presenting with otherwise unexplained acute neurological symptoms, and the association may be more common than is generally recognised.

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Sialochemistry in evaluating bromhexine treatment of Sjögren's syndrome

Frost-Larsen *et al*[1] found that lacrimal gland secretion, measured by the Schirmer test, increased during bromhexine treatment for Sjögren's syndrome (SS). They did not find that bromhexine had any effect on salivary gland function, but their methods of estimating salivary secretion "were crude and of doubtful value." Changes in the composition of saliva are a sensitive indicator of salivary gland disease in SS. Significantly raised concentrations of Na, IgA, and IgG in saliva have been reported.[2 3] We therefore decided to study the effect of bromhexine on the quantity and quality of saliva in patients with SS.

Patients, methods, and results

Twenty patients under the age of 60 were divided into two groups. Group 1 (SS group) consisted of five patients with sicca syndrome who had no associated disease and who had been followed up for at least 18 months, and seven patients with Sjögren's syndrome associated only with seropositive rheumatoid arthritis. Group 2 (control group) consisted of eight patients with seropositive rheumatoid arthritis without sicca complex. The criteria for sicca and Sjögren's syndrome were decreased tear flow to less than 5 mm/min by Schirmer's test, staining of the cornea with rose bengal dye, diminished salivary flow, and abnormal salivary composition. All patients with rheumatoid arthritis fulfilled the American Rheumatism Association's criteria for either definite or classical rheumatoid arthritis.

Bromhexine 16 mg three times daily was given for four weeks. The medical treatment remained unchanged during this period. Saliva was collected before and at the end of the course of bromhexine. Total mixed unstimulated saliva was collected for 10 minutes. The rate of flow was measured and the saliva analysed for Na, IgA, and IgG as described.[2] Student's *t* test was applied for statistical analysis. Symptoms were alleviated to a varying degree during bromhexine treatment. They recurred when bromhexine was discontinued and improved when bromhexine was again given. None of the control group had sialorrhoea or excessive lacrimation. No side effects were recorded even during prolonged treatment. The SS patients had significantly higher initial concentrations of Na, IgA, and IgG when compared with the controls, whose saliva was normal (table). Bromhexine had no effect on salivary composition in the control group, but in the SS group concentrations of Na, IgA, and IgG were significantly reduced towards normal without an increase in salivary flow. Concentrations were not always uniformly reduced in all patients. In a few the concentration of only one component was significantly lower. Four SS patients took bromhexine continuously for months and a further gradual lowering of Na, IgA, and IgG concentrations was noted. Two SS patients took part twice in the trial, with a two-weeks interval between courses of treatment. The concentrations of Na, IgA, and IgG had returned to their original levels after the interval. Further treatment lowered them, as before.

Comment

The change in salivary composition towards normal without a significant increase in salivary flow raises the question whether the clinical improvement with bromhexine treatment could be due to the change in the quality of the saliva. Bromhexine reduces sputum viscosity in chronic bronchitis.[4] A reduction in sodium concentration may affect salivary viscosity, which changes with the cationic concentration.[5] How bromhexine alters salivary composition in SS is unknown. Since it lowers the concentrations of IgG and IgA perhaps it inhibits the local transformation of B lymphocytes.

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Effect of PUVA on serum 25-OH vitamin D in psoriatics

The action of ultraviolet radiation (UVR) on 7-dehydrocholesterol in the epidermis is one of the main sources of vitamin D in man. It is important to know whether treatment of psoriasis with PUVA (8-methoxypsoralen and long-wave ultraviolet light) may lead to excessive production of vitamin D and to toxic concentrations in the blood.

Patients, methods, and results

Twenty-five patients with chronic plaque psoriasis were studied. They had never had PUVA treatment and had not recently had UVR. They were irradiated two hours after taking the 8-methoxypsoralen (8-MOP), when the peak concentrations of the drug are believed to occur in blood and skin. Further details of treatment, which was given three times a week till the rash was clear and approximately weekly after that, are described elsewhere.[1]

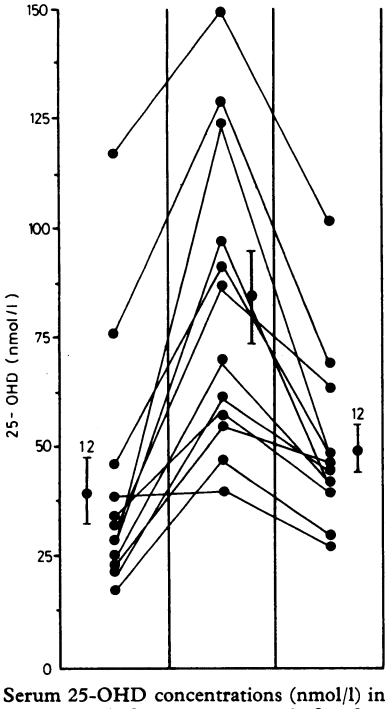
Mean (± SD) flow rate and composition of saliva before and after bromhexine treatment in a control group and a group of patients with Sjögren's syndrome (SS group)

	Rate of flow (ml/min)		Na (mmol(mEq)/l)		IgA (mg/l)		IgG (mg/l)	
	Before	After	Before	After	Before	After	Before	After
Control group (n = 8)	0·30	0·31	4·6 ± 1·4	4·3 ± 1·3	97 ± 52	105 ± 61	< 10	< 10
SS group (n = 12)	0·08	0·07	22·6 ± 17·1	13·6 ± 12·3	423 ± 205	296 ± 174	133 ± 42	45 ± 39

Statistical analysis
(1) Pretreatment control/pretreatment SS: Na $P < 0.01$; IgA and IgG $P < 0.001$ (Student's *t* test).
(2) Pretreatment/on treatment. A control group—no significance. B SS group—Na and IgA $P < 0.001$; IgG (n = 6) $P < 0.01$; rate of flow, no significance (*t* test for paired comparison).

The patients comprised, firstly, 19 in whom serum 25-hydroxy vitamin D (25-OHD) concentrations were measured before and 24 hours after the first PUVA treatment. In seven of the 19 plasma 25-OHD was also measured two hours after the psoralen but before the UVA, and in 12 of the 19 it was also measured 24 hours after the third PUVA treatment when pigmentation was just beginning to appear. Secondly, six patients in whom the psoriasis had been cleared and who were receiving maintenance treatment. They were very pigmented. For comparison the results were compared with the summer and winter concentrations in 30 normal subjects. 25-OHD was measured by competitive protein binding.[2 3]

The mean (±SEM) serum 25-OHD concentration in the 19 patients was 40±5·5 nmol/l (16·0±2·2 μg/l) before treatment and rose significantly to 81·2±7·8 nmol/l (32·9±3·1 μg/l) after the first PUVA treatment. The concentrations reached were significantly higher than the summer mean of 57·5±5·5 nmol/l (23·0±2·2 μg/l) for 30 normal individuals ($P < 0.001$). We found no significant difference in the concentrations in the seven patients studied before and two hours after 8-MOP who were not irradiated. After the third treatment the mean serum 25-OHD concentrations had returned almost to normal (fig). The longer term effects were that the mean (±SEM) serum 25-OHD concentration in the patients on maintenance treatment was 28·5±3·5 nmol/l (11·4±1·4 μg/l), which was not significantly lower than the winter mean of 38±7 nmol/l (15·2±2·8 μg/l) in normal people.



Serum 25-OHD concentrations (nmol/l) in 12 patients before treatment and after first and third PUVA treatments. Mean ±SEM is shown for each group.

Conversion: SI to traditional units—Plasma 25-OHD: 1 nmol/l ≈ 0·4 μg/l.

Comment

Although the action spectrum for the conversion of 7-dehydrocholesterol to vitamin D_3 is thought to be within the UVB range (280-310 nm), our results suggest that the higher wavelengths of UVA (310-400 nm) may have an effect too at least in the presence of psoralen. Nevertheless, we have not ruled out the possibility that the small amounts of UVB emitted by the lamps we used[4] may explain the increase either alone or in combination with UVA or psoralen, or both. The stimulation of vitamin D synthesis by PUVA was short-lived. It had returned almost to normal by the third irradiation. By then there may have been screening by melanin even though clinical pigmentation was only just beginning. The magnitude of the rise in serum 25-OHD was not great even in the early stages, and additional measurements of serum calcium and inorganic phosphate concentrations showed them to be normal. Thus PUVA is unlikely to lead to harmful concentrations of vitamin D in the blood. The converse possibility, that the pigmentation caused by PUVA could lead to vitamin D deficiency by impairing its synthesis by natural UVR,[5] seems unlikely from our data, though they are insufficient to answer this question completely.

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Chloroquine-resistant falciparum malaria in a Bangladeshi girl with acute lymphoblastic leukaemia

A girl from Bangladesh with acute lymphoblastic leukaemia was found on admission to have *Plasmodium falciparum* malaria. She was treated with chloroquine with rapid eradication of the parasites. Large numbers of ring forms of *P falciparum* were found in blood smears 23 days later, and she was then treated with intravenous quinine and Fansidar. The malaria may have been acquired from blood transfusions given in Bangladesh.

Case report

An 11-year-old Bangladeshi girl developed general malaise and bone pains four weeks before admission to hospital in Dacca, where acute lymphoblastic leukaemia (ALL) was diagnosed. She was transfused with three units of whole blood, started on chemotherapy, and transferred to the United Kingdom for further management on 19 March 1979.

On arrival she was well and afebrile but her liver and spleen were enlarged. A blood count showed: haemoglobin 11·3 g/dl, white cell count $0·8 \times 10^9$/l with 22% neutrophils, 52% lymphocytes, 24% blast cells, and platelets 49×10^9/l. Examination of the peripheral blood film showed 4% parasitaemia of the red cells with *P falciparum*. No parasites had been found on a blood film made in Bangladesh before blood transfusion. Microscopy and cell surface marker studies on her bone marrow confirmed the diagnosis of common ALL. She was treated with chloroquine, a total of 1·5 g base by mouth, and intravenous vincristine 1·5 mg/week, with prednisone 40 mg/day by mouth. The malaria parasites disappeared from her peripheral blood within 72 hours. She remained neutropenic ($< 1·0 \times 10^9$/l) but relatively well.

Two days later she developed fever (40°C) and signs of peritonitis. No parasites were found in the peripheral blood. A laparotomy did not show any localised lesion, but *Klebsiella aerogenes* was grown from the peritoneal exudate and the blood, for which she received gentamicin and granulocyte transfusions. Her postoperative course was complicated by continued severe neutropenia and delayed healing of the abdominal incision.

Twenty-three days after admission she became unwell and developed a swinging fever (up to 41°C). There were no specific clinical findings apart from an open granulating abdominal wound, from which a gentamicin-resistant *Klebsiella* was grown. Her haemoglobin concentration fell from 14·4 g/dl to 5·4 g/dl over the next few days, the serum bilirubin concentration reached 53 μmol/l (3·1 mg/100 ml) (normal 5-20 μmol/l (0·3-1·2 mg/100 ml)), and large amounts of urobilinogen and haemoglobin were found in the urine. A blood smear showed a 26% parasitaemia with ring forms of *P falciparum*. She was treated with intravenous quinine, 10 mg/kg in 10 ml normal saline per kg, infused over four hours at 12-hourly intervals on four occasions, followed by a single dose of Fansidar (sulphadoxine 500 mg and pyrimethamine 25 mg). Clinical improvement was slow and her temperature did not return to normal until 24 hours after the last dose of quinine. The parasitaemia showed minimal decrease during the first 24 hours of quinine therapy, but thereafter the parasites rapidly cleared and none were found at 92 hours or during the subsequent month. The patient is