Study the Impact of Neuroleptics Features on the Hypothalamic-Pituitary-Adrenal (HPA) in Schizophrenic Patients Admitted To Psychiatric Hospital-Annaba-Tested For Suppression to Dexamethasone (0.5 Mg)

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Abstract: Schizophrenia is a disease with the determinants multi-factors, it was announced to be associated with an abnormal activity with the hypothalamic-pituitary-adrenal axis (HPA). It is a study referred to before and after, it focused on 32 patients hospitalized at the emergency admission unit of the psychiatric hospital ER-Razi Abu Bakr Annaba; the period from September 2012 to December 2013. Two blood samples were taken, one before the administration of dexamethasone (0.5 mg tablet) (pre dex) and the other after administration of the tablet (post dex). Our results revealed 56% of no suppression cortisol after suppression test of dexamethasone. The results of this research claim that neuroleptics do not affect the suppression test with dexamethasone. The high rate of non-suppression told us a lot about the quality of hospital care is insufficient.

Key words: Dexamethasone • Schizophrenia • Neuroleptics • Cortisol

INTRODUCTION

Schizophrenia is a disease with the determinants multi-factors, interactions of a genetic vulnerability tested by external factors [1]. It was announced to be associated with an abnormal activity with the hypothalamic-pituitary-adrenal axis (HPA) [2, 3]. This last, is one of the two principal systems of answer to the neuro endocrine stress [4]. The phenomenon of stress is generally associated with one on activation of the axis and an increase resulting from glucocorticoïdes, studies found plasmatic cortisol levels high among certain schizophrenic patients compared to the pilot subjects [5-7]. Cortisol is a peripheral marker of the operation axis (HPA) [8].

The dexamethasone is a hormone glucocorticoïde of synthesis. It removes the endogenous cortisol secretion for one period of 24-48 H by an effect of negative feedback on the hypothalamic-pituitary-adrenal axis [9].

It was brought back by Carroll et al. [10] that the test of suppression of dexamethasone (DST) is specific for the diagnosis of the melancholy with a sensitivity of 67% and one specificity of 96%. Although one believed being a test which was very specific for the melancholy or endogenous depression, of many reports/ratios revealed considerable rates of prevalence of no suppression of other groups of diagnosis such as schizophrenia, the insanity and the disorders panics [11, 12].

In 1985, A. Baumgartner et al. [13] made a first study using the test of suppression to the dexamethasone (DST) among seriously sick acute schizophrenes and at healthy volunteers, the result of this study shows that the cortisol level post DEX among schizophrenes was higher than that found at the subjects centres. The most probable explanation of the high incidence of nonsuppression among the schizophrenes in this study it is the fact that there are only acute schizophrenic patients seriously sick. Another group of researchers noted that the schizophrenes presented a frequency of 30% of abnormal answer to the DEX [12, 14, 15, 16].

The nerve sedatives are the principal drugs used in the treatment of schizophrenia. They do not cure the disease, but they contribute to look after it by attenuating some symptoms. While taking in consideration interest that the nerve sedatives bring to this pathology and while basing on opinion contradictory of Arana et al. [11] which affirms that the nerve sedatives do not assign the result
of the test of suppression to the dexamethasone (DST), of Dewan et al. [15] which ensure in their turn that it not removal of cortisol after the DST could be due to the nerve sedative treatment and of Tandon et al. [17] which found a reduction in the rate of no removal of cortisol after DST after a nerve sedatives treatment and on the fact that none of these researchers evoked the characteristics of these treatments (type of treatment, routes of administrations, posology, type of therapy, duration of treatment), our study focuses on highlighting the impact of neuroleptics on the DST in studying the influence of their features on this test.

**MATERIALS AND METHODS**

It is a study referred to before and after, it focused on 32 patients hospitalized at the emergency admission unit of the psychiatric hospital Abu Bakr ER-Razi Annaba; the period from September 2012 to December 2013.

We received the authorizations on behalf of the legal guardians of the patients for the development of the subject and the publication of the data.

**Characteristics of the Studied Population:** Our sample consists mainly of schizophrenic patients admitted to the emergency department. He was selected randomly within this group. The diagnosis of the disease was made by the psychiatrist doctor at the first interview with the patient and that based on the diagnostic criteria of DSM-IV [18].

We excluded from the study Outgoing schizophrenic patients were on immunosuppressive, chronic carrier or they did not accept this study.

100% of the recruited patients were under nerve sedatives treatment.

**Work Method:** Consultation of the files of the patients and collection of important information (age, place of habitat, factors starting pathology, pathology), (type of treatment, number of treatment prescribe, their routes of administrations, posology and lasted of treatment), (number of admission). The duration of treatment is the period of treatment taken from the first psychiatric admission until the time of the study.

We also recorded the treatments which did not form part of the psychiatric range, the biochemical assessment of admission of the patients, any pathology which is not related to the psychiatric disorder.

We measured the intensity of the disease based on the items of the BPRS (Brief Psychiatric Rating Scale) [19]. The Brief Psychiatric Rating Scale (BPRS) [19] includes 18 items (distinct symptoms), the listing of these items and as a result (Figure 1):

The items of the BPRS questionnaire were completed by a single person and in the presence of the psychologist service.

**Tests with the Dexaméthasone, Taking Away Blood and Proportionings:** The blood samples are carried out in two recoveries before and after test with the dexaméthasone (Pre-DEX and Post-DEX). The blood collected in dry tubes is centrifuged to 3000 rpm during 15 minutes with 4°C. The plasma obtained aliquot in tubes éppendorf and is preserved at a temperature (-20°C). It will be used for proportionings of cortisol.

A first taking away is carried out the first day (Pre-DEX) with jeun eight hours of the morning. The dexaméthasone is managed by oral way in the form of compressed with low dose (0.5 Mg) at 11 o'clock in the evening the same day [20]. The following day per same hour (eight hours of the morning), a second blood sample obtained (Post-DEX). Plasmatic cortisol is measured by proportioning immunological in electro chimiluminescence (ECLIA, module Elecsys 1010, Roche).

We recorded the time between taking antipsychotic treatment (patient admission) and the administration of dexamethasone is the "duration of DST", this period begins with the admission of the patient and stops the time of testing by against the intake period is extended even after the test.

Sampling was carried out by nurses of the service.

**Statistical Analysis of Data:** Differences between means were assessed by Student's t test, a Pearson correlation test was also carried out when necessary. The level of statistical significance \( p \) retained was 0.05. These tests were carried out by the statistical software XLSTAT in its version 7.5.2. The mean values were presented with the standard deviation as a dispersion index.

After exploratory analysis aimed at uncovering outliers and collinearity, a linear model using cortisol Post Dex as a response variable and other explanatory variables (age, gender, treatment, length of treatment, etc.) was performed using the package “leaps” which looks for best subset selection. A forward stepwise selection was also carried out to check for the best model based on Mallow’s Cp. Following the unsuccessful attempts to fit a linear model. Statistical analyses were carried out using R (R Development Core Team 2014). The level of statistical significance \( p \) retained was 0.01.
RESULTS

Our study was carried out on a troop of 18 patients of male sex (56%) with a Middle Age of (34, 79±9, 74 years) and 14 patients of female sex (44%), with a Middle Age (34, 14±9, 66 years).

Our results show a significant difference between the rate of cortisol pre dex (15,508±5,578) and post dex (9,326±8,369) with a significant difference (p=0.001). The dexamethasone suppression test (DST) showed: 56% of no suppression and 44% suppression of cortisol after DST.

100% of patients have experienced stressful events, which are: unemployment was reported by 19% of patients, sentimental deception (25%) and the death of a loved one (3%), family conflicts (50%), addiction (3%).

This study can not be said that these factors are the cause of the outbreak of the disease; because the medical records of patients do not provide information on the subject, but they play an important role in the persistence of the disorder, worsening of the disease which responds to relapse. Outgoing schizophrenic patients.

The BPRS total score of the questionnaire indicated 81% of patients with schizophrenic symptoms are severe. The results of the questionnaire will be illustrated in Figure 2.

The Characteristics of Neuroleptics: We recorded 2 groups of patients with "times DST" close to the inlet (2 ± 1.9 days) and away from the inlet (34 ± 44 days), the difference is significant between the duration (p = 0.007).

(84%) of patients were on antipsychotics against first generation (16%) were of Second-generation antipsychotics (Table 1). The most common neuroleptic association was: Haldol-Nozinan with (66%).

Table 1: presentation of types according to their generation antipsychotics

Typicals neuroleptics (first generation): Nozinar®(lévomépromazine), Haldol®(halopéridol), Largactil®(chlorpromazine), Loxapac®(loxapine)

Atypical neuroleptics (second generation): Risperdal® (rispéridone), Zyprexa®(olanzapine), Solian®(amisulpiride).

Our study showed that (53%) of patients were on antipsychotics orally.

Figure 3 shows the relationship between cortisol post dex "CortPost" and other variables collected (age, duration of treatment, duration of admission and number of admission).

This figure indicates that there is no significant correlation between these cortisol post dexamethasone and quantitative variables. The values of the correlation coefficient "r" will be indicated in Figure 3.

Similarly, boxplots between cortisol post dexamethasone and qualitative variables (sex, routes of administration, Dosage and type of neuroleptic, number of neuroleptic), no correlation is identified. This will be demonstrated in Figure 3.

Two analyzes of variance have nevertheless been performed to confirm the boxplots (routes of administration and Dosage). They confirm the no correlation between the two variables and cortisol post dexamethasone. One-way ANOVA: F1, 30 = 2.8, not significant "ns" for Ways and F2, 29= 1.2, ns Dosage).

We performed a correlation test between cortisol post dex and duration of DST, no association is obtained by this test (p = 0.4).
Fig. 3: The link between cortisol post dex "CortPost" and other variables collected ("age", "duration of treatment", "duration of admition" and "number of admission").

The legend of Figure 3:
CortPost=cortisol post dexamethasone
Durée Tr: duration of treatment
Durée Ad: duration of admission
Nadmi: number of admission
This figure indicates that there is no significant correlation with cortisol levels post dex (CortPost) and:
- age avec r=0,099
- duration of treatment (DuréeTr) avec r=-0,031
- duration of admission (DuréeAd) avec r=-0,14
- number of admission (Nadmi) avec r=-0,19

P is obtained (p > 0.05)

DISCUSSION

The present investigation proceeded in hospital medium and comprises many de features:

- The choice of the subject: no research studied the anomalies of the axis hypothalamic-pituitary-adrenal caused by the test of suppression to the dexamethasone among schizophrenes in Algeria.

- Few scientific investigations even aucunes did not study the influence of the characteristics of nerve sedatives on the result of DST and thus on axis HPA, such as the routes of administrations (oral and injectable) which different by their speed of resorption and their biodisponibility [21].

Our investigation did not record any significant association between the quantitative or qualitative variables and the cortisol rate post dex. This wants to say that these parameters did not influence the answer of DST (suppression/ no suppression). This report comes in agreement with the results from Arana et al. [11] and Carroll et al. [10], but contradicted those of Dewan et al. [14] or Tandon et al. [17].

The duration of the DST does not explain cortisol levels post dex, this parameter is very important because the time between the admission of the patient (treatment socket) and when the test dexamethasone suppression was achieved can be indication of the effect of neuroleptics on this test. To confirm this observation, a Pearson correlation test was performed (p = 0.4).

All these findings argue that neuroleptics with their prescribing patterns do not affect the test.

This report pushes us to seek the factors which could influence these data, one can already draw aside the anomalies related to the gland suprarenal or hypophyseal likely to influence the results of this test, much of studies noted a relation between the age and the result of DST [22, 23], but this factor is not excluded seen the no correlation of this one with the cortisol rate post dex. Separately the nerve sedative treatment, the patients did not take any drug which could deteriorate the result of the DST and which did not form part of the psychiatric range.
Sex

Number of neuroleptic

Type of neuroleptic

Dosage

Routes of administration

Fig. 4: Representative diagram of box plots between cortisol post dex and qualitative variables (Sexe, routes of administration, dosage, type of neuroleptic and number of neuroleptic)
The assessment of this study affirms that the treatment of schizophrenia cannot be reduced to the therapeutic use of only one method, the psychotropic ones must be associated with no pharmacological measurements aiming at supporting the observance, to make acceptable lived of the patient and with stage these deficiencies. They must be thus accompanied by psychotherapy. On those, this article has as an obligation to propose a therapy easy to include/understand and easy to practice and which is taking scale and interest by the experts around the world especially in France and which is the cognitivo-behavioral therapy which was started with much success [28].

The doctor psychiatrist must also help the schizophrenic patient to include/understand his pathology, to recognize the schizophrenic symptoms, to put the patient in contact with reality, to discuss the causes of the release of their pathology and their hospitalization and especially to make take part the family of the patient in the meetings of therapy.

Apart from the hospital structure, the Algerian state must provide intermediate structures of readjustment and of rehabilitation, because, after their exit of the hospital, one finds the patients wandering in nature, completely rejected by their family or folded up in a corner.

**CONCLUSION**

The results of this research have been able to achieve the main objective of the study by stating that the neuroleptic treatment with prescription methods practiced does not influence the result of the suppression test with dexamethasone.

The feature that makes this survey addition to the result of the effect of neuroleptics on the DST, is the highlight of a reverse very inadequate hospital treatment vis-à-vis these patients.

Indeed, the strong positivity of DST (56%) is higher than that found in the literature in schizophrenia and the lack of effect of neuroleptics on the DST, support idea discussed in the article that schizophrenics of this institution are not treated as they should be.

Suites results of this study, we affirm that the effectiveness of antipsychotic treatment depends on the quality of work that the practitioner to the patient.

Finally, improving the quality of life of schizophrenic patients in the hospital of Annaba is a necessity.
REFERENCES


