Brief Report

Low-Dose Cortisol for Symptoms of Posttraumatic Stress Disorder

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Objective: Because elevated cortisol levels inhibit memory retrieval in healthy human subjects, the present study investigated whether cortisol administration might also reduce excessive retrieval of traumatic memories and related symptoms in patients with chronic posttraumatic stress disorder (PTSD).

Method: During a 3-month observation period, low-dose cortisol (10 mg/day) was administered orally for 1 month to three patients with chronic PTSD in a double-blind, placebo-controlled, crossover design.

Results: In each patient investigated, there was a significant treatment effect, with cortisol-related reductions of at least 38% in one of the daily rated symptoms of traumatic memories, as assessed by self-administered rating scales. In accordance, Clinician-Administered PTSD Scale ratings assessed after each month showed cortisol-related improvements for reexperiencing symptoms and, additionally, in one patient for avoidance symptoms.

Conclusions: The results of this pilot study indicate that low-dose cortisol treatment reduces the cardinal symptoms of PTSD.

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Posttraumatic stress disorder (PTSD) is characterized by traumatic memories that can manifest as daytime recollections, traumatic nightmares, or flashbacks in which components of the event are relived (1). These symptoms reflect excessive retrieval of the traumatic memory, which usually retains its vividness and power to evoke distress for decades or even a lifetime. We have reported previously that an elevation of glucocorticoid levels inhibits memory retrieval in animals and healthy human subjects (2, 3). Because excessive retrieval of traumatic memory is a cardinal symptom of PTSD and, additionally, patients with PTSD often show low baseline cortisol levels (1), we investigated whether administering cortisol might attenuate the incidence or intensity of traumatic memories.

Method

Patients were diagnosed with the German version of the Clinician-Administered PTSD Scale (4) and fulfilled the diagnostic criteria for chronic PTSD according to DSM-IV. Exclusion criteria included alcohol or substance abuse and changes in psychotherapy or pharmacotherapy within 3 months of the start of the study. After complete description of the study to the patients, written informed consent was obtained. The study was approved by the ethics committee of the University of Zurich, Switzerland.

During a 3-month observation period, low-dose cortisol (10 mg/day of hydrocortisone; Galepharm, Küsnacht, Switzerland) was administered orally for 1 month (mean=27.3 days, SD=1.2) by using a double-blind, placebo-controlled, crossover design. Study medication was administered once a day in the late morning to Mr. A and twice daily (5 mg at noon and 5 mg in the evening) to Ms. B and Mr. C.

To assess possible treatment effects on traumatic memories, the patients daily rated the intensity and frequency of the feeling of reliving the traumatic event and the physiological distress felt in response to traumatic memories and nightmares (self-administered rating scales from the Clinician-Administered PTSD Scale questions). In addition, reexperiencing/intrusion, avoidance, and hyperarousal symptoms were rated by a trained interviewer each month by using the Clinician-Administered PTSD Scale.

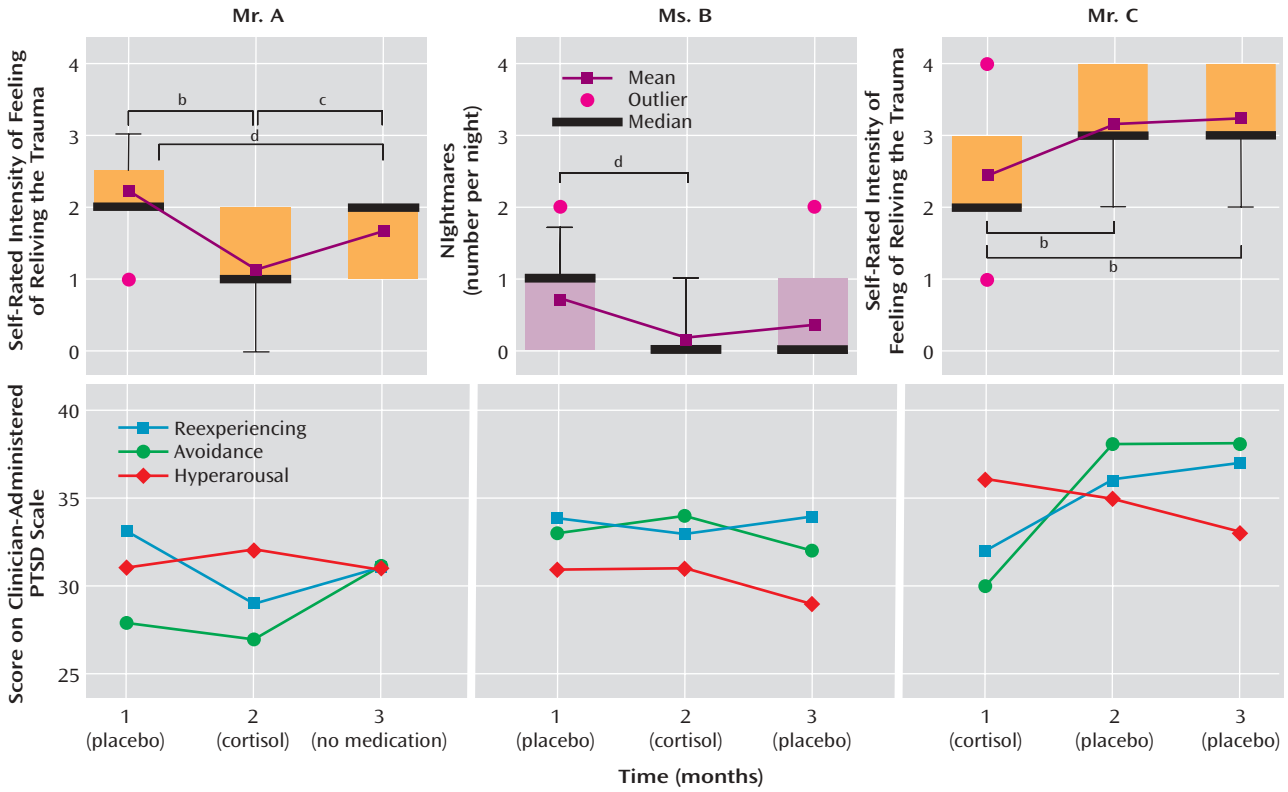
Single-case statistical analyses with Kruskal-Wallis nonparametric tests were performed to assess treatment effects on daily symptom ratings over the 3 months. Post hoc comparisons used Bonferroni-corrected Mann-Whitney U tests.

Results

Mr. A was a 50-year-old man who survived a terrorist attack 4.5 years before inclusion into the study. Psychotherapy and pharmacotherapy (oxazepam for sleep disturbances) was continued during the study. There was a significant treatment effect for the intensity—but not frequency—of the feeling of reliving the traumatic event (χ^2= 32.1, df=2, p<0.001, Kruskal-Wallis nonparametric test) (Figure 1). Of interest, the intensity ratings during the last study month (with no medication) were significantly lower (Mann-Whitney U=213, df=53, p<0.005, with Bonferroni correction) compared to those during the first month (placebo), suggesting a carryover effect of cortisol. There was also a significant treatment effect for the intensity—but not frequency—of physiological distress (χ^2=6.7, df=2, p<0.05, Kruskal-Wallis nonparametric test; data not shown). Twenty-four-hour urinary cortisol excretion for Mr. A was 307 nmol/24 hours at baseline and 336 nmol/24 hours during the last day of the cortisol month.

Ms. B was a 40-year-old woman who experienced a life-threatening physical assault 1 year before inclusion in the study. Pharmacotherapy (tramadol hydrochloride for pain) was continued during the study. She underwent no psychotherapy before or during the study. There was a signifi-

FIGURE 1. Effects of Cortisol Administration on Symptoms of Three Patients With Chronic PTSD[a]



[a] The panels at the top show the most significant treatment-related change in frequency or intensity among the daily self-rated symptoms of traumatic memories for each patient. Whiskers that start at the boxes indicate the 10th and the 90th percentiles of the distribution, respectively; the top and bottom of each box indicate the 75th and 25th percentiles. The panels at the bottom show symptoms from the Clinician-Administered PTSD Scale that were assessed by a trained interviewer each month.
[b] Significant difference between time points ($p<0.001$, Bonferroni-corrected Mann-Whitney U test).
[c] Significant difference between time points ($p<0.01$, Bonferroni-corrected Mann-Whitney U test).
[d] Significant difference between time points ($p<0.005$, Bonferroni-corrected Mann-Whitney U test).

cant treatment effect for the frequency—but not intensity—of nightmares ($\chi^2=13.9$, df=2, $p<0.001$, Kruskal-Wallis nonparametric test) (Figure 1). No significant treatment effects were detected for the feeling of reliving the event and physiological distress in the self-administered rating scales. Collection of urine for cortisol analysis was not possible in this instance.

Mr. C was a 55-year-old man who had a severe car accident 8 years before inclusion in the study. Pharmacotherapy (chlorprothixene and mianserin for agitation and sleep disturbances) was continued. He underwent no psychotherapy before or during the study. To control for possible treatment order effects, he received cortisol in the first month, followed by 2 months of placebo medication. Significant treatment effects were detected for the intensity of the feeling of reliving the traumatic event ($\chi^2=30.4$, df=2, $p<0.001$, Kruskal-Wallis nonparametric test) (Figure 1), the physiological distress ($\chi^2=64.0$, df=2, $p<0.001$, Kruskal-Wallis nonparametric test; data not shown), and the frequency of nightmares ($\chi^2=7.8$, df=2, $p<0.05$, Kruskal-Wallis nonparametric test; data not shown). Twenty-four-hour urinary cortisol excretion was 87 nmol/24 hours at baseline and 206 nmol/24 hours during the last day of cortisol treatment. None of the patients complained about treatment-related disturbances of everyday memory upon questioning.

Discussion

The major finding of this study was that in all three patients investigated, low-dose cortisol treatment had beneficial effects with significant reductions of at least 38% (average rank) in one of the daily rated symptoms of traumatic memories. Notable improvements were also observed in Clinician-Administered PTSD Scale ratings for reexperiencing and avoidance symptoms but not for hyperarousal symptoms (Figure 1). It is possible that cortisol administration reduced avoidance by reducing reexperiencing symptoms.

Of importance, patients with chronic PTSD often show low basal cortisol levels, and people with reduced cortisol excretion in response to a traumatic event have a higher risk of developing subsequent PTSD (1). Moreover, there is evidence for the preventive effects of cortisol as prolonged administration of stress doses of cortisol during intensive care treatment reduces the risk for later PTSD (5). In view of our previous findings in animals and healthy human

subjects (2, 3) together with the present results, it is possible that cortisol reduces the risk and symptoms of PTSD by inhibiting excessive retrieval of traumatic memories. Furthermore, by inhibiting memory retrieval, cortisol may have weakened the traumatic memory trace over time and thereby reduced symptoms even beyond the treatment period. Findings of a recent neuroimaging study (6) indicate that cortisol acts in the medial temporal lobe to reduce memory retrieval. Alternatively, cortisol administration may have reduced PTSD symptoms by altering cortisol feedback regulation. The findings that cortisol administration (10 mg/day) for 1 month did not cause side effects and does not suppress endogenous cortisol production (7) suggest a low risk of chronic cortisol treatment at this dose.

The present findings provide the first evidence to suggest that the administration of cortisol reduces the symptoms of PTSD. Future studies with more patients and longer treatment periods are required to evaluate the efficacy of cortisol treatment for PTSD.

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