OBJECTIVES: To assess the influence of the serotonin transporter variable number of tandem repeat (HTT-VNTR) polymorphism and the serotonin transporter-gene-linked polymorphic region (HTTLPR) polymorphism on development of side effects under antidepressant therapy. METHODS: A total of 109 depressive in-patients treated with various antidepressants according to local clinical practice were included in the investigation. Four weeks after admission to hospital, side effects were assessed by using a modified version of the dosage record and treatment emergent symptoms scale (DOTES). Differences in side effects between the genotype groups of both polymorphisms were analyzed using the Fisher’s exact test. RESULTS: A total of 65 patients received mirtazapine (25 of them in combination with other antidepressants), and 44 patients were predominantly treated with antidepressants acting via HTT, such as selective serotonin re-uptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs). When patients were treated with HTT-blocking antidepressants, a significantly higher occurrence of side effects in patients with the HTTVNTR 2.10/2.10 genotype (52.6%) than in patients with the 2.10/2.12 (12.5%) and 2.12/2.12 (0%) genotypes (p = 0.004) was found. With regard to the HTTLPR polymorphism, patients predominantly on HTT-blocking antidepressants with the s/s genotype...
suffered more frequently from side effects (50.0%) than heterozygotes (40.0%) and homozygotes for the l-allele (0%) (p = 0.002). In contrast, no association of the HTTVNTR polymorphism was found in patients treated with mirtazapine. The risk groups defined by a combined genotype from both polymorphisms demonstrated a major effect on the incidence of adverse drug events in patients treated with predominantly HTT-blocking antidepressants (p = 0.00018; low risk: 0%, 0/13, medium risk: 13.3%, 2/15, high risk: 62.5%, 10/16). CONCLUSION: These results support the hypothesis that both polymorphisms influence tolerability to drugs primarily acting via HTT inhibition, such as SSRIs, TCAs and venlafaxine. Tolerability to mirtazapine was not influenced, probably owing to a different mode of action. As there are limitations due to the heterogeneity of treatment and concomitant therapy, further studies are required to confirm the obtained results.