Ocular side-effects of Ibuprofen

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Ibuprofen (2-4'-isobutylphenylpropionic acid) is an anti-inflammatory, analgesic, and antipyretic agent which is now frequently used in the treatment of rheumatoid and osteoarthritis. The drug is remarkably free of side-effects and no serious toxicity has been demonstrated in extensive clinical trials, apart from one case of gastrointestinal bleeding (Dick-Smith, 1969). Minor toxic effects which have been reported are listed in Table I (Boardman, Nuki, and Hart, 1967; Jasani, Downie, Samuels, and Buchanan, 1968; Thompson, Fox, and Newell, 1968; Chalmers, 1969; Dick-Smith, 1969).

Table I *Minor side-effects of Ibuprofen*

Gastrointestinal tract	Anorexia; nausea and vomiting; dyspepsia; upper abdominal pain; constipation
Skin	Irritation; rash
Central nervous system	Headache; giddiness; tinnitus; deafness
Miscellaneous	Tiredness; malaise; heavy perspiration; nocturnal frequency of micturition

No ocular side effects have been described in the literature. Recently two patients, whose case histories are reported below, presented at the Eye Clinic with visual disturbances related to Ibuprofen therapy, and as a result of this we examined a series of patients who were taking Ibuprofen, to assess the effects of the drug on ocular function. Our findings are reported.

Case reports

Case 1, a woman aged 71, was seen at the Eye Clinic in February, 1970, complaining of deteriorating vision, particularly in the right eye, over a period of 2 months. She had suffered from rheumatoid arthritis for 31 years and had been treated with an assortment of drugs including Plaquenil, which was stopped in November, 1968. When her vision started to deteriorate her treatment was prednisolone 5 mg. daily, a dose which had remained unaltered for 9 months, and Ibuprofen 0.4 g. daily, which she had been taking for 8 months. She had received a total of 90 g. Ibuprofen at the time of presentation.

Examination

The corrected visual acuity of the right eye was 6/18 and of the left 6/9. The media were clear and the fundi normal. A visual field examination, performed on the Goldmann perimeter, revealed a centrocaecal scotoma in the right eye (Fig. 1) and an enlargement of the blind spot in the left (Fig. 2).

FIG. 1 Visual field of right eye in Case 1

FIG. 2 Visual field of left eye in Case 1

Treatment

Ibuprofen was thought to be the cause of the reduced visual acuity and visual field defects, and was therefore withdrawn. The patient reported an immediate improvement in her vision and one month, later although she still complained of some residual dimness of vision, the visual acuity had improved to 6/9 in the right eye and 6/6 in the left.

Result

This improvement was maintained, and when the visual fields were examined in August, 1970, the defects had disappeared and the fields were full. The vision then was 6/6 in both eyes unaided.

Case 2, a 67-year-old woman, was seen at the Eye Clinic in June, 1970, because of the sudden appearance of "a moving mosaic of coloured lights in front of both eyes". Her medication at that time was digoxin 0.25 mg. twice daily, Lasix 80 mg. three times a day, Etophylate 500 mg. three times a day, Aldactone A 25 mg. daily, Tofranil 25 mg. three times a day, and Eltroxin 0.1 mg. three times a day. None of these drugs had been increased in dosage or added to her treatment within the previous 3½ weeks, but 7 days before her visit to the Eye Clinic she had started on Ibuprofen 200 mg. three times a day for arthritis of the sacroiliac joints and within 2 days the coloured mosaic appeared and gradually increased in intensity.

Ocular examination

No abnormality was found and, as it was thought that the symptoms could be due to Ibuprofen, this drug was withdrawn. There was an immediate decrease in the intensity of the symptoms and the vision had returned to normal in 11 days.

Investigation of patients on Ibuprofen

38 patients receiving Ibuprofen were examined. The visual acuity, fundus, and visual fields, including macular sensitivity, were assessed. The findings are summarized in Table II (overleaf).

Discussion

The first patient, who was on treatment with Ibuprofen, presented with reduced visual acuity in both eyes, an early centrocaecal field defect on the right side and an enlarged blind spot on the left. On withdrawal of the drug the visual acuity returned to normal and the visual field defects disappeared. This is the typical presentation of a toxic amblyopia. Harrington (1964) has listed a number of agents which can cause a central

Table II *Summary of investigations of 38 patients on Ibuprofen*

Case no.	Diagnosis	Duration of Treatment (mths)	Sex	Age (yrs)	Dose (g./day)		Other drugs
					Current	Total	
3	RA	3	F	46	0.6	50G	Indocid; predisone
4	RA	12	F	54	1.2	353	Tofranil; Mandrax
5	RA	1	F	74	Nil	13	Distalgesic
6	RA	18	F	62	0.6	303	Plaquenil; Indocid
7	RA	12	F	43	0.8	202	Nil
8	RA	12	M	61	0.6	202	Gold; disprin
9	RA	6	F	48	0.8	168	Plaquenil
10	RA	20	F	49	0.6	360	Predisalone; Indocid
11	RA	18	M	49	0.6	324	Plaquenil
12	RA	7	F	58	Nil	118	Nil
13	RA	24	F	57	0.8	470	Nil
14	RA	2	F	65	1.2	67	Digoxin; predisalone
15	RA	5	F	64	0.6	83	Gold
16	RA	3	F	63	1.2	101	Predisone; gold; aspirin
17	RA	1 wk	M	68	0.6	3	Predisolone
18	RA	6	M	43	1.0	146	Mandrax
19	RA	5	F	60	0.8	157	Aspirin
20	RA	16	F	72	Nil	358	Nil
21	RA	4	M	65	0.6	67	Digoxin; Aldactone
22	RA	9	M	61	1.0	237	Valium; Avomine
23	RA	6	F	40	1.2	202	Plaquenil
24	RA	6	M	64	0.6	101	Plaquenil
25	RA	4	F	48	1.2	136	Plaquenil; gold
26	RA	4	F	58	1.2	135	Aspirin; Betamethasone
27	RA	4	F	42	1.2	125	Plaquenil; Phenylbutazone
28	RA	12	F	49	0.6	230	Aspirin; Nucil
29	RA	2	M	58	0.8	45	Nil
30	RA	7½	F	13	0.4	84	Nil
31	RA	9	F	16	0.2	22	Plaquenil
32	RA	4	F	58	0.8	111	Nil
33	RA	6	M	59	0.4	67	Nil
34	RA	1	F	59	0.6	17	Nil
35	RA	5	F	38	0.8	111	Decadron
36	RA	10 days	F	73	0.6	6	Nil
37	OA	21	F	69	0.6	353	Plaquenil
38	PA	6	M	21	0.6	110	Librium
39	PA	8	F	35	1.2	184	Indocid; aspirin
40	SC	6	M	60	0.6	83	Nil

RA : Rheumatoid arthritis   OA : Osteoarthritis   PA : Psoriatic arthropathy   SC : Supraspinalis cordis

Type of visual disturbance	Corrected visual acuity		Fundi	Visual fields	Remarks
	Left	Right			
Fall in left visual acuity 3 wks Ibuprofen	6/4	6/4	N	N	See Discussion
	6/4	6/6	N	N	
	6/18	6/60	Bilateral circinate retinopathy R > L	Right normal Left central scotoma	
	6/6	6/6	N	N	
	6/6	6/6	N	N	
	6/6	6/5	Peripheral retinal degeneration	N	
	6/5	6/6	N	N	
	6/6	6/5	N	N	
	6/4	6/4	N	Reduced central retinal sensitivity	
	6/6	6/6	N	N	
General fall in vision after 5 days Ibuprofen	6/6	6/6	N	N	See Discussion
	6/18	6/18	Bilateral macular pigment changes	Bilateral centrocaecal scotoma	
	6/9	6/6	N	N	
	6/9	6/5	N	N	
	6/6	6/4	N	N	
	6/6	6/6	N	N	
	6/9	6/9	N	N	
	6/18	6/6	N	Reduced sensitivity	
	6/4	6/6	N	N	
	6/5	6/5	N	N	
	6/6	6/6	N	N	
	6/6	6/4	N	N	
	6/5	6/4	N	N	
	6/6	6/6	N	N	
	6/4	6/4	N	N	
	6/5	6/5	N	N	
	6/5	6/5	N	N	
	6/4	6/4	N	N	
	6/4	6/4	N	N	
	6/5	6/12	N	N	
Reduced vision after 5 days Ibuprofen	6/4	6/9	N	N	Old left iritis
	6/5	6/6	N	N	
	6/4	6/4	N	N	
	6/6	6/6	N	N	
	6/6	6/6	N	N	
	6/4	6/4	N	N	
	6/9	6/9	N	N	
Reduced vision after 5 days Ibuprofen	6/6	6/6	N	N	See Discussion
	6/4	6/4	N	N	
	6/4	6/4	N	N	
	6/9	6/9	N	N	

or centrocaecal scotoma, including tobacco, ethyl alcohol, methyl alcohol, lead, carbon disulphide, iodoform, thallium, digitalis, chloramphenicol, plasmocid, streptomycin, sulphonamides, and isoniazid. The exact site of the toxic action is unknown in most cases and may be situated in the retina, the optic nerve, or even further back in the post-chiasmal section of the visual pathway. Usually the amblyopia induced by the agent is reversible on withdrawal of the drug but permanent visual loss may occasionally result.

The second patient, who was seeing a mosaic of lights, was receiving a variety of drugs at the time of onset of her symptoms, including digoxin, which can cause visual hallucinations, scintillations, and xanthopsia. The onset and regression of symptoms, however, were so closely related to the commencement and withdrawal of Ibuprofen that we have little doubt that this drug was responsible. This type of visual disturbance is almost certainly cortical in origin and is unrelated to the toxic amblyopias.

Three patients of the 38 examined in the survey had visual disturbances which they related to Ibuprofen. In Case 5 bilateral circinate retinopathy explained the reduced visual acuity and, although she had a reduction in vision within 3 weeks of starting Ibuprofen, we do not think that it is justified in this case to relate the drug to the visual disturbance. In Case 14 there were also macular changes but these were of the senile type, and were first recorded in 1964, at which time the visual acuity had been normal. When she presented with her recent visual failure, after being on Ibuprofen for 2 months, the visual acuity was 6/18 in both eyes and visual field examination on the Goldmann perimeter showed bilateral centrocaecal defects. When the drug was withdrawn there was an immediate subjective improvement in her vision and this was confirmed not only by an improvement in the visual acuity to 6/9 in each eye but also by the disappearance of the centrocaecal field defects. A minute paracentral scotoma persisted in each field, however, and this was consistent with her preexisting maculopathy. There seems little doubt that this patient's visual deterioration was related to Ibuprofen therapy, although the clinical picture was complicated by the maculopathy.

In Case 36 blurring of vision developed a few days after starting treatment with Ibuprofen for a rheumatoid synovitis of the left wrist. After 10 days of treatment her ocular symptoms had not improved and she stopped taking the drug. She did not consult her doctor and her vision returned to normal within the next few days. She was not referred to the Eye Clinic until 7 weeks later at which time the ocular examination showed normal results. This patient may have had a toxic reaction to Ibuprofen though this supposition is based entirely on her subjective history.

In summary, therefore, Patients 1 and 14 developed centrocaecal field defects and reduced visual acuity while on Ibuprofen therapy, and in both there was a marked improvement when the drug was withdrawn. Although in Case 14 there was a pre-existing maculopathy, we believe that both patients had a toxic amblyopia due to Ibuprofen. In Cases 5 and 36, a toxic reaction may have taken place, but the evidence is not conclusive. The symptoms exhibited by Patient 2 are unrelated to those of the previous four cases, and are probably cortical in origin.

Summary

Two patients with ocular symptoms related to Ibuprofen therapy are reported and the findings in a survey of 38 patients taking this drug are discussed.

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