Cognitive performance and attention of csU patients: Objectifying measurements by computer-assisted memory and attention tests (MAT)- first results

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INTRODUCTION
- Histamine release from mast cells is a key component in chronic spontaneous urticaria (csU).
- Nonsedating H1-receptor antagonists at licensed dose are 1st line of csU.
- Increasing the dose up to 4x has been recommended in non-responders.
- In more than half of all treated csU patients disease control is not achieved by first line therapy.
- Likewise, histamine is relevant intracerebally.
- Histamine producing neurons are interconnected to almost all cerebral areas.
- They influence alertness, arousal, cognition, motivation, susceptibility to pain and stress.
- Drugs interfering with the histamine system may influence also the higher cognitive performance.
- Information on cognitive performance in csU-patients is lacking.

AIM
To obtain objectifying measurements by computer-assisted memory and attention tests (MAT) of the cognitive performance in csU patients on second generation H1-receptor antagonists at licensed or up-dosed doses.

METHOD
- Multicenter non-interventional observational study (12 German centers)
- Standardized documentation of socio demographic data and current medication of csU
- Disease burden: UAS7 (start: 6 days before MAT), UCT
- Quality of life: CU-Q20L, DLQI
- Depression: Beck-Depression-Inventory 2 (BDI II) (14 – 63 points depression)
- Investigation of the cognitive performance in csU patients by computer-assisted memory and attention tests (MAT)

- MAT distinctive measurements:
  - Selective attention
  - Episodic working memory
  - Episodic short-term memory and executive functions

RESULTS
- MAT results include a normalization and validation concerning age, gender and education
- High sensitivity and specificity, robust results
- Disturbing factors: postprandial, rage, alcohol, sleep deprivation
- Cross-sectional and longitudinal studies (e.g. Alzheimer, MS, Parkinson)
- Reached points (out of maximum of reachable points) are compared with individual comparison group
- Percentile rank (PR) and interpretation
- The PR indicates how many % of the participants from the norming sample had identical or fewer points.
- PR ≥ 84: above average; PR ≤ 16: alarming

- 52 csU patients
- 31 women, 21 men
- Age: 19 - 72 years (median: 52)
- Duration of csU: 1 month to 26 years (median: 35 months)
- UAS7: mean 11 ± 12; min=0, max= 40 (median: 7)
- Disease burden: Urtikaria control test (UCT): 0-16 (median: 10)
- Control of disease is achieved ≥ 12 points (here: 42.3 %)

- 1 Maurer M et al. Chronic spontaneous urticaria: It’s worse than we thought – first results of the multicenter real-life AWARE study (submitted)

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considered, the prevalence of attacks was higher in treated vs non-treated patients at night-time (χ² test = 4.5, P = 0.03). Considering the two subgroups at night-time we found fewer attacks onset during the numbness (n = 538) than during awakening period (n = 1960). In term of severity the two groups did not show differences.

**Conclusion:** A daily circadian variability in onset of attacks in patients with CI-INH-HAE is not supported. The presence of a significant pick (20.6% of all attacks) between 7.00 and 8.00 am probably relates to the fact that patients detect the attacks when they wake-up. In contrast to patients’ frighteness, attacks detected at awakening are not more severe.

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**1457 Cognitive performance and attention of csU patients: objectifying measurements by computer-assisted memory and attention tests (MAT)- first results**

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**Background:** Histamine release from mast cells is a key component in the pathophysiology of chronic spontaneous urticaria (csU). Likewise, histamine is relevant intracerebrally: Histamine producing neurons are interconnected to almost all cerebral areas. They influence alertness, arousal, cognition, motivation, susceptibility to pain and stress. Drugs interfering with the histamine system may influence also the higher cognitive performance.

Nonsedating (ns) H1-receptor antagonists at the licensed dose are the first line therapy of csU. In patients who do not obtain complete control with this treatment, increasing the dose up to four times has been recommended. In more than half of all treated csU patients disease control is not achieved by first line therapy.

Objectifying measurements (by computer-assisted memory and attention test (MAT)) of the cognitive performance in csU patients on second generation H1-receptor antagonists at licensed or up dosed doses have not been done, yet.

However, detection of cognitive impairment is crucial with regard to the risk of accidents in specific occupations and/or traffic. This may also have implications for the physician with regard to informed consent and liability issues.

**Method:** In a multicenter non-interventional observational study, the cognitive performance is investigated in csU patients by computer-assisted memory and attention tests (MAT): The performance in selective attention, episodic working memory, episodic short-term memory and executive functions are distinctively measured.

**Result:** The first n = 46 MAT-investigated csU-patients on H1-receptor antagonists (12 at licensed dose; 34 updosed) displayed in 6 patients (5 of them on a high dose treatment) a score of less than 4 concerning selective attention (i.e., strong impairment).

**Conclusion:** Our data indicate that approximately 10–15% of csU-patients on treatment with antihistamines are impaired in their selective attention (and consequently in their fitness to drive).

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**1458 Chronic spontaneous urticaria treated with omalizumab: personalized treatment for a cohort of 64 patients between 2013 and 2016**

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**Background:** In clinical studies, efficacy and tolerance of Omalizumab to treat severe forms of Chronic Spontaneous Urticaria (CSU), has been well established. The licensed dose is 300 mg every 4 weeks. Yet few data extracted from real life analysis exist. Our goal is to assess feasibility and relevance of such personalized Omalizumab treatments, for patients with severe CSU, followed in Grenoble Alpes University Hospital.

**Method:** A retrospective, monocentric study (Grenoble Alpes University Hospital) of a French Cohort of patients with CSU resistant to fourthfold dose of anti-histamines treated with Omalizumab between May 2013 and January 2016. Our analysis aimed to evaluate the quality and delay of treatment responses, treatment duration and patients’ tolerance to Omalizumab. Treatment efficacy was measured from clinical data: response to the treatment (scores Cu-QoL, AE-QoL, UCT, AA28 et UAS7) and the interval between 2 injections was individually tailored.

**Result:** 64 patients (including 51 women), aged between 16 and 89, suffering from severe CSU, were cared for over an average period of 32 months. 81% of these patients developed angioedema because of superficial urticaria. The disease’s average length fluctuated between 6 months to 15 years. 90% of patients taking Omalizumab completely responded to the treatment after 6 months, 70% after the second injection, 6% partially responded and only 4% did not respond at all. A complete response is defined as an upgrade in quality of life above 80%, followed by UAS = 0 and AAS = 0. On average, the Omalizumab intake lasted between 2 and 38 months. In terms of time interval between two injections, it fluctuated between 2 and 16 weeks. It was decided to put a halt to the treatment in cases for which patients did not respond after 6 months. Verdicts to stop Omalizumab were never a result of secondary symptoms. Only one patient stopped his own treatment without consulting medical advice, and had not relapsed a year later. 30% of patients showed non-severe adverse events which disappeared after several injections.

**Conclusion:** In real life, out of 64 patients, individual and personalized treatment intervals when prescribing Omalizumab, allowed for a response rate far superior to clinical tests, with a clear progress with regard to patients’ quality of life.

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**1459 Efficacy of bilastine updosing in refractory moderate to severe chronic spontaneous urticaria**

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**Background:** Second generation H1-antihistamines (sgAHs) in licensed dose are the first-line treatment in chronic spontaneous urticaria (CSU). However, many subjects do not achieve a sufficient symptom reduction with this approach and require an updosing (refractory CSU). Evidence for the efficacy of sgAH-updosing in CSU is still limited.

**Objective:** To assess efficacy and safety of the sgAH bilastine in licensed (20 mg) and higher doses in refractory moderate to severe CSU.

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