoholic liver disease, as evidenced by clinical features and histological changes, as well as the male:female ratio, were analysed in relation to the mode of presentation and to prognosis.

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Since considerable interest has recently focused on the role of immune mechanisms in perpetuating alcoholic liver damage, we also investigated laboratory manifestations of autoimmunity.

Patients and methods

The 293 patients were admitted to the liver unit, King's College Hospital, in 1967-75 with a diagnosis of alcohol-related liver disease. Regular daily ingestion of at least 100 g ethanol could be substantiated, either on the patient's own account or by information from a relative or close friend.

The histological features of all patients were assessed by biopsy on referral and, in 45 patients, by a follow-up biopsy. The patients were classified according to the following seven histological diagnoses: (*a*) fatty infiltration alone; (*b*) fatty infiltration and portal fibrosis; (*c*) alcoholic hepatitis (with foci of lobular inflammation, spotty necrosis or hyaline inclusions, or both)[5]; (*d*) central sclerosing hyaline necrosis[6]—same pattern as in *c* with a centrilobular distribution and much tissue loss together with fibrous tissue deposition surrounding hepatic vein radicals; (*e*) cirrhosis; (*f*) cirrhosis and alcoholic hepatitis; (*g*) primary hepatocellular carcinoma, in all cases superimposed on cirrhosis.

Laboratory investigations included standard tests of liver function, measurement of serum immunoglobulin levels,[7] and tests for serum autoantibodies.[8] ^{99}Tc-scintiscanning of the liver and spleen was performed in most cases, and the splenic peak count rate was calculated as a measure of portosystemic shunting.[9]

Results

Sex ratio—There were 215 men and 78 women—a male:female ratio of 2·7:1. The mean age at presentation was similar in both sexes (men 51·7±10·2 years; women 51·9±11·1). One hundred and six patients presented in 1967-71 and the remaining 187 in 1972-5. Over the period of survey there was a significant increase in the proportion of women referred, particularly with cirrhosis or alcoholic hepatitis. Thus in 1967-71 the male:female ratio was 4·88:1 compared with a ratio of 2·11:1 in 1972-5 ($\chi^2=7·14$; $P<0·01$). Over this period the proportion of men aged under 55 who showed features of alcoholic hepatitis or cirrhosis also significantly increased (34/54 in 1967-71 and 64/76 in 1972-5; $\chi^2=6·57$; $P<0·025$).

Reasons for referral—Forty-four (15%) patients were asymptomatic and had been referred for investigation of suspected liver disease after abnormal liver function values or hepatomegaly had been