

# Efficacy of antiprostaglandin therapy in vernal conjunctivitis

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**SUMMARY** Twenty-seven patients with vernal conjunctivitis who remained symptomatic following treatment with corticosteroid drops and/or Opticrom drops (sodium cromoglycate 2%, benzalkonium chloride 0.01%) were treated with aspirin. Aspirin produced marked improvement in all patients apart from three. The possible mechanism of the efficacy of aspirin in vernal conjunctivitis is discussed.

Vernal conjunctivitis is a severe perennial form of allergic conjunctivitis involving the conjunctiva and often also the cornea. The condition is found predominantly in children or young adults. The main symptoms are those of severe itching, photophobia, and the production of a tenacious, stringy, mucous discharge. The disease generally affects the upper tarsal conjunctiva with papillary hypertrophy and cobblestone appearance. In severe cases the limbal conjunctiva may also be affected, causing localised oedema and hyperaemia or fleshy isolated vegetations. Punctate keratitis and indolent corneal ulceration may also occur.

The topical application of corticosteroids may be of considerable benefit. But control is not complete in all cases, and its long term use can produce glaucoma. The efficacy of sodium cromoglycate 2% (Opticrom) remains controversial.<sup>1-3</sup>

Aspirin therapy in mastocytosis was found to be beneficial, and, since the pathophysiology of both mastocytosis and vernal conjunctivitis involves mast cell abnormalities, the use of aspirin in treating the latter was tried in three patients.<sup>4</sup>

We report here the effect of aspirin therapy on 27 patients with vernal conjunctivitis.

## Material and methods

Twenty-seven patients aged 4-18 years were treated with aspirin; 24 were males and three were females. All the 27 patients had been treated prior to aspirin

with steroid drops topically and 15 with Opticrom drops too; nevertheless they remained symptomatic. In three patients the disease was so severe that they received prednisone tablets. The patients had been under our follow-up before aspirin treatment for an average of 1.5 years, and the duration of the disease had lasted up to 4 years.

The patients were questioned for photophobia, lacrimation, and itching. On examination they were divided into cases of palpebral, limbal, and mixed type of vernal conjunctivitis, with special emphasis on superficial punctate keratopathy. Twenty-three patients complained of severe photophobia, 22 of itching, and 18 of lacrimation. On examination 14 patients presented with the palpebral type, three with the limbal type, and 10 with mixed vernal conjunctivitis. Twenty patients presented with superficial punctate keratopathy and two had corneal ulcers (nos. 5, 10) prior to aspirin therapy.

The dosage of aspirin in our patients varied between 0.5 g and 1.5 g daily, depending on the patient's age. During aspirin treatment corticosteroid as well as Opticrom drops were withheld. The duration of therapy for the acute inflammatory stage was six weeks, followed by gradual weaning from the drug, clinical findings permitting.

## Results

The results are summarised in Table 1. Symptoms improved in 24 patients after treatment with aspirin, though in 20 patients the palpebral hypertrophy remained visible. In four out of 19 patients superficial

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Table 1 Summary of clinical findings prior to and after aspirin treatment

Pat. no.	Sex	Age	Treatment prior to aspirin		Symptoms before aspirin treatment			Signs before aspirin treatment			Symptoms after treatment			Signs after aspirin treatment		
			C-steroids	Opti-crom	Photo-phobia	Lacri-mation	Itch-ing	Palpe-bral type	Super-fic. corneal stippling	Limbal type	Photo-phobia	Lacri-mation	Itch-ing	Palpe-bral type	Super-fic. corneal stippling	Limbal type
1	M	4	+	+	+	+	+	+	+	-	-	-	±	±	-	-
2	M	8	+	+	+	+	+	+	+	-	-	-	-	+	-	-
3	F	18	+	-	+	+	+	+	+	++	-	-	-	±	-	-
4	M	4	+	+	+	+	+	+	-	++	-	-	-	±	-	-
5	M	5	+	+	+	+	+	+	+	-	-	-	-	+	-	-
6	M	7	+	+	+	+	+	+	+	+	-	-	±	+	-	-
7	M	18	+	+	-	-	+	-	-	-	-	-	-	+	-	+
8	M	7	+	+	+	+	+	+	+	-	-	-	-	±	-	-
9	M	7	+	+	-	+	+	+	+	+	-	-	-	±	-	-
10	M	11	+	-	+	++	+	-	+	++	+	+	-	+	-	+
11	M	6	+	+	-	+	-	+	+	-	-	-	+	+	±	-
12	M	8	+	+	++	+	+	+	-	+	-	-	+	++	+	-
13	M	8	+	-	±	+	+	+	+	-	-	-	-	+	-	-
14	M	8	+	-	+	-	-	+	+	-	-	-	-	+	-	+
15	M	4	+	+	+	+	-	+	+	++	-	-	+	±	-	-
16	M	4	+	-	+	+	+	+	+	+	+	+	+	+	+	-
17	F	6	+	-	+	+	+	+	-	+	-	-	-	+	-	-
18	M	13	+	-	+	+	+	+	-	-	-	-	-	+	-	-
19	M	5	+	-	+	-	+	+	+	+	-	-	-	-	-	-
20	M	11	+	+	+	-	-	+	+	-	-	-	-	-	-	-
21	M	10	+	-	+	-	+	+	+	-	-	-	-	+	-	-
22	M	8	+	-	++	-	-	+	+	-	-	-	-	+	-	-
23	M	6	+	-	+	-	+	+	±	+	-	-	-	+	-	-
24	M	9	+	+	+	+	+	+	-	-	-	-	-	+	-	-
25	M	7	+	+	+	-	+	+	+	-	±	-	-	+	-	-
26	M	6	+	+	+	+	+	-	-	+	-	-	-	-	-	-
27	F	6	+	-	+	-	+	+	+	-	±	-	±	±	+	-

punctate keratopathy remained, and in three other patients limbal papillae were still visible. In this group of patients no adverse reaction to aspirin was observed.

## Discussion

The incidence of vernal conjunctivitis is particularly high in Israel, and apparently some of its features are different from those in temperate zones.<sup>5</sup> The disease in this country seems to be less seasonal than has been reported elsewhere. It has also been stressed that the incidence of other atopic disorders in children with vernal conjunctivitis was only 11%, which is similar to the incidence of atopic disorders among other children of the same age. This finding may explain why only a selective group of children with vernal conjunctivitis, namely those who present with other allergic conditions, react well to cromoglycate.

In spite of treatment with steroids and cromoglycate our patients remained symptomatic. Mast cell abnormalities characterise both vernal conjunctivitis and mastocytosis, a generalised disease of mast cell proliferation with increased serum levels of hista-

mine and prostaglandin D<sub>2</sub>.<sup>6</sup> Prostaglandin D<sub>2</sub> is the mast cells' most prevalent prostaglandin, and its role in inflammation has been recently appreciated.<sup>7</sup>

In vernal conjunctivitis the percentage of degranulated mast cells is increased, probably signifying prostaglandin release.<sup>8</sup> The process of degranulation is believed to be due to antigen induced bridging of IgE molecules which are bound to specific receptors on the mast cell surface. Aspirin acts by acetylating the active sites of cyclo-oxygenase, thus interrupting the production of prostaglandin D<sub>2</sub> from its precursor arachidonic acid.<sup>9</sup> Hence aspirin may block the production of the inflammation producing prostaglandin in mast cells released in vernal conjunctivitis by an antigen-dependent mechanism. Indeed, application of arachidonic acid, the precursor of prostaglandin D<sub>2</sub> produces conjunctival redness and chemosis in rabbits.<sup>10,11</sup>

We have administered aspirin to 27 patients who, in spite of local steroid drops and/or opti-crom, remained symptomatic. After treatment with aspirin the symptoms and signs improved in all but three patients (nos. 12, 16, 27). Aspirin produced marked improvement in the punctate keratopathy and limbal

infiltration in most patients. The cobblestones of the upper tarsus did not disappear but were smaller and less inflamed.

The limitation of this study is that the efficacy of acetylsalicylic acid treatment was not evaluated in a masked fashion. The gravity of the disease in this group, however, prevented us from applying a procedure using a placebo. We believe that the marked improvement in signs and symptoms of vernal conjunctivitis in most patients receiving aspirin only for extended periods of time, following the failure of corticosteroids and cromoglycate, strongly suggests the efficacy of this treatment beyond a placebo effect.

We conclude that aspirin is an additional therapeutic tool in the treatment of vernal conjunctivitis and can be tried as the only treatment in new cases of vernal conjunctivitis, in conjunction with tear drop substitutes to help prevent punctate keratopathy by lubricating the cornea. The clinician must, however, be alert to the possible side effects of aspirin, namely increased bleeding tendency, gastritis, and Reye's syndrome. It may also worsen the bronchial asthma which occasionally occurs in these allergic children.

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