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RESISTANT DEPRESSIONS

Giuseppe Stranieri

Mental Health Center, Catanzaro Lido, Italy

SUMMARY

The concept of Resistant Depression was introduced for the first time in 1974 by Leiman. Despite the numerous studies in this regard, it was not possible to give a precise definition of this problem and to identify a safe etiology. This work aims to contribute through a literature review and exposure of two clinical cases, to better define and analyze this phenomenon by assuming the possible therapeutic strategies for patients with resistant depression.

Key words: *Resistant Depression – antidepressants – tricyclics – Monoamine oxidase inhibitors*

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INTRODUCTION

The term "Resistant Depression" is commonly used to indicate all cases of patients suffering from depression who do not respond to drug treatment in a satisfactory manner. From existing data in the literature, 30 up to 50% of Major Depressive disorders do not respond adequately to treatment with psychiatric drugs. When it is considered that Depression affects 121 million people worldwide with impaired work capacity and compromised social skills, and that in the most severe cases can cause suicide and is becoming in 2030, according to the WHO, the leading cause of inability and disability around the world, resistance to the treatment of depression becomes a key point for research and in the clinic, which surely needs to go deeper and be better specified, in order to limit the incidence and increase positive outcomes for people suffering from this disease.

The main instrument used to measure the severity of a depressive disorder and the improvements resulting from the treatment, is the Hamilton Scale (HAMD): the scale contains 17 variables, with a score of 3 to 5, a score of less than 7 indicates absence of disease, a score of 8 to 17 indicates mild depression, while a score of 18 to 24 shows moderate depression and a score of more than 25 a severe depression. It is possible to speak of healing when remission (defined as the condition in which the patient is free from depressive symptoms, with values at the Hamilton scale less than seven, and the maintenance of this state for six consecutive months), responds to treatment with a reduction of at least 50% of the baseline score on the HAM-D. and of non-response when the symptoms persist to the point of requiring a change of therapy, this condition corresponds to a reduction of less than 25% HAM-D.

The difficulties encountered in clinical practice in determining whether the failure to respond to a treatment protocol for patients with depression is due to a real resistance to therapy or as often happens to a pseudo-resistance, are often due to factors that are not taken into account, and that if on the contrary duly considered would reduce the incidence of DR reported in the literature.

Many authors have studied and identified several factors that promote resistance to the depressive therapy, with proper caution in interpreting the different clinical records, some factors seem to be consistent and predictive for a non-response to Depressive treatment, including: female sex, the age of onset of depressive disorder (before age 30 and over 65 years of age), family history of mood disorders, depressive symptom severity, chronic depressive episodes, which lasted more than two years, symptomatologic subtypes, psychiatric comorbidity, medical comorbidity, endocrine disorders, neurodegenerative diseases, dementia, tumors, head trauma, and premenstrual syndrome in women.

There is also a staging of the resistant depression proposed by Thase & Rush (1997), which includes six stages (from the O stage to the V stage), where the O level corresponds to a pseudo resistance, with no response to a first trial with AD proven inadequate to the doses and times, stage I as a non-response to a trial with AD at doses and with appropriate modalities; stage II indicates a non-response to two trials with AD of a different class; stage III shows a non-response to two or more trials of which at least one with a TCA (tricyclic antidepressant); stage IV a non-response with two or more trials of which at least one with MAOI (Monoamine oxidase inhibitor); stage V corresponds to a non-response to two or more trials of which at least one is associated to a cycle of bilateral ECT.

The current guidelines in the literature for the treatment of DR substantially provide the optimization of the pharmacological treatment, which consists in bringing the dosage of the drug to the maximum permitted. Such an attempt must be continued for a sufficient time to allow the appearance of a response. When this attempt does not work, there are two different ways to proceed:

- with switching, the replacement of the drug used with another antidepressant;

- with the strengthening, based on two different strategies: the augmentation (addition of an antidepressant drug which in itself is not antidepressant) and the combination (combination of two different antidepressants). Among the non-pharmacological therapeutic strategies there is furthermore electroconvulsive therapy/TEC.

There is not, at the moment, an optimal strategy and the pharmacological treatment of these non-responder patients is often empirical, a modality which can often become malpractice in failing to take into account other variables that frequently determine the "treatment resistance".

FIRST CLINICAL CASE

38 years old man, married with two children, a boy and a girl of four and seven years respectively. Positive medical history for psychiatric disorders (mother with depressive disorder). Graduate, he worked as a cattle farmer, a heavy smoker, he suffered before the entry into prison, from panic attacks which he treated with SSRIs that have allowed him to have an acceptable psychic balance.

Sentenced to life imprisonment for murder, he is in prison with the regime of 41a since four years. From the clinical diary of the prison we know that he is suffering from a major depressive disorder resistant to therapy and for this reason has been subjected to various treatment protocols, starting with the optimization of the treatment, proceeding with the switching and finally with the combination. He currently takes: Cypralex 20 mg daily; Cymbalta 60 mg daily; Seroquel 400 mg daily; Alprazolam 30 gtt. Stilnox 10mg in the evening. His clinical condition requires admission to a hospital ward, also considering the suicidal intentions manifested by the patient. From the MMPI personality test, the Hamilton Scale score higher than 24, the Roscharch test and the from the physical examination, the patient shows all the requirements for a diagnosis according to DSM 5, of a grave Major Depression.

SECOND CLINICAL CASE

35 years old woman, married with two daughters aged 15 and 12, currently unemployed graduate, has been working in a commercial studio until seven years ago. Came to our attention after several hospitalizations in SPDC and after practicing various drug therapies, whereof the last one included the consumption of: Daparox 20gtt. per day; Chrono Depakote 500 mg twice a day and 100 mg of Seroquel, which had not altered the health condition of the woman. From the interview and physical examination emerged a clinical picture compatible with a Major Depressive Disorder, characterized by marked weight loss, depressed mood with episodes of crying, social withdrawal, anhedonia, apathy and fatigue, insomnia and irritability. After a few sessions, in a climate of trust and empathy, the patient spoke of what she said she had never told anyone. Her husband, a businessman, used to beat her up for being morbidly jealous as well as forcing her to leave her job and demanding sexual performances with various perversions and obliged her to accept wife swapping. She did not have the strength to divorce because she was not economically independent and she was afraid of revenge by her husband, also knowing that their children adored their father. About a year ago she fell in love with a man much younger than herself whom she met on Facebook, and now she is afraid that her husband might come to know.

DISCUSSION

It should be said that the response to pharmacological treatment with antidepressants and with all psychiatric drugs in general, as shown by a recent meta-analysis of meta-analyses is superior to many other medical maintenance therapies, six times more, for example, than the response to ACE inhibitors in heart failure, and that the improvements made from the 50's to the present day in the treatment of depression have been remarkable. This does not mean that a certain percentage of depressions do not respond to drug therapy. But what is important is to check whether the resistance to drug therapy is due to the drug itself or to all those variables that are often not considered and that are instead significantly affecting the outcome of the treatment.

The two clinical cases that we have presented show that it is not enough to base a diagnosis on a diagnostic manual such as DSM IV or DSM 5, and that a non-response to a therapeutic protocol is not sufficient to speak of "treatment resistance", because some living conditions such as a life sentence under the 41a and the daily violence suffered by the patient in the second case, cannot be cured by the administration of drugs, but with something different that often cannot be found.

So, apart from considering that depressions that perhaps are not simply depressions, which should make us psychiatrists think about how far we have gone beyond the psychopathology in talking about depression, it is important to carefully evaluate the patient's medical history, to consider the factors that affect the resistance to therapy as the clinical and psychiatric comorbidity, the non-adherence to therapy, the subtypes of depression, and primarily determine whether it is a depressive disorder or a state of existence that inevitably flexes the mood in a depressive sense.

Regardless of the innocence or guilt of the patient in the first case, to know that he must spend the rest of his life in a prison, living isolated with one hour out of the cell per day, seeing his family once in two months for one hour, will originate despair and sadness of life that cannot ever be eliminated with drug therapy. As well as living with a pathologically jealous and violent man, a controlling father, this cannot be solved by the use of medicines.

It is therefore a necessary to train psychiatrists not only on the pharmacological side, but also on the psychological and relational one, so as to encourage taking charge of the depressed patient 360 degrees and so as to be able to identify and treat those human and existential factors, which often are the cause of a non-response to therapy.

CONCLUSIONS

There is no "depression," but there are "depressions".

Today depressions respond to drug therapy as much as other medical pathologies. The resistance to therapy in depression is in a high percentage of cases not directly due to the action of the prescription.

A training for psychiatrists that is able to deal not only with the pharmacological aspects, but also with the psychological, social and existential ones is essential. The biological variables that determine resistance to treatment are not yet known.

Resistant depression is a problem that should not be underestimated in terms of epidemiological, clinical and financial issues.

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Correspondence:
Dr Giuseppe Stranieri
Mental Health Center
via Milano 28, 88024 Girifalco, Italy
E-mail: straniti@virgilio.it