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Plasma concentrations of atrial natriuretic peptide in hypothyroidism

Atrial natriuretic peptide may play an important part in plasma volume homeostasis in normal humans because of its ability to cause natriuresis, diuresis, and vasodilatation. Hypothyroidism is accompanied by abnormalities in both the cardiovascular system and water balance.^{1,2,3} Our study investigated the plasma concentrations of atrial natriuretic peptide in hypothyroidism.

Patients, methods, and results

We studied a group of 15 patients in whom clinical and biochemical hypothyroidism had been newly diagnosed (mean age 49, range 23-73) and a group of 21 healthy normal subjects (mean age 43, range 27-86). In addition, 10 patients were restudied after treatment with thyroxine for six to 12 weeks. None had signs of heart failure, valvular heart disease, or hypertension (blood pressure >150/90 mm Hg). Venous blood from the forearm was drawn between 0900 and 1100 after 30 minutes of quiet sitting and placed into cooled tubes containing sequestrene and aprotinin. On the same day the peptide was extracted from plasma with octadecyl silica and methanol.⁴ The mean recovery was 70%, and the results are given uncorrected for the losses.

The concentration of atrial natriuretic peptide was measured with a previously described radioimmunoassay using a polyclonal antibody to the carboxy terminus of atrial natriuretic factor 99-126 (Peninsula Laboratories) and an iodine-125 label (Amersham).⁴ Intraassay and interassay variations were 10% and 12% respectively, and samples from before and after treatment were measured in the

same assay. The concentration of plasma atrial natriuretic peptide increases in normal subjects who are receiving a high intake of sodium, so the 24 hour urinary sodium excretion was also measured on the day of the study. Diet was unrestricted. Because of the small numbers of subjects and the finding that plasma concentrations in each group showed a skew distribution the results are expressed as median and range, and the groups were compared with the Wilcoxon paired and unpaired tests.

The concentration of plasma atrial natriuretic peptide in the hypothyroid group (median 3.3 pmol/l, range 2.1-10.2 pmol/l) was lower ($p<0.01$) than in the controls (median 6.5 pmol/l, range 2.3-18.1 pmol/l) (figure). In 10 patients the median pretreatment value (3.0 pmol/l, range 2.1-10.2 pmol/l) increased significantly after treatment with thyroxine (median 7.6 pmol/l, range 1.4-11.8 pmol/l; $p<0.01$). There was no significant difference between the 24 hour urinary sodium excretion of the control group (median 148 mmol, range 45-288 mmol) and the hypothyroid group (median 130 mmol, range 65-191 mmol).

Comment

The decreased median concentration of atrial natriuretic peptide in hypothyroidism confirms the results of a smaller study in which urinary sodium excretion was not measured.⁵ By contrast, we have reported increased plasma concentrations of peptide in patients who have untreated hyperthyroidism,⁴ a disease associated with an increased plasma volume.¹ A low plasma volume has been reported in myxoedema,¹ and this may decrease secretion of the peptide. A lack of circulating atrial natriuretic peptide may partly explain the impaired ability to excrete a water load, which recovers after treatment,² and the enhanced arterial pressor response to angiotensin II³—both are features of hypothyroidism.

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Plasma concentrations of atrial natriuretic peptide in normal subjects and hypothyroid patients before and after treatment.

Rubber glove asthma

Rubber gloves are well known to dermatologists as causes of allergic dermatitis, the chemical responsible usually being an antioxidant or an accelerator added to the latex in its production.^{1,2} So far as we are aware asthma provoked by vapour given off by rubber gloves has not been described, though rhinitis and anaphylaxis due to contact have.³

Case report and investigations

A 36 year old male laboratory technician presented with a two year history of increasingly troublesome attacks of cough and wheeze. These tended to occur about one hour after starting work and lasted until evening. Two weeks before attending the clinic he had a prolonged and more severe attack which required treatment with prednisolone. For the past 10 years he had been performing serological investigations for hepatitis and, more recently, the acquired immune deficiency syndrome and he was required to wear gloves, which he changed frequently. He attributed his attacks to the starch with which the gloves were powdered. He recalled one attack after drinking red wine.

Over three weeks he recorded his peak flow rate four times daily. During a week at work it averaged about 530 l/min, whereas during two weeks on holiday it averaged about 570 l/min. During work he used an aerosol bronchodilator 14 times; he did not need it when off work.

Formal challenge tests with talc (control) and glove starch produced no reaction. Two sets of outwardly identical gloves were obtained from the manufacturers (Surgikos Ltd), microtouch and general purpose. The latter was the type he used at work. Putting on and taking off the microtouch gloves again produced no reaction, but after 10 minutes of the same manoeuvre with the

general purpose gloves his peak flow fell from 580 l/min to 350 l/min within 15 minutes, necessitating inhalation of a bronchodilator. This challenge test with suspected and control gloves was repeated, and again a pronounced fall in peak flow occurred only with the general purpose gloves.

A dozen each of the microtouch and general purpose gloves were enclosed in conical flasks. Pure filtered air was drawn over them at 0.5 l/min and passed through a tube of activated charcoal; this was desorbed with carbon disulphide and analysed by gas chromatography and mass spectrometry. The vapours from the two types of gloves were compared and included many chemicals in common. Nevertheless, one peak was observed in the vapour from the general purpose gloves which was not present in the microtouch glove vapour; this was identified as a bicyclic terpene, probably carene. Semiquantitative analysis by selected monitoring showed that it was given off from the gloves in concentration of about 10 parts per billion per glove.

Comment

The patient remained symptom free after changing the gloves he used at work to the microtouch type, and in view of his sensitivity to the vapour we thought that it was inadvisable to carry out formal challenge testing with pure carene.

Carene is a terpene produced naturally by plants and may protect them from boring insects. It is found particularly in pine resin and is one component of the distillate that made oil of turpentine such an important skin sensitiser, leading to its replacement by the petroleum derived turpentine substitute.⁴ Curiously, the solid residue after distillation of pine resin, rosin or colophony, is also an important skin and lung sensitiser.⁵

Inquiries of the manufacturers of gloves showed that the general purpose ones were imported ready made from Malaysia and had been supplied to the patient's employer about three years previously. No pine resin or terpenes were added to the latex in manufacture and these substances were probably present in the raw latex. Chemically this is quite possible, as carene may be produced from two molecules of isoprene, and latex is a polymer of the same chemical (figure).

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Natural latex is a polymer of isoprene. Bicyclic terpenes such as 3-carene are made up from two isoprene units as shown.

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Meningitis complicating acute otitis media

Meningitis is a potentially fatal complication of acute otitis media. We report on four adults who were admitted to this hospital during the past six months with meningitis secondary to acute otitis media. None of the patients had received antibiotic treatment before admission. In one case the disease was fatal.

Case reports

The table shows details of the patients. In two patients high resolution computed tomograms of the temporal bones showed defects in the roof of the tegmen and in one of these patients the scan also showed air in the middle cranial fossa. It was presumed that the air and bacteria from the acute otitis media had penetrated through the defect in the tegmen; this defect was closed with muscle and tissue glue.

Comment

Intracranial sepsis is a well recognised complication of chronic suppurative otitis media but is probably more common after acute otitis media.¹ In one series acute otitis media was the source of infection in 30% of patients with pneumococcal meningitis.² The routes of spread from the middle ear to the meninges are through defects in the tegmen, through emissary veins running from the mastoid to the dura, or through the labyrinth.

The role of antimicrobial treatment in children is controversial. Most clinicians treat acute otitis media with antibiotics,³ and the rate of

suppurative complications after otitis media in childhood has decreased in the antibiotic era.⁴ In one trial, however, antibiotics were not shown to be superior to xylometazoline nosedrops and analgesics in childhood otitis media. In this particular study no complications of otitis media occurred.⁵ Acute otitis media in adults is fairly uncommon, and the four patients reported on here show that the complications can be severe. We therefore believe that adults should receive antimicrobial treatment as soon as acute otitis media is diagnosed. Failure to respond to antibiotics should be an indication for immediate referral for specialist treatment.

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Details of patients with acute otitis media and meningitis

Case No	Sex	Age (years)	Symptoms	Duration	Organism	Outcome
1	F	25	Left otalgia, headache	2 Days	Pneumococcus	Died
2*	F	37	Left otalgia	12 Hours	Streptococcus	Paralysis of left vocal cord and left hemiplegia
3	F	53	Left otalgia, headache	24 Hours	Streptococcus	Full recovery
4	F	64	Right otalgia, right otorrhoea	5 Days	Streptococcus	Full recovery

*This patient had had a similar episode when aged 25. The symptoms had lasted for two weeks and were due to haemophilus; she recovered fully.