

ASSOCIATION BETWEEN AFFECTIVE DISORDERS AND THE USAGE OF LOW AND MEDIUM DOSES OF CORTICOSTEROIDS

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SUMMARY

It is well known that high doses of corticosteroids can induce psychiatric disorders, especially the maniacal states. However there are only a few studies that investigate the effects of low and medium doses of such drugs used for a long period of time on the patient's mental health. The aim of the study was to investigate the prevalence and severity of affective disorders among the patients using up to 40 mg of corticosteroids (prednisone or equivalent). 54 patients during the corticosteroid therapy and 51 healthy controls were assessed with the use of the following questionnaires: Hypomania Checklist 16 (HCL-16), Beck Depression Inventory (BDI) and authors' questionnaire. The results were analysed using SPSS Statistics version 12.5. The results indicated statistically significant differences in the prevalence of hypomania and depression between controls and study group. There were no evident correlations between either the dose or the length of the therapy and the severity of affective disorders. The study has shown that the usage of corticosteroids doses below 40 mg does have an effect on the prevalence of affective disorders. The occurrence of hypomania and depression was more common among the study group. To assess correlations further studies are needed.

Key words: affective disorders – hypomania - corticosteroids

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INTRODUCTION

It is well known that corticosteroid can induce the occurrence of psychiatric side effects including mania and depression. Many studies have shown that the prevalence of those symptoms is dose dependent, which means that higher doses are more likely to cause the psychiatric side effect (Sherwood 1999). These led to the assumption that psychiatric side effects are reversible on dose reduction (Michael 1981). Studies suggest that around 10% of patients taking high doses of corticosteroids develop affective disorders (Stiefel 1989). Most of the studies suggest that psychiatric side effects of corticosteroid therapy have rapid onset and that they develop in the first two weeks of the treatment (Hall 1979). The data imply that doses of at least 30 mg of prednisone per day are sufficient to induce the psychiatric symptoms (Chan 1981). However there were a few studies that examine the effect of low and medium doses on prednisone or equivalent on the affective disorders. Varney et al. (1984) report the occurrence of dementia after 2 weeks of 20mg/d prednisone therapy, which was a reduction from 100mg/d used for 4 months. The aim of this study was to investigate the association between the occurrences of depression and hypomania and the usage of up to 40 mg of prednisone of equivalent per day.

MATERIALS AND METHODS

The study was approved by the Bioethical Committee of the Medical University of Silesia. The participants were selected from adults on internal, rheumatoid and pulmonology wards in Katowice. The patients

were divided into two groups, the study group containing 54 patients and the control with 51 healthy adults; an informed consent was obtained from every participant. The patients were questioned using the following scales: Authors' Questionnaire, Beck Depression Inventory (BDI), Hypomania Checklist-16 (HCL-16). The effect of steroids on psychiatric disorders was calculated by converting all the doses into their prednisone equivalent.

MEASURES

The authors' questionnaire

The authors questionnaire consisted of 6 questions regarding age, sex, diagnosis associated with steroid usage, type of the steroid drug, dosage and the length of the therapy.

Beck Depression Inventory

The Beck Depression Inventory (BDI) is a 21-item, self-report rating inventory that measures characteristic attitudes and symptoms of depression (Beck 1961). It is designed for individuals aged 13 and over, and is composed of items relating to symptoms of depression such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex. (Beck 1972).

Hypomania Checklist-16 [HCL-16]

The Hypomania Checklist 16 is a shortened version of Hypomania Checklist 32, which is a questionnaire

aimed to identify hypomanic features in patients with major depressive disorder. It asks about 16 behaviours and mental states that are either aspects of hypomania or features associated with mood disorders. The sensitivity (83%) and specificity (71%) of the 16-item version were very similar to those for the full 32-item HCL (Kelly 2010).

Data analysis

The statistical analysis was performed using SPSS Statistics version 12.5. The results were considered statistically significant when the significance level (p) was lower than 0.05.

105 people were originally enrolled in this study. Subjects were divided into two categories; the research group consisted of patients and the control group of healthy persons. The first set consisted of 21 men and 35 women aged from 24 to 78 years (mean 49.6, SD 13.7). In this group every patient was undergoing corticosteroid therapy. The second set consisted of 22 men and 29 women aged from 21 to 74 years (mean 41.6, SD 14.5). None of them was receiving corticosteroid treatment.

The average result obtained by the first group in the BDI was 15.1 (SD 7.3) which stands for mild depression. An interesting thing is that women achieved greater score in the analysis as their result was 16.3 (SD 7.8) while men obtained 13.0 (SD 6.0). Whereas the mean score received by the patients from control group was 5.1 (SD 4.6) which stand for minimal depression. In this group of women and men the result for women was 4.6 (SD 4.7) and for men 5.8 (SD 4.5). The Student t-test for independent samples revealed statistically significant difference between the result of BDI in control group and study group ($p=0.00$, $t=8.4$) (Figure 1).

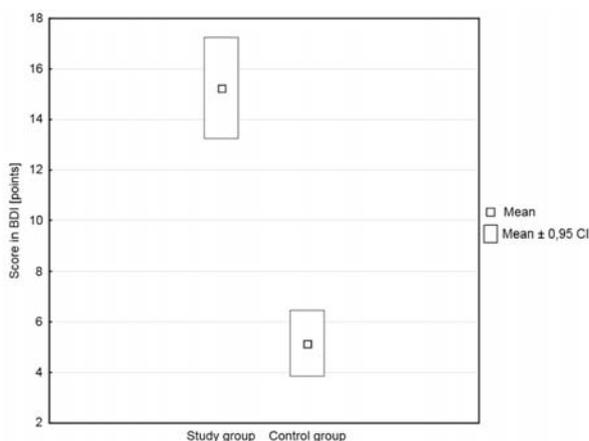


Figure 1. Framed chart illustrating differences in BDI score between study and control groups

The results of HCL-16 scale are more complex. Patients receiving steroids achieved 8.4 (SD 4.0) while healthy people obtained 7.1 (SD 2.5). What is more The Spearman's rank correlation coefficient revealed sta-

tistically significant correlation between duration of treatment and score in HCL-16 ($R=-0.33$, $p=0.043$) (Figure 2, 3).

Neither the dose of steroids nor sex had statistically significant effect on score.

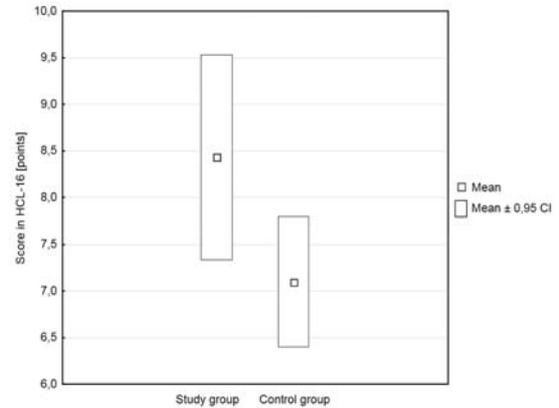


Figure 2. Framed chart illustrating differences in HCL-16 score between study and control groups

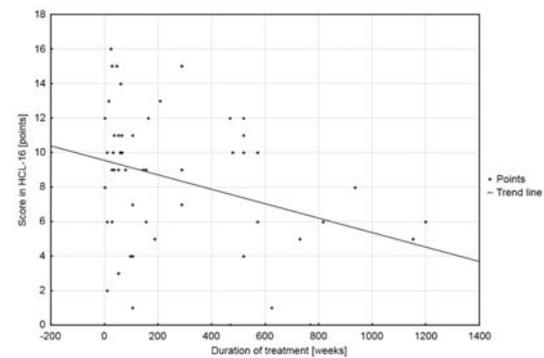


Figure 3. Correlation between the duration of the corticosteroid treatment and HCL-16 score

DISCUSSION

The effect of corticosteroid therapy on induction of depression (Ismail 2002) and other affective disorders has been observed for a long time (Ahmad 1999, Wada 2001). This is a well-known and documented phenomenon (Murphy 1998, Sherwood 1999), but the mechanisms of its formation remain unclear. According to some authors, the dose received does not affect the severity and duration of affective disorders (Ismail 1995), while others suggest that such a connection exists (Stiefel 1989). This study has shown a correlation between the duration of corticosteroid usage and higher results in the Hypomania Questionnaire (HCL-16). Patients who were undergoing the corticosteroid therapy for longer period of time presented less severe hypomanic syndromes. This implies a decrease in the occurrence of hypomania and the severity of its symptoms along with the time of the treatment. The authors believe that a reason for this is that longer exposure to elevated corticosteroids concentration can lead to

downregulation of corticosteroid receptors in the central nervous system. It occurs when receptors have been chronically exposed to an excessive amount of neurotransmitters, whether endogenous or drugs, and thus prevents the disruption of hypothalamo-pituitary-adrenocortical axis. In addition to this, the average result in the control group was 7.1 (SD 2.5) compared to 8.4 (SD 4.0) in the study group which suggests that the effect of long term steroid therapy does not have a serious impact on the exaggeration of symptoms of hypomania.

Another test used by the authors was Beck Depression Inventory (BDI). The mean result obtained by the study group was 15.1 (SD 7.3), which indicates mild depression while in the control group the mean score was 5.1 (SD 4.6) what indicates minimal depression. The increased severity of depression in people in the group cohorts confirms the effect of corticosteroid medication on the induction of depression. However another reason for such results may be the primary disease itself rather than the corticosteroid usage. Some illnesses, which require steroid treatment, are severe and there are no chances for the full recovery, while other may be less serious. This affects the patient's mental health and results in increased intensity of affective disorders. The study did not demonstrate that higher corticosteroid doses increase the risk of developing symptoms of depression. Some of the patients who were taking 40 mg of prednisolone or equivalent showed less severe symptoms of depression than those who were on lower than 12 mg doses. In addition, there is no correlation between gender and the prevalence of depression.

Interestingly, the women in the trials scored higher, as their mean result was 16.3 (SD 7.8), while men scored 13.0 (SD 6.0). This observation is consistent with the results of other studies, which show that depression is second most common disease among women (Kantorska-Janiec 2012) and much more frequent than in men, although there are many factors in such a distribution. Men choose to visit a doctor less often (Real 2011). In addition, a man can perceive the disease as a weakness and because of this, many of them do not undergo diagnosis. The authors presume that the reason for this is the stereotypical male representation in Poland as a head of a family. Other important causes may be "male depression" (Walinder 2001), and this results in the failure to recognize depression despite having reported the patient to a specialist (Dudek 2016). It has a different course and it is noticed in the patient's behaviour, which is difficult to catch during a medical history. It is worth noting that in the control sample the situation is reversed. The mean score of women was 4.6 (SD 4.7) and was lower, on average by men 5.8 (SD 4.5). Perhaps this is the problem of under diagnosing depressive disorders in men. The BDI questionnaire is anonymous, which gives the patient the feeling of comfort and the ability to freely and honestly assess his mental state. Other factors

considered by the authors may be the different number of men in both groups. Equalizing the numbers of men in both groups could result in obtaining similar results to the study group.

CONCLUSION

The aim of this study was to investigate the effect of low and medium doses of corticosteroids on the prevalence of hypomania and depression. The analysis revealed that there is a correlation between the usage of up to 40 mg of prednisone or equivalent and the occurrence of hypomania what matches the results of other studies. In case of prevalence of depression no correlation was found what makes the authors assume that the primary disease rather than the corticosteroid usage causes the incidence of this disorder.

No psychiatric intervention was administered during the course of our study, given its observational nature. One limitation of the research is its relatively small sample size; all of the presented results should, therefore, be confirmed in a large prospective study.

As data suggest the rapid onset of psychiatric side effects the patients should be seen in a follow-up soon after imitating therapy, preferable within a week. Along with monitoring weight, glucose and blood pressure patients should be asked about mood swings and symptoms of depression and observed for signs of mania, such as increased energy, rapid speech and insomnia (Sherwood 2001). Since the psychiatric side effects of these medications are of concern to all the physicians it is essential to raise awareness among them about the possibility of mentioned disorders in order to improve the efficacy of the treatment.

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Contribution of individual authors:

Marcelina Czok: design and conception of the study, collection and analysis of data;

Aleksandra Ćwiek: design of the study, data collection;

Bartłomiej Kurczab: data analysis, literature searches;

Krzysztof Kramarczyk: data collection, literature searches

All authors participated in the final revision of the manuscript and approved it.

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