Brief report on cognitive function and corticosteroid therapy in elderly

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Abstract

Glucocorticoids (GCs) are drugs commonly used for the treatment of a great number of acute or chronic pathological conditions. In a cross-sectional study we analyze a cohort of elderly patients treated for at least four weeks with a glucocorticoid (GC), exactly prednisone therapy, for a renal or rheumatological condition pointing out on functional, mental and clinical status. The main purpose was to assess change in cognitive performances. Corticosteroids administration also at low dosage in older subjects could enhance cognitive function. This observation should be proved in larger population and underlying mechanisms studied in deep.

Introduction

Glucocorticoids (GCs) are drugs commonly used for the treatment of a great number of acute or chronic pathological conditions. In particular are often the first choice for inflammatory or autoimmune disorders in rheumatological and nephrological field. It’s well known that GCs cause, among other side effects, also a significant alteration in behavior reaching in some circumstance personality traits modification and psychiatric events.1 Corticosteroid psychosis was the term adopted to describe a rapid and dramatic onset with psychotic and manic symptoms after acute or also chronic administration of GCs.2 In addition, they cause cognitive impairment of different severity from mild cognitive impairment to dementia1,3 but except through case-reports or series with few cases the relationship between GCs and cognitive function was less evaluated. In a cross-sectional study we analyze a cohort of elderly patients treated for at least four weeks with a glucocorticoid (GC), exactly prednisone therapy, for a renal or rheumatological condition pointing out on functional, mental and clinical status. The main purpose was to assess change in cognitive performances.

Materials and Methods

Study population

Our analysis comprised patients over 65 years old recruited from January to October 2018 starting corticosteroid therapy for a rheumatological or renal condition. Prednisone treatment was a continuous und current daily prednisone medication (between 5 and 25 mg) for at least 4 weeks. Clinical and laboratories data were collected. The local Ethic Committee approved the study and all patients gave written informed consent. Subjects underwent a geriatric assessment of functional and cognitive status. We excluded subjects with: i) toxic or pharmacological exposure, excessice alcohol use and pre-existing pharmacological treatments associated with cognitive impairment; ii) severe reduction of renal function (estimated glomerular filtration rate (GFR) under 30 mL/min stage 4 National Kidney Foundation); iii) tumor.

Patients’ history was carefully recorded by interview and confirmed by checking patients’ record, also recording drug prescription. Clinical examination, including assessment of BMI and blood glucose, was performed. Blood pressure was measured three times, and the average value was considered for data analysis.

Assessment of cognitive functions

Cognitive functions were assessed by Montreal Cognitive Assessment (MOCA) a brief screening instrument to detect Mild Cognitive Impairment that assesses multiple cognitive domains including attention, concentration, executive functions, memory, language, visuospatial skills, abstraction, calculation and orientation.4 5 Behavioral symptoms were evaluated with Neuropsychiatric Inventory Scale (NPI, score 0-144).

Clinical and laboratories data

Health status was assessed by the Cumulative Illness Rating Scale (CIRS, score 0-14) scoring system that can classify all medical conditions within 14 organ systems: cardiac, vascular, hematological, respiratory, ophthalmological-oto-rhino-laryngological, upper gastrointestinal, lower gastrointestinal, hepatic-pancreatic, renal, genitourinary, musculoskeletal-tegmental, neurological, endocrine–metabolic-breast and psychiatric.6 Daily life functions were assessed by Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL). The Medical Outcomes Study (MOS) Sleep Scale assessed sleep outcomes.7

Blood samples were taken in the morning before any food intake. Traditional biochemical parameters were measured at baseline in all subjects, following standard methods in the routine clinical laboratory. eGFR was assessed using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation8 in according with European Renal Best Practice Group guidelines for the management of older patients with CKD.9

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 20 and the Prism package (ver. 4.0; GraphPad Software, La Jolla,
CA, USA) package. The level of significance was set at p-values <0.05. Continuous variables are expressed as means±standard deviations or medians, as appropriate. Comparisons between continuous data were performed by 2-sample t test or analysis of variance for continuous variable.

Results

Our analysis comprised 40 patients (30 women, 10 men). 33 with a rheumatologic disease and 7 with a primary glomerulonephritis. No racial differences were present in the population. Participants had a mean ± SD age of 73.90±8.07 (ranging from 67 to 82 years old). Tables 1 and 2 show the main demographic, clinical and laboratory characteristics of enrolled patients. Daily life functions were assessed preserved in our population. The MOCA yielded a mean score of 21.38±4.32 before treatment (T0) and 24.30±3.30 after (T1) steroid therapy (P<0.000). Neuropsychiatric Inventory Scale doesn’t change significantly between T0 and T1. Analysis of single MOCA items showed a difference from T0 to T1 significative in visuospatial/executive domains (P<0.000), attention (P<0.000), abstraction (P<0.000) and Short-Term Memory/Delayed Recall (P=0.001), but not significative for orientation and language. MOS Sleep Scale showed not significant differences.

Discussion

Main findings from this pilot study suggest that low dosages of corticosteroids are able to positively affect cognitive function. In particular we showed significative differences in visuospatial/executive domains, in attention, in abstraction and in short term memory/delayed recall. Among many other well-known systemic effects GCs have a direct action on central nervous system. Endogenous release of GCs, acting on receptors located in different areas of the brain, control sleep-wake cycle, stimulate memory and learning processes and influence moods and hunger regulation. In literature is documented the appearance of psychic signs after prolonged treatment with corticosteroids. Acutely enhanced GCs level increases synaptic plasticity and facilitate hippocampal-dependent cognition while enduring exposure worsens cognition with long-lasting detrimental influences on hippocampal function, including altered adrenal steroid receptor density, neurotransmitter content and dendritic atrophy. GCs could act eliciting specific brain area with changes in glutamate release. The downstream effect resulting from GCs- Glutamate receptors interaction could be specific of neuronal populations and possibly individual neurons. There is evidence that acute increases of GCs and chronic stress decrease synaptic glutamate re-uptake and clearance. Acute and chronic stress stimuli differ in GCs exposure length (from hours to days to weeks), and investigations into whether this differentially modulates neurotransmission are ongoing. Regarding the significative positive effect of GCs on memory in our population, acutely administered glucocorticoid are known to dose-dependently enhance memory consolidation but as De Quervain et al. previously demonstrated, a single administration of cortisone (25 mg) 1 h before retention testing impairs free recall of words that have been learned 24 h earlier.

Conclusions

In this pilot study, we investigated patients treated with low to moderate doses of prednisone, widely used in clinical practice. Corticosteroids administration in older subjects could enhance cognitive function. This observation should be proved in larger population and underlying mechanisms studied in deep.

| Variable                                      | T0 (n=40) | T1 | P       |
|-----------------------------------------------|-----------|----|---------|
| Cumulative Illness Rating Scale (CIRS)        | 27.9±4.90 | 7.1±3.8 | NS      |
| NPI                                           | 6.0±5.3   | 18.1±4.7 | NS      |
| MOS Sleep Scale                               | 21.38±3.32| 24.30±3.30 | <0.0001 |
| MOCA score*                                   | 4.82±1.10 | 4.95±1.19 | NS      |
| Orientation                                   | 3.2±1.12  | 3.8±1.10 | 0.001   |
| Short-Term Memory/Delayed Recall              | 3.32±0.99 | 3.9±0.95 | <0.0001 |
| Executive Function/Visuospatial Ability*      | 2.8±0.40  | 2.7±0.46 | NS      |
| Language Abilities                            | 0.82±0.78 | 1.25±0.54 | <0.0001 |
| Abstraction*                                   | 2.17±0.59 | 2.35±0.48 | NS      |
| Attention*                                    | 4.2±1.20  | 5.25±0.74 | <0.0001 |

*P statistically significant.
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