

Reduced thirst in patients with a vasospastic syndrome

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ABSTRACT.

Purpose: To compare thirst, drinking behaviour, and endothelin-1 (ET-1) plasma levels between vasospastic and non-vasospastic subjects.

Methods: We compared 67 subjects with a primary vasospastic syndrome with 64 age- and sex-matched non-vasospastic control subjects. A detailed medical history was recorded, including a questionnaire containing queries about thirst and drinking behaviour, history of migraine or unspecific headache, history of episodes of low blood pressure, and smoking habits. Body mass index (BMI) was calculated and blood samples were drawn for ET-1 measurements.

Results: Subjects with a vasospastic syndrome reported a reduced desire to drink and a lower estimated quantity of daily fluid intake, more often forgot to drink, more often had both migraine and unspecific headache, more often had episodes of low blood pressure, and had an increased plasma level of ET-1. These features differed statistically significantly between the two groups. There was also a non-significant trend among vasospastic subjects to smoke less and to have a smaller BMI.

Conclusion: A reduced desire to drink is found frequently among vasospastic subjects.

Key words: glaucoma – vasospasm – endothelin – thirst

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Introduction

There is some evidence that vascular dysregulation may be a risk factor for a number of diseases, including eye diseases such as glaucoma (Drance et al. 1988; Flammer et al. 1999, 2001, 2002; Nitenberg et al. 2004). Therefore, a detailed description of this condition is of interest for clinicians, including ophthalmologists.

Vascular dysregulation occurs in the context of so-called vasospastic syndrome (VSS). Subjects with VSS have a tendency to respond to stimuli such as

coldness or emotional stress with inappropriate vasoconstriction or insufficient vasodilatation in the microcirculation (Flammer et al. 2001). The eye seems often to be involved, justifying the term ‘presumed ocular vasospastic syndrome’ (Goldberg et al. 1999; Hasler et al. 2002; Gugleta et al. 2003). Primary vasospastic syndrome occurs in the absence of an underlying disease (Flammer et al. 2001). The first symptoms usually appear during puberty and eventually attenuate as subjects become older, especially after the menopause. The syndrome seems

often to be inherited. A secondary VSS can occur in the context of an underlying disease such as multiple sclerosis (Swank et al. 1983; Haufschild et al. 2001), rheumatoid arthritis (Pache et al. 2002a), giant cell arteritis (Pache et al. 2002b) or fibromyalgia (Pache et al. 2003). Only the primary VSS seems to be associated with glaucoma (Flammer et al. 2001). Indeed, affected individuals often have a disturbed autoregulation of the ocular perfusion (Gherghel et al. 1999), similar to the altered blood flow regulation observed in progressive glaucoma patients (Hafez et al. 2003).

The key symptoms of a person with VSS are cold hands and, sometimes, cold feet (Flammer et al. 2001). Often, patients indicate a history of migraine, although not all subjects with VSS suffer from migraine, and not all patients with migraine are vasospastic (Hegyalijai et al. 1997). They often suffer from low blood pressure, especially when they are young, and from prolonged sleep-onset latency (Pache et al. 2001). Furthermore, they often exhibit a higher drug sensitivity, possibly due to an altered expression of ABC transporter genes (Gaudez et al. 2003; Wunderlich et al. 2003). There exist well established methods for diagnosing a VSS, including nailfold capillaroscopy combined with a cold provocation test (Saner et al. 1987; Gasser & Flammer 1991). In a busy clinical setting, however, it is often not possible to screen with sophisticated methods. A detailed patient history, however, may help in establishing the likelihood of the diagnosis (Singhal 2004). Better knowledge

of the syndrome will obviously facilitate such an approach. Because increased plasma levels of ET-1 have been reported in patients with a vascular dysregulation (Flammer et al. 2001), and because ET-1 has an antidipsogenic effect (Stocker et al. 2001), the present study investigated differences in thirst and drinking behaviour between vasospastics and non-vasospastics.

Patients and Methods

A notification in the University Eye Clinic Basel informed potential volunteers (collaborators, students, parents and friends of patients) of the opportunity to participate in a scientific research project. A total of 67 subjects with VSS (14 men and 53 women), with an average age of 53 years (range 26–85 years), and 64 non-vasospastic controls (14 men and 50 women), with an average age of 55 years (range 26–82 years), were enrolled in the study. The distribution of age-, sex- and occupational characteristics were comparable between the two groups.

After informed consent had been obtained, a detailed medical and ophthalmic history was recorded, and all subjects completed medical and ophthalmological examinations. Subjects were not included if they had a history of a systemic disease (e.g. diabetes, renal diseases or systemic circulatory diseases) or any chronic systemic medication.

The diagnosis of VSS was based on both a positive history of cold hands or feet and an abnormal reaction in the local cold exposure test in the nailfold capillaroscopy (Gasser & Flammer 1991). The group of non-vasospastic controls included subjects who had neither a history of cold hands nor a pathological reaction in the local cold exposure test. The capillaroscopy was carried out in individuals acclimatized for 15 minutes to a 23 ° room temperature. Baseline measurements were obtained during 60 seconds and then a fingertip was exposed to carbon dioxide at – 15 ° for 60 seconds. Subjects found to have a blood-flow standstill of at least 12 seconds in one or more capillaries were defined as vasospastic (Saner et al. 1987).

Subjects were asked to fill out a detailed questionnaire containing queries about desire to drink (high, moderate

or low), estimated quantity of daily fluid intake, motivation for drinking (thirst or wilful decision), and forgetfulness regarding drinking during the daytime. They were also questioned regarding migraine and unspecific headache, episodes of low blood pressure and smoking habits. Their BMI (body mass index) was calculated. Blood samples were taken after 30 minutes of rest in a supine position and ET-1 levels were determined by specific radioimmunoassays as described previously (Haufschild et al. 2001).

Comparisons between the groups were performed using chi-squared test, Mann–Whitney *U* test or Kruskal–Wallis test, as appropriate. P-values smaller than 0.05 were considered as significant.

Results

When compared to the 64 non-vasospastic subjects, the 67 subjects with VSS had significantly less thirst (Table 1), significantly lower estimated quantities of fluid intake, and significantly more often forgot to drink. They suffered from both migraine and unspecific headache significantly more often, and had a history of low blood pressure significantly more often. They tended to smoke less (NS) and to have a lower BMI (NS). The ET-1 plasma level was significantly increased.

Discussion

The results of this study indicate that patients with VSS have both a reduced

desire to drink and a reduced fluid intake. The study further confirms previous reports of patients with VSS having migraine more often (Hegyalljai et al. 1997), and unspecific headache as well as a history of low blood pressure (Huang et al. 1986; Gherghel et al. 2001). It further confirms that patients with VSS have a significantly increased plasma level of ET-1 (Flammer et al. 2001). While an increased ET-1 plasma level might, on one hand, have an impact on circulation, specifically of the eye (Strenn et al. 1998), it might also, on the other hand, be the cause of reduced feelings of thirst (Stocker et al. 2001).

Many hormones, such as renin, angiotensin, vasopressin, oxytocin and neurotransmitters, are involved in the regulation of thirst. Angiotensin II, for example, is a powerful stimulus for sodium appetite. When injected into the sensitive area of the brain it causes an immediate increase in water intake followed by an increase in salt intake. ET-1 has an antidipsogenic effect, mediated by ET-A receptors (Samson & Murphy 1993).

A slight increased ET-1 plasma level might also partially explain the low blood pressure. It probably not only leads to a slight dilatation of the veins, but also to a reduced re-uptake of sodium in the tubuli of the kidneys (Masereeuw et al. 2000).

The present results rely partly on answers to a questionnaire, and, consequently, on subjective ratings. Nevertheless, they indicate with a high probability that patients with VSS may have an altered desire to drink and a reduced intake of fluid. This observation is well in line with the

Table 1. Frequency of signs and symptoms.

		Vasospastic subjects	Controls	p
Desire to drink (% of subjects)	Low	64.2	26.6	0.0001
	Average	34.3	62.5	
	High	1.5	10.9	
Estimated daily fluid intake (litres, mean ± SD)		1.4 ± 0.4	1.8 ± 0.6	0.001
% of subjects who sometimes forget to drink		71.6	45.3	0.001
Prevalence of migraine (%)		40.3	11.0	0.001
Prevalence of unspecific headache (%)		25.4	7.8	0.008
History of low blood pressure (%)		50.7	14.1	0.001
Smoking (%)	Regularly	4.5	15.6	0.067
	Sometimes	7.5	10.9	
	Never	88.1	73.4	
BMI (mean ± SD)		22.6 ± 2.8	23.8 ± 3.8	0.051
ET-1 plasma level (mean ± SD)		2.7 ± 0.6	1.5 ± 0.4	0.01

report of an increased plasma level of ET-1 (Flammer et al. 2001).

The reported observation may help the clinician in that it may strengthen the likelihood of a presumed VSS. Beside the symptoms of cold hands, low blood pressure and migraine, a reduced desire to drink characterizes a subject with a VSS.

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