FC79 *Neurosciences, psychopharmacology and biological psychiatry*

CLONAZEPAM IN THE MANAGEMENT OF BENZODIAZEPINE ADDICTION

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Consurrent abuse of benzodiazepines (BDZs) is a major clinical problem, both among street addicts and during methadone maintenace (MM). Flunitrazepam shows high reinforcing properties and produces severe chronic intoxication because of its pharmacodynamic and pharmacokinetic characteristics, but many other BDZs (including midazolam, temazepam, lorazepam, lormetazepam, triazolam and others) have shown abuse liability both in animal models and in clinical settings. Social-cultural factors and the availability on the "gray market" account for further differences in the choice of specific BDZs in a given pharmaceutical form and way of administration. Adverse consequences of severe BDZ abuse/dependence include cognitive and behavioural disturbances and the BDZ discontinuance syndrome requires treatment. Clinical problems are even more severe among HIV infected clients. A first therapeutical step in the pharmacological management is substitution with drugs showing cross-tolerance and less or non abuse liability, like oxazepam and carbamazepine, followed by gradual tapering of the dose. Clonazepam, is a well-known anti-epileptic, mood-stabilizing and anti-panic agent sharing these characteristics. We report three clinical cases of methadone-maintained clients showing severe BDZ dependence treated with clonazepam. Oral clonazepam was given up to 10 mg/day in the first period of treatment, according to the level of tolerance and was prescribed for self-administration in an outpatient setting. After an initial titration of the daily dose, patients underwent medical counselling every few weeks in order to adapt the pharmacological regimen and reinforce their compliance with the treatment. Case 1. Male, 25 years was first prescribed BDZ when 8 for anxiety disorders, became addicted to opiates at 18. In MM at 35 mg/day, he was taking orally and/or injecting i.v. up to 50 mg/day of lormetazepam. Clonazepam was first administered 6-8 mg/day and successfully tapered within 2 months. Case 2. Female, 29 years, polydrug user since 16, suffering from dysthemia and gender identity disorder, asymptomatic HIV infected. In MM at 50 mg/day, she was taking oral flunitrazepam up to 20 mg/day and had already failed a substitution with carbamazepine. Clonazepam was started 8-10 mg/day and slowly tapered after 12 months since the patient decided to stop her MM in advance. Case 3. Female 32 years, polydrug abuser since 20 with seizures at 26, HIV infected with peripheral neuropathy. In MM at 90 mg/day, she was taking flunitrazepam 6 mg/day and lorazepam 10 mg/day orally. Clonazepam was given 6 mg/day and is still maintained as a substitution at 2-4 mg. Clonazepam proved to be effective and safe in the management of BDZ abuse/dependence among motivated MM clients, including those HIV infected and/or psychiatrically comorbid. Clonazepam may be viewed as a drug of choice since it seems non-addictive and well accepted. Anecdotal evidence of good outcome deserves controlled studies of retention and effectiveness among unselected patients.

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AFFECTIVE DISORDERS IN GENERAL HEALTH CARE

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We have previously demonstrated that paroxetine and amisulpride have comparable efficacy in the treatment of Dysthymic Disorder (DD). In the present study we evaluated whether there is a differential response to amisulpride and paroxetine in DD patients divided according to the age of onset. Moreover we analysed the clinical impact of these two drugs on relieving the cognitive symptoms as described by the alternative research criteria (Appendix B, DSM-IV). Eighty-four outpatients with a DSM-IV diagnosis of DD were included in the study. They were randomly allocated to treatment either with paroxetine or amisulpride. Patients who completed at least 8 weeks of treatment were considered for outcome analysis. Early- and Late-onset dysthymic patients showed a different response to study drugs. Comparing amisulpride-treated patients, a trend to a better improvement of both depressive and anxious symptomatology was observed in the Early-onset group. Conversely, Late-onset patients responded better to paroxetine showing at week 4 and 8 a lower MADRS score than Early-onset subjects ($p<0.05$). Preliminary results indicate that amisulpride improved a higher number of cognitive symptoms in the Early-onset group after 4 weeks of treatment even if at the end of the study there were no differences. Paroxetine improved a higher number of symptoms in the Late- than in the Early-onset dysthymic patients both at week 4 and 8 of the treatment.

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ADDITIONAL DISORDERS IN SCHIZOPHRENIA: INFLUENCE OF NEUROLEPTIC TREATMENT AND CORRELATION BETWEEN COGNITIVE PERFORMANCES AND CLINICAL FEATURES

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It's generally admitted that patients with schizophrenia present various degrees of attention disorders. With computerized tests, elaborated in our unit and aimed at evaluating quantitatively various attention modalities (attention centered on one sensorial modality, divided attention, selective attention and attention disturbances induced by various perturbers), we tried to determine the attention disorders in patients (30 cases) fulfilling the DSM-IV criteria for schizophrenia compared to normal subjects matched for age, sex, study level and marital status. In one group, the subjects were clinically stabilized under neuroleptic treatment for at least 15 days and in the other, the subjects were without psychotropic treatment for at least one month. Our data showed a global drop of the scores obtained by schizophrenics in all the tests regarding the mean reaction time and the error ratio. The schizophrenics are disturbed by aleatory stimuli and by orders referring to a category. They have difficulties in extracting pertinent information from context. NL seemed to have little influence: the results show a slight but significative tendency for a cognitive improvement under NL treatment. Our tests, however, showed great differences in attentional processes between patients which were correlated with negative and positive symptoms scored with the P.A.N.S.S. From this we conclude that correlational studies between cognitive deficits and clinical features are definitely possible. Our new research projects consist of specific studies about selective attention and information extraction from contexts which seem to be particularly disturbed in schizophrenic patients.

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ATTENTIONAL DISORDERS IN MAJOR DEPRESSIVE DISORDERS: RESULTS OF A COMPARATIVE STUDY USING COMPUTERIZED TESTS

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It is generally admitted that patients suffering from major depression present various degrees of attention disorders. Computerized tests, elaborated in our unit, are aimed at evaluating quantitatively various attention modalities (attention centered on one sensorial modality, divided attention, selective attention and attention disturbances induced by various perturbers). In this study, we tried to determine the attentional disorders in patients (15 cases) fulfilling the DSM III-R criteria for major depressive disorders compared to normal subjects matched for age, sex and study level. The first part of this study consisted of testing the drug free patients recognised as depressed (MADRS score >25). Secondly, these subjects were evaluated again one month later under antidepressive treatment and after clinical recovery. Our data showed globally low levels of the scores obtained by the depressed patient before treatment in all the tests. The main reaction times were particularly increased but the number of errors observed were similar to those of the healthy volunteers. These results can be explained as an adaptative cognitive strategy used by the patients in order to avoid errors. In the second part of the experiment the recovered patients have globally increased their performance. However, some attentional disorders seem to remain: the patients are still disturbed by aleatory stimuli and disynchronized informations even with a good clinical recovery (Mean MADRS score <5 and feeling by the patient of being not depressed). From this we conclude that our tests are sensitive and that standardized data collection allows studies of the cognitive tasks without bias due to non standardized stimuli. The results obtained by the depressed patient still showed some deficits indicating a potential subclinical attentional vulnerability. If we compare these results with our studies concerning schizohrenic patients we can emphasize that the attentional disorders between these two pathologies have rather different profiles.

https://doi.org/10.1016/S0924-9338(97)80525-1 Published online by Cambridge University Press