The role of quetiapine in the treatment of dissociative episodes in the acute phase

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Summary

Dissociative phenomena are characterised by alterations in the functions of conscienceness, memory, identity and perception. These are placed along a continuum ranging from normal daily experiences to real mental disorders that interfere with the performance of usual activities.

Dissociation may represent the foundation for specific disorders, Dissociative Disorders, as well as the prospect of symptoms of psychopathological conditions of various kinds.

This study has evaluated the clinical efficiency of quetiapine during dissociative episodes in the acute phase in patients referred in the last year to the Mental Health Centre (NHS Salerno). Participants in the study were subjected to the administration of a series of tests at the onset of symptoms (T0); after two weeks (T1); and after four weeks (T2). The assessment tools used were: the Dissociative Experience Scale (DES); the Brief Psychiatric Rating Scale (BPRS); the Clinical Global Impressions (CGI); the Global Assessment of Functioning (GAF). All observed patients showed an improvement in symptoms, no patients discontinued pharmacological therapy and side effects did not emerge which would have required the discontinuation of therapy. The analysis of the results showed that quetiapine monotherapy next to a good efficacy and tolerability may be a viable therapeutic option for the pharmacological treatment of dissociative episodes in the acute phase.

Key words

Dissociative episodes • Quetiapine • Treatment • Effectiveness

Introduction

The term "dissociation" refers to a separation of the different mental functions, which are no longer operating in parallel and in synchronisation [1].

Janet, introduced this concept for the first time at the end of the 1800s, which was defined as "a failure to integrate experiences normally associated with one another in the stream of consciousness" [2].

Apart from theories formulated by Janet many studies have dealt with the "phenomenon of dissociation", which has taken on different meanings over time, referring to set-ups sometimes antithetical.

Currently, the term lacks a coherent concept, as demonstrated by the different definitions and classifications of conversion and dissociative disorders present in the 'ICD-10 and DSM-IV.

According to the latter, the disconnection of functions, which are usually integrated, such as conscious, memory, identity and perception, represent the essential feature of dissociation. The ICD-10 defines it instead as a "partial or total loss of the normal integration between the memory, awareness of their own identity, sensations, and control of body movements". Both classification systems agree that the dissociation is of interest for the system, memory, conscious and personal identity.

However, the ICD-10 recognizes that it may also involve the sensory and motor systems, giving rise to so-called conversion symptoms; while the DSM-IV restricts the dissociation functions and systems of purely psychic nature [3 4].

On the other hand, it would be simplistic to refer to the dissociation only in pathological terms. Empirical evidence has shown that this is not an all or nothing phenomenon but rather how it should be placed along a continuum, which from transitional forms, of its own subclinic population, leads to episodes of greater qualitative and quantitative importance, so it can theorize the existence of a "dissociative spectrum".

Dissociative experiences from a descriptive and phenomenological point of view may arise as transitory and modest phenomena altering the sense of reality and itself, present in the non-clinical population. The phenomenon of *absorption* falls into this category, which refers to the tendency to engage their minds in situations of altered and highly focused attention, so as not to be aware of what is happening around.

Dissociation can also be seen as a fundamental and per-

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vasive symptom of specific diagnostic categories, such as *dissociative disorders*. In addition, many psychopathological conditions present dissociation as an associated symptom, including Schizophrenia, Post Traumatic Stress Disorder, Obsessive Compulsive Disorder, Eating Disorders, Borderline personality disorder [1 5 6].

Drug treatment and quetiapine

Quetiapine is a derivative dibenzotiazepinico multirecettoriale antagonist of serotonergic 5-HT2A, dopamine D1 and D2, istamimergici H1, α1 and α2 adrenergic receptors and partial agonist of the serotonin 5-HT1 receptors, and has a weak anticholinergic action, which is of limited clinical relevance [7].

Considering the 5-HT2A and D2 receptors, there is a higher affinity towards the former than the latter. This particular receptor activity profile gives uniqueness to the pharmacodynamic properties of the drug. It acts on mesocortical and mesolimbic dopaminergic structures, responsible for antipsychotic activity, and has a minimal effect on the nigrostriatal dopaminergic system, responsible for extrapyramidal side effects, and infundibular tuber, whose activation causes hyperprolactinemia [8 9].

The clinical pharmacokinetic studies have demonstrated that quetiapine is absorbed well and extensively metabolized in the liver, with a high "first pass effect" that results in a low bioavailability [10].

Quetiapine also has the ability to stabilize mood, reduce anxiety symptoms and, more generally, to have a positive impact on some psychopathological dimensions such as irritability, impulsivity, aggression, hostility and somatization [11].

Materials and Methods

There were 16 patients included in this study (6 males and 10 females) between the ages of 16 and 59 years (average age 43 years), all from the province of Salerno, referred last year to the Centre for Mental Health in the Local Health Authority of Salerno, during an episode of dissociative behaviour.

The sample recruited, belonging to the general population, it has not been subjected to any kind of sampling.

All participants in the study, at the time of that displayed no organic disease or mental, as well as detected by interview prior medical history, and that otherwise would have resulted in the exclusion from the research, nor traumatic elements have emerged noteworthy

It has also taken steps to inform about the aims of the study, treatment modalities, inviting participants to sign the informed consent, consistent with the standards of care in place [12 13].

The patients were tested with the following assessment scales, administered at the onset of symptoms (T0); after two weeks (T1); after four weeks (T2):

- the Dissociative Experience Scale (DES);
- the Brief Psychiatric Rating Scale (BPRS);
- the Clinical Global Impressions (CGI);
- the Global Assessment of Functioning (GAF).

The DES is a self-assessment scale designed to measure the level and type of dissociative experience present without going into the merits of the diagnosis. The 28 questions of the scale, describe a series of dissociative experiences, some of which fall within normal experiences, for which the patient has to indicate the frequency with which they occurred. The psychometric properties of the DES have been extensively studied and have proved to be excellent [14-16].

The BPRS is a hetero-assessment scale suitable for the evaluation of the clinical course and is an almost constant reference parameter in psychopharmacological clinical research. The scale consists of 18 items that explore many symptoms, characterized, each by a description. The total score of the scale can be taken as an expression of the severity of the disease.

Also were isolated 5 factors: I. Anxiety-Depression (ANDP), II. Anergy (NARES), III. Thought disorder (THOT), IV. Activities (ACTV), V. Hostility-Suspiciousness (HOST) [17-21].

The CGI is a global psychopathological rating scale that evaluates the effectiveness of treatment for psychiatric patients compared to the following three areas: severity of the disease; overall improvement; therapeutic/side effects effect. Each item is priced separately. There is a total score.

The scale being suitable for the evaluation of the clinical course is expected that the severity of the disease should be evaluated at the pre-treatment and at least once a post-treatment, in contrast to the improvement and the Global Effectiveness Index, for which no evaluation to the pre-treatment but only started treatment. Are possible (and advisable) mid-term evaluations at the discretion of the clinician [18].

The GAF allows a comprehensive assessment of the psychosocial and working functioning of the patient, placing him/her in a hypothetical continuum ranging from mental health to serious mental disorder.

It is a "universal" scale that can be used for all categories of patients and gives a single item rated on a scale from 1 to 100 [12].

The scale is suitable for the evaluation of the clinical course; the first evaluation (relative to the current condition) is performed at the time of taking charge of the patient and at least another assessment must be made at discharge [14 22-27].

The entire sample was treated with quetiapine IR at doses ranging between 200 and 900 mg; patients during the study did not undergo any other psychological or pharmacological therapies, with the exception of low doses of benzodiazepines.
The use of a pharmacological therapy, indicated in the literature as a possible therapeutic strategy, albeit secondary to an intervention of psychological and psychotherapeutic type, it was necessary after a careful assessment of the active symptoms, mainly characterized by dysregulation and emotional instability, disorganization thinking, irritability [28 29].
Quetiapine was found to be between molecules at lower risk of side effects, leading to higher long-term clinical compliance, going to act, specifically, on the psychopathological dimensions described above, favoring a reduction in quantity and quality.

Results

Statistical analysis was performed using the t-test for paired samples. As regards the assessment of specific symptoms, evaluated by the DES, significant differences emerged between the mean scores, onset, after two and four weeks, which over time tend to decrease, indicating a remission of dissociative symptomatology.
When visited at T0 and T1, all patients scored higher than 30, while when visited at T2, 6 patients (37.5%) had scores between 20 and 30, indicating a greater therapeutic effect of the drug after four weeks of intake (Table I).
With regard to the evaluation of changes in clinical and therapeutic effects, significant differences between the mean scores at T0 and T2 for the five factors investigated by the BPRS emerged (Table II).
This significant difference appears to be present also in the three areas of CGI and specifically:

- seriousness of the disease shows significantly lower scores between T0 and T2 ($F(2.36) = 80.75$, $p < .005$) (Table III);
- global improvement significantly in the first 4 weeks;
- effect therapeutic/side effects: no patient discontinued therapy and the side effects (dry mouth, drowsiness, restlessness) were not sufficiently serious to require interruption of the therapy (Table IV).

TABLE I.
Paired tests for DES.

		Mean	SD	t	df	p (2-code)
Pair 1	DES T0 - DES T1	10.8700	3.59071	12.109	15	.000
Pair 2	DES T0 - DES T2	27.0081	5.70916	18.923	15	.000

TABLE II.
Paired tests for BPRS.

		Mean	SD	t	df	p (2-code)
Pair 1	BPRS T0 BPRS T1	21,75000	4,20317	20,699	15	.000
Pair 2	BPRS T0 BPRS T2	45,56250	5,79619	31,443	15	.000

TABLE III.
Paired tests for CGI (Severity).

		Mean	SD	t	df	p (2-code)
Pair 1	Severity T0-T1	.50000	.51640	3.873	15	.002
Pair 2	Severity T0-T2	1.50000	.51640	11.619	15	.000

TABLE IV.
Paired tests for CGI (Improvement/Efficacy).

		Mean	SD	t	df	p (2-code)
Pair 1	Improvement T1-T2	.37500	.50000	3.000	15	.009
Pair 2	Efficacy T1-T2	1.56250	2.09662	2.981	15	.009

TABLE V.
Paired test for GAF.

		Mean	SD	t	df	p (2-code)
Pair 1	GAF T0-T2	-38.25000	4.80971	-31.811	15	.000

Finally, as regards the scores obtained from GAF, these had significantly increased after four weeks (Table V).
While at the first visit, all patients had a value less than 70, indicator of a pathology, at the next administration only seven patients (43.8%) achieved a score of less than 70, six (37.5%) between 71 and 80 (marginal presence of psychopathology) and three above 80 (absence of psychopathology).

Conclusions

Currently it seems to be accepted that there is a continuum in the dissociative experience which incorporate within it qualitative or quantitative symptoms different from dissociative phenomena present in the general population.
Although recent studies have shown high rates of prevalence of pathological dissociation in psychiatric patients, data appear to be still lacking as regards the types of treatment which are most appropriate for the dissociative symptoms.
The great handling and tolerability of quetiapine, as widely documented in the literature and confirmed by our clinical practice, suggests the possibility of its use also in psychopathological conditions other than schizophrenia.
Although the limitations of the study resulting from the small sample size and the sampling mode, which make little generalizable results, the data resulting from our studies, suggest that quetiapuine can be efficient and well-tolerated in the treatment of the dissociative episodes in the acute phase, showing an improvement in the psychopathological picture in terms of dissociative and social symptoms.

Conflicts of interest
None.

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