

Disorders of Corticotrope Axis: Hypercortisolemia and Post Traumatic Syndrome at Women Raped and Abused by Their Spouses, Algeria

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Abstract: To emphasize the importance of violence against women and to measure the consequences in terms of health for the female population; our study has been launched on traumatized women who were raped and subject to domestic assaults. The aim is to explore the response of the HPA axis (The hypothalamic–pituitary–adrenal axis or Corticotrope axis) and locate a possible predisposing hypercortisolism installing a PTSD (Post Traumatic Stress Disorder). The dosage of morning cortisol calculated in 38 abused women within the structure AFAD (Association Female Algerian for Development) compared with seven (07) control women who have not suffered any trauma, our results clearly indicate depression suggested desensitization of the HPA axis (Adrenocorticotrophic Axis) and validate significantly higher rate than the control. The move towards PTSD is imminent to support the neurophysiological damage in these subjects.

Key words: Women • Domestic Violence • Cortisol • PTSD • Depression • Stress

INTRODUCTION

Violence is a major problem that affects billions of women: globally at least a third of these women have already been beaten; forced to have sex or abused in some other way, most often by someone from their knowledge including their husbands. The family and especially the couple are indeed places where violence against women are the most numerous [1]. Name-calling, hurtful, humiliation, excessive jealousy, exit ban, confiscation of revenues, slapping, beating, rape, forms of violence are many and they compromise heavily social, economic and political women's inclusion. Violence-related trauma can occur after a person has been victim of sexual, physical or emotional abuse or neglect [2]; this trauma is seriously disrupting the balance of the victim. It can lead to mental disorders: disorders of appetite, anorexia/bulimia, disorders of sleep, nightmares, cognitive disorders, anxiety, feelings of shame and guilt, loss of self-esteem, self-confidence and spontaneity, psychological distress, depression, suicide [3]. Some authors address injuries as a psychosocial stress, it involves the memory, learning, so emotional and limbic Brain [4]. Sometimes adds stress posttraumatic depression (PTSD) associating with nightmares,

"flashback" [5], which can occur when a person feels the effects of trauma long after the event in question occurred [6].

The hypothalamic - pituitary - adrenal axis called axis ACTH is particularly involved in the responses of the body facing a stressful situation. Disturbance of this axis are undoubtedly the neuroendocrine anomaly the more extensively described in Psychiatry and during severe depressive episodes where the vast majority of studies, hypersecretion of cortisol [7], has highlighted it especially. This hormone has many effects on most of the organs; to control the protein metabolism; mostly carbohydrates and fats. It intervenes mainly in Adaptive responses to stress [8]. Through this study, we proposed to explore the response of the axis adrenocorticotrophic via morning cortisol levels in women who have suffered various attacks. The aim expected to identify any hypercortisolism to substantiate the neurophysiological attacks, predisposing the facility of a PTSD.

MATERIALS AND METHODS

Experimental Lots: The present study conducted on 47 female sex individuals between the ages of 14 to 84 years; including 38 suffered various violence (physical, sexual...).

They are selected at time of their takeover by the AFAD and are compared to a control population of seven women has not undergone any violence. The patients selected for this study, were distributed after the trauma they have suffered, more or less violent, depending on the nature and duration of violence, they are broken down into 4 lots, compared to a seven women healthy control lot.

Control Lot T: Women volunteered for the experiment (n = 7).

Lot V1: They suffered rape during the last 12 months (n = 7).

Lot V2: These women suffered rape for at least three years (n = 7).

Lot AC1: They have been victim of spousal assault in the year past (n = 12).

Lot AC2: Women of this lot (n = 12) were a spousal assault for at least three years.

Blood Samples and Determination Cortisol: The venous blood sampling is performed, the admission of patients at 8 o'clock in the morning, to the medical analysis

laboratory. The blood sample is doing on a disinfected skin at the level of the elbow, collected into EDTA tubes. After centrifugation, immediate, for 20 minutes at 3500 rpm, plasma, aliquot in Eppendorf tubes, frozen to -14°C. The determination of plasma cortisol was make by electrochimiluminescence (E.C.L.I.A.) that test is suitable for immunoassay analyzers Elecsys 1010 [9]. This immunological test allows determining quantitative *in vitro* cortisol in serum and human plasma.

Analysis of the Results: The results are expressed as mean (X), multiplied by the standard deviation (S) and analyzed by ANOVA testing, Student's t test and the test of Dukey.

RESULTS AND DISCUSSION

The results show an increase in the number of affected women, so since 2008 the number to almost triple at the end of 2011. Studies in this area are consistent with these data; this progression explained according to the World Health Organization (WHO) by means of supports as well as the increase in associations (UNIFEM, CMHC, FNSF, CLFC and SOS) local and international supported bringing statistics at higher levels.

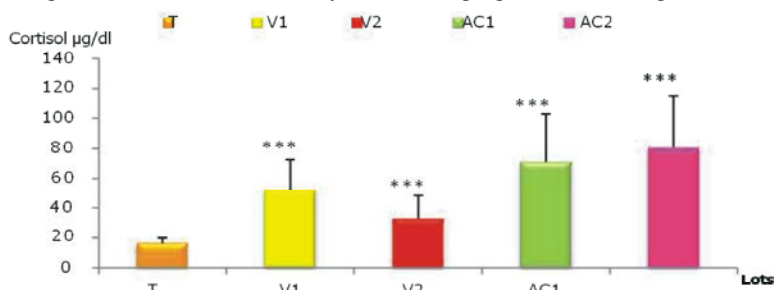


Fig. 1: Cortisolemie from 8: 00 in the morning: T (n=7), V1 (n=7), V2 (n=7), AC1 (n=12), AC2 (n=12).

*** p<0.001: difference very highly significant T (n=7) vs V1 (n=7), V2 (n=7), AC1 (n=12), AC2 (n=12). We find that regardless of the time there are significant differences between the witness and lots who have suffered trauma.

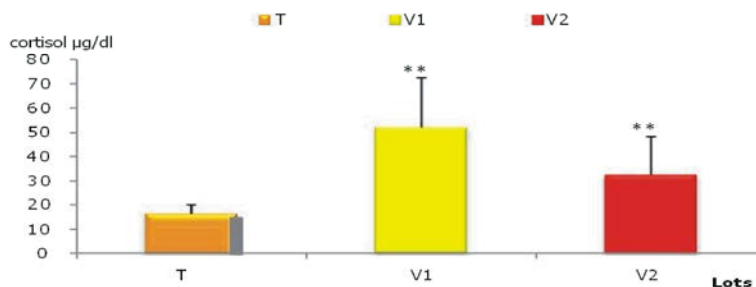


Fig. 2: Cortisolemie from 8: 00 in the morning: T (n=7), V1 (n=7), V2 (n=7).

** p<0.005: highly significant difference T (n=7) vs V1 (n=7), V2 (n=7).

We can see that regardless of the time there are significant differences between the control and violated lots.

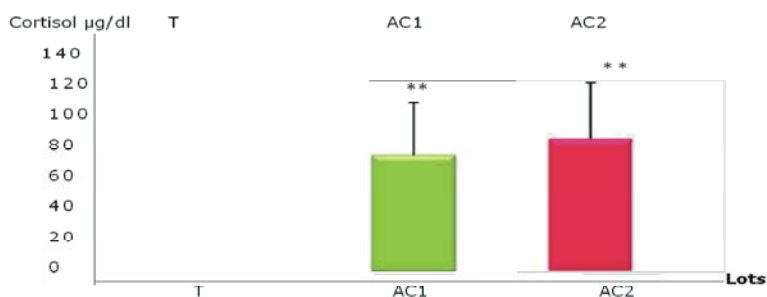


Fig. 3: Cortisolemie from 8: 00 in the morning: T (n=7), AC1 (n=12), AC2 (n=12).

** p<0.005: highly significant difference T (n=7) vs AC1 (n=12), AC2 (n=12).

We find that regardless of the time there are significant differences between the control and the lot of spousal assault.

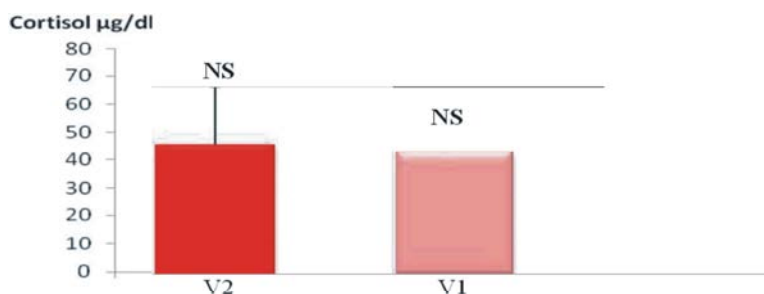


Fig. 4: Cortisolemie from 8: 00 in the morning: V1 (n=7) vs V2 (n=7).

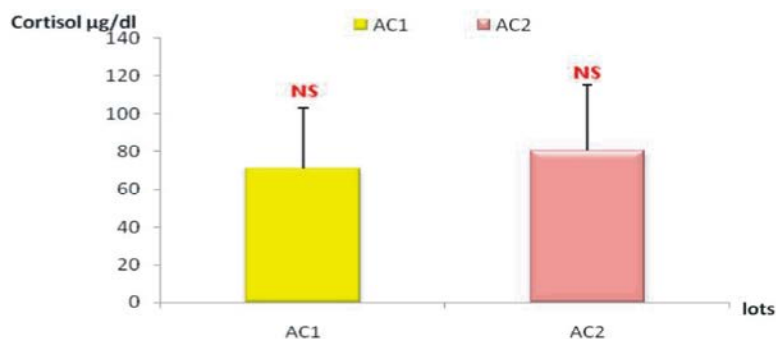


Fig. 5: Cortisolemie from 8: 00 in the morning: AC1 (n=12) vs AC2 (n=12).

The comparison intra-lots of the raped and spousal assault. is statistically insignificant. Time has no effect on the deregulation of cortisol levels.

Table 1: The Morning Cortisol Levels (8 hours).

| Parameters / Lots | Mean (X) | Deviation type (s) |
|----------------------------------|-------------|--------------------|
| Control T (n= 7) | 16.38428571 | 3.675748709 |
| Raped 1 « V1 » (n=7) | 52.05857143 | 20.57391101 |
| Raped 2 « V2 » (n=7) | 32.63428571 | 15.70965187 |
| spousal assault 1 « AC1 » (n=12) | 71.0375 | 32.17642534 |
| spousal assault 2 « AC2 » (n=12) | 80.55916667 | 34.59943627 |

During this survey addressed women express a deep malaise that sometimes dispute them unable to expressed their feelings fully. This malaise is a clear sign of a victimization maintained by taboos and often-demeaning practices. The violence that occurs most often in marital homes isolate victims and disputes often-nonexistent

harder contact. Silence observed after attacks helps make the victim more isolated and allows the progressive installation of depression, attempted suicide and anxiety symptoms often ignored. These disturbances sometimes directly perceived hide most important violations affecting the psychological neuro-immuno sphere [10-12]. The development of phobias and immune disturbances are the index a disturbed brain homeostasis [13-15].

Since the work of Cannon [16] and Selye [17] on stress, Corticotrope Axis is placing at the center of these perturbations mainly from work on laboratory animals. Thus, trauma are acting in a manner similar to stress but affect cognitive abilities in an indelible time [18, 19]. It was

during the phase of resistance resulting from the reaction of alarm that the activation of the hypothalamic-pituitary axis moved by activating the secretion of hormones glucocorticoids from the adrenal glands [20, 21]. It was then thought that the general adaptation syndrome (GAS) was a general response stereotype; In fact, the conditioning of subjects, aimed to prepare for the stress, shows that the answer is not as stereotypical, it therefore appears that the general reaction can be adjusted specifically according to the experience of the subject [22-24].

It is the Limbic System, which is directly involved in this modulation of the hypothalamic depending on experience reaction since the limbic system receives information from the environment and the body [25-27]. The evaluation of stress through the complex limbic system / cortex is therefore more important than the stress itself for the programming and implementation of the response to stress [28]. Here, the acquisition or training are essential to easily produce a specific response [29-31]. Hypothalamic stimulation causes a general stereotypical inappropriate response to stress which increases the impact of stress and the emotional discharge [32].

Above a certain threshold ; Glucocorticoids (GR) exert a negative feedback on brain structures and thus limited the duration of exposure of the body to these steroids to minimize the deleterious effects (catabolic and immunosuppressive effects). Keller and Wood [33] have shown that activity and reactivity of the Corticotrope axis depend on two types of receptors: Mineral Receptor (MR) and GR. It is classically well established; that the GR control the secretion of corticosteroids in response to stimulation [34, 35], while the MR determine the basal activity of the Corticotrope axis [36, 37].

The Corticotrope axis varies during the circadian rhythm, so the intensity of the negative feedback by glucocorticoids is increasing at the time of the active phase of the Diel cycle [38]. The intensity of feedback on brain structures such as the hippocampus is higher under acute stress than in a situation of chronic stress [39-41]. Three structures are clearly distinguishable as the key players of the negative feedback of glucocorticoids on the Corticotrope axis: hypothalamus, pituitary and adrenal glands [41, 42].

Extra structures Hypothalamic (seahorse) also mediate negative feedback by glucocorticoids [43, 44]. Corticosteroids, by their affinity receptors, play a key role as well on the basal activity control of axis adrenocorticotrophic (MR) on the modulation of the intensity and the duration of response to stress (MR and

GR) [45, 46]. Glucocorticoids regulate electrical activity of some neurons in the hippocampus, which could explain the change in behavior involving the limbic structures [47].

At the same level of adrenal glands, glucocorticoids directly regulate steroidogenesis [48] by inhibiting the expression of the enzymes involved. The sensitivity of adrenal to ACTH (Adreno Cortico Tropic Hormone) is a key control factor in plasma levels of glucocorticoids in basal situation after a stress. Many factors and conditions may determine the tissue sensitivity to corticosteroids [49]; it comes to the availability of extracellular and intracellular hormones, levels of expression of glucocorticoid receptor and the affinities of binding [39]. The secretion of corticosteroids is the result of implementing various neuroendocrine factors, whose action is not only regulated by environmental factors (circadian rhythm, stress), but also to regulating them [50]. Thus the slightest imbalance of a complex system and involved in many vital functions, causes a failover of the body to a medical condition [51, 52].

The activation of receptors for glucocorticoids (GR) has a facilitator action on serotonin synthesis by activating the synthesis of tryptophan hydroxylase, key enzyme in the synthesis of 5-HT [53]. The GR are also abundant in the adrenergic neurons and activate the synthesis and the release of noradrenaline in response to stress following the activation of the Locus coeruleus that causes an increase in vigilance and anxiety in animals [54, 55]. In our study, we recorded an increase in plasma cortisol, for 4 lots: the raped less than a year (52.058 ± 20.573 $\mu\text{g/dl}$), the raped more than one year (32.634 ± 15.709 $\mu\text{g/dl}$), less than a year domestic assault (71.037 ± 32.176 $\mu\text{g/dl}$), over a year spousal assault (80.559 ± 34.599 $\mu\text{g/dl}$) compared to control. We talk about (PTSD) post-traumatic stress syndrome when the symptoms last more than a month (they begin often several weeks after the event). The duration of disorders can be from a few months to several years. Without treatment, time brings no improvement. Flashback, contorted almost 'impossible to control, punctuate the life of the subject. It relives in imagination, in standby or sleep state, the memory of the traumatic event in detail (images, smells, etc.) [32, 56].

In about half of cases, a complete healing occurs in three months while many other topics have symptoms that persist for more than 12 months after the trauma. We have to treat the condition of Stress Post causes car: 30%, of people suffering posttraumatic stress may develop depression, 25% have anxiety disorders (panic attack,

obsessive-compulsive disorder, generalized anxiety disorder, phobias...) [57, 58]. Taking as example veterans of the Viet Nam veterans, having developed a PTSD, have a strong decrease in the urinary excretion of cortisol compared to normal subjects [27] and an average of the lowest cortisolemie measured at several periods of Diel [59-61].

Galman and Angelin [62], working on a valid model of PTSD in macaque monkeys where the animal was housed in cages with a device allowing it to injure voluntarily called self-injurious behavior (SIB), examined the relationship between the animal behavior and changes in the cortisolemie. Monkeys with SIB showed persistent dysregulation of the Corticotrope axis would thus be able to modify the functioning of certain populations of receptors in the brain and in particular corticosteroids selectively and final at the level of the limbic system.

Studies forms among the suffering PTSD Viet Nam veterans reported that the right hippocampus volume decreased 8% [35, 63 and 64]. In PTSD who had a history of sexual abuse, the volume of the hippocampus (left) reduced by 12% [65, 66]. These same subjects recorded a surge in the rate of CRF. More the hippocampus is big, it is efficient and therefore more information forwarded to the memory to long term [67, 47, 66]. The hippocampus is a cervical structure very vulnerable to stress, which can cause, under chronic exposure, a neurotoxic effect including the destruction of the dendritic connections, Inhibition of neuronal Genesis and a disorder in the metabolism of glucose [68, 69]. This neurotoxic effect can result in atrophy of the hippocampus, which makes it small and becomes less effective, increases vulnerability to stress and brings holes of memory [70]. In short, a smaller hippocampus is less effective and so hampers memory, thus harming the learning process.

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