Cognitive Dysfunction in Patients with Renal Failure Requiring Hemodialysis

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ABSTRACT

Background and Objectives: Renal failure patients show significant impairment on measures of attention and memory, and consistently perform significantly better on neuropsychological measures of memory and attention, approximately 24 hours after hemodialysis treatment. The objectives are to determine the cognitive dysfunction in patients with renal failure requiring hemodialysis. Materials and Methods: A total of 60 subjects comprising of 30 renal failure patients and 30 controls were recruited. The sample was matched for age, sex, and socioeconomic status. The tools used were the Standardized Mini-Mental State Examination and the Brief Cognitive Rating Scale. Results: The patients showed high cognitive dysfunction in the pre-dialysis group, in all the five dimensions (concentration, recent memory, past memory, orientation and functioning, and self-care), and the least in the 24-hour post dialysis group. This difference was found to be statistically significant (P=0.001). Conclusion: Patients with renal failure exhibited pronounced cognitive impairment and these functions significantly improved after the introduction of hemodialysis.

Key words: Cognitive dysfunction, hemodialysis, uremia, renal failure

INTRODUCTION

Uremia was characterized as being, primarily, a neurobehavioral syndrome, as far back as 1839.[1] Sustained attention and mental processing speed appeared to be the neuropsychological functions most sensitive to uncorrected uremia in patients with end-stage renal disease.[2]

Till the early 1960s, a diagnosis of chronic renal failure meant a long, agonizingly slow, or an abrupt painful death, as the ultimate outcome for most of the patients. However, with the advent of dialysis and later of transplantation, this scenario has changed to a large extent.

The importance of understanding these issues was highlighted as far back as 1967, when Crammond,[3] commented on the need to study the psychological aspects of renal transplantation. Other researchers like Kemph,[4] Short and Harris,[5] Ferris,[6] and Penn[7] also reported prominent psychiatric morbidity existing in chronic renal failure.

In the modern era, neuropsychological testing on uremic patients, who showed significant impairment on measures of attention and memory, performed significantly better on neuropsychological measures approximately 24 hours after their last hemodialysis treatment, compared to non-dialyzed patients.[1]

This study, therefore, examines the neurocognitive deficits in renal failure patients requiring hemodialysis, before and 24 hours after hemodialysis, and compares them with individually matched controls.
Also, we realize that most of these chronic renal failure patients mainly interact with a purely medical unit, with no access to mental health professionals, resulting in their mental health needs remaining unfulfilled.

**MATERIALS AND METHODS**

**Participants**

We recruited participants with renal failure, requiring hemodialysis, from the Inpatient Department of Medicine of the Father Muller Medical College and Hospital (FMMC). The subjects in the ‘control group’ were recruited from the medical and surgical wards, with well-preserved renal function, from the FMMC.

Individuals were eligible to participate if they at least had a primary level of education, were diagnosed to have renal failure requiring hemodialysis for the first time. No subject (case or control) had a history of dementia, clinically evident cerebrovascular disease, depression, any emergency conditions requiring immediate hemodialysis, for example, pulmonary edema, hyperkalemia, or the like, or use of glucocorticoids or medications with known effect on neuropsychological functions, prior to six months.

All participants provided their written informed consent after the purpose of the study was explained to them.

**Data collection**

The study was cross-sectional in design and consisted of 60 subjects. Recruitment was accomplished using a screening proforma containing the inclusion / exclusion criteria. Among the subjects fulfilling the criteria, two did not consent to participate in the study, while one recruited subject expired before the assessment could be completed.

The instruments were administered in two sessions, one prior to hemodialysis and the second 24 hours post dialysis. The order of presentation of the instruments was kept identical for all the subjects: The sociodemographic and clinical profile proforma, Standardized Mini-Mental State Examination, (SMMSE), and Brief Cognitive Rating Scale (BCRS).

The SMMSE is a simplified scored form of the cognitive mental status examination. On account of its brevity and ease of use, the SMMSE is commonly used to screen and follow patients with cognitive impairment. In the Standardized Mini-Mental State examination, reasonable time limits for answers, commensurate with the tasks based on clinical trials are given. It takes less time to administer the Standardized Mini-Mental State examination than the Mini-Mental State examination. The mean time required for an interview with the Mini-Mental State examination was 13.39 minutes, which was significantly greater than that required for the Standardized Mini-Mental State examination (10.47 minutes). This was due to the clearer guidelines for the administration, scoring, and timing of the responses in the Standardized Mini-Mental State examination. Therefore, the expanded guidelines in the Standardized Mini-Mental State examination made the Mini-Mental State examination easier to administer and increased the reliability of the instrument.

This instrument is divided into two sections, where section I requires verbal responses and covers orientation, memory, and attention, and the maximum score on this section is 21. Section II tests the ability to name, follow verbal and written commands, write a sentence spontaneously, and copy a complex polygon, and the maximum score on this section is 9. Thus, the maximum total score on SMMSE is 30, and a score of less than 24 suggests impairment.

The BCRS is an assessment tool developed by Reisberg. The BCRS is part of the triad of assessments with the Global Deterioration Scale (GDS) and the Functional Assessment Staging (FAST). The BCRS is designed specifically to assess the syndrome of cognitive decline. The BCRS differs virtually from all other presently used clinical rating instruments for cognitive disturbances, in that, it excludes mood changes such as anxiety, depression, agitation, and psychosis. Thus, the effects of interventions on cognition and associated functioning can be specifically assessed.

The investigator clarified any doubt and provided an answer for any query asked by the subjects regarding the study. All the subjects were discussed with the nephrologist and the diagnosis was ascribed by him.

**Data analysis**

We compared the sociodemographic and clinical characteristics of cases and controls in our sample using the Chi-Square test from a contingency table and Student ‘t’ test for continuous numerical values.

All data are expressed as a mean±SE. P<0.05 was used to establish the statistical significance.

**RESULTS**

**Demographic and clinical characteristics**

The study was cross-sectional in design; the subjects were recruited on a purposive basis from the Inpatient Department of the hospital. Recruitment was accomplished using a screening proforma containing the inclusion / exclusion criteria. Among the subjects
fulfilling the criteria, two did not consent to participate in the study, while one recruited subject expired before the assessment could be completed. The study consisted of 60 subjects, 30 renal failure patients who were divided into two groups based on the onset of the hemodialysis treatment modality (cases) and 30 patients who were admitted to the general medical wards (controls).

The study subject’s sociodemographic background showed that a majority were males, and had completed a minimum primary education, were married, and belonged to the middle socioeconomic class. These demographic characteristics may not be representative of the general population; especially in terms of education and socioeconomic class, but they do give a descriptive account of the sample population.

The mean age of the subjects [Table 1] recruited here was 46.16 (±13.23) years, and the groups were found to have no differences in terms of the clinical presentation of renal failure. A majority of patients had chronic renal failure (63.3%), while only 36.7% had acute on chronic renal failure ($P=0.200$, [Table 2]). The mean urea of the case group was 124.60 mg/dl (±48.77) and the mean creatinine was 6.89 mg/dl (±3.12), which was statistically significant ($P=0.001$, [Table 3]).

Neuropsychological tests
Two tests were administered to study the cognitive functions (1) SMMSE and (2) BCRS, although these instruments have been well-validated, they have not been used in any of the previous studies.

The tests revealed significant neurocognitive impairment in all the five dimensions (concentration, recent memory, past memory, orientation and functioning, and self-care) in the cases when compared to the control group, in all the tests used here.

The SMMSE revealed significant differences ($P = 0.001$) in orientation, registration, attention, recall, language, and construction [Figure 1]. The BCRS test also revealed significant differences in concentration, recent memory, past memory, orientation and functioning, and self-care [Figure 2]. The findings of the current study suggest that the cognitive functions are significantly impaired in the pre-dialysis patients group, when compared to the 24 hours post-dialysis case group and the control group.

However, in this study there was a significant difference among the 24-hour post dialysis case group and controls, in contrast to the previous studies.[12,9] This finding was probably due to the higher educational level in the control group (based on the cognitive reserve

| Table 1: Comparison of age between controls and cases |
|-----------------------------------------------|
| Age                                           |
| Mean | Std. deviation | t     |
| Cases | 46.16 | 13.23 | 0.021 \(P=0.984\) ns |
| Controls | 46.23 | 11.63 |           |

| Table 2: Medical diagnosis data |
|--------------------------------|
| Diagnosis | Frequency | Percent |
| Chronic renal failure | 19 | 63.3 |
| Acute on chronic renal failure | 11 | 36.7 |
| Total | 30 | 100.0 |

Binomial test $P=0.200$ NS

| Table 3: Comparison of renal function test between cases and controls |
|-----------------------------------------------|
| Urea | Cases | Mean | Std. deviation | t |
| Cases | 124.60 | 48.77 | 11.16 |
| Controls | 24.66 | 5.12 |           |
| Creatinine | Cases | 6.89 | 3.12 | 10.50 |
| Controls | 0.88 | 0.166 | P=0.001vhs |

Figure 1: SMMSE – total score

Figure 2: BCRS total score
hypothesis, which proposed that a higher educational level could delay the expression of cognitive deficits, (this hypothesis was studied primarily in dementia)).

DISCUSSION

As the concept of ‘General Hospital Psychiatry’ or better put as ‘Consultation Liaison Psychiatry’ is gaining ground, a lot more research focusing on the psychiatric aspects of medical diseases in coming forth. Today we are witness to specialties like ‘Psychology,’ and ‘Psycho-Nephrology,’ which talk about the psychological aspects of cancer and renal disorders, respectively. This study has been undertaken to contribute to the growing body of literature in psycho-nephrology worldwide, especially as the data in this respect is limited to Indian Population.

The importance of neurocognitive dysfunction and the associated disability with any medical disease has been better understood in recent years, and has probably been more disabling than the medical illness itself. Research into the neurocognitive dysfunction of renal failure patients has been an area of recent interest, in view of the potential for full recovery, with initiation of the hemodialysis treatment modality. Deficits in cognitive functioning may thus make a difference between a normal life and chronic disability, which in turn is likely to affect the psychosocial functioning, insight, and treatment adherence.

The study consisted of 60 subjects. The renal failure patients were matched with normal renal functioning subjects on age and gender, to avoid overestimation of the cognitive deficits.

The control group consisted of 30 subjects, who had normal renal functions, with no psychiatric illness. Although randomization of the sample would have been best for this sort of comparative study, it was a fundamental problem that chronic renal failure patients were never randomized to receive hemodialysis.

The subjects’ renal function status was established based on the clinical records from the consulting unit, as well as cross-sectional assessment, both by a structured and unstructured clinical interview. Thus, renal failure was clearly defined and any pre-existing decline in cognitive functions was ruled out.

Earlier investigators have mainly used other varieties of instruments to determine cognitive dysfunctions like the Stroop color word test, trail making test, digit span subtest of the Wechsler Adult Intelligence Scale, Paced Auditory Serial Addition Test, Boston Naming Test, Finger Tapping Test, Wechsler Adult Intelligence Scale - Revised, Wechsler Memory Scale, Rey Auditory–Verbal Learning Test, Kaufman Brief Intelligence Test, and so on.

Although there are a variety of instruments available to assess the cognitive functions, we decided to use the SMMSE and BCRS - simple scale, which is short and easy to understand and administer, and basically measures cognition across five dimensions. The other reason to use SMMSE and BCRS is because they consume less time, and hence, minimize the possible worsening of uremia (ethical considerations).

The mean age of the subjects recruited here was 46.16 (±13.23) years. Most of the subjects who were assessed previously were in the higher age group 59.8 (±15.5) years.[1,9] This could be one of the confounding factors, as normal aging could lead to cognitive deficits or there could be an underlying dementing process ongoing. This difference in age could be due to the fact that either older patients were not always medically suitable for dialysis or their families refused dialysis. Gender matching was done case by case, so as to rule out the differences in neurocognitive functions between the genders [Table 2]. However, we found that females performed better than males before dialysis, but after 24 hours of dialysis, there was no statistical difference between the groups.

However, when we look at the education, there was a significant difference, as most of the case groups were less educated when compared to the control group. This difference in education could be a confounding variable for the other aspects being studied. In a majority of the previous studies the mean educational level was 10.4 years.[9] The majority of patients in the group had chronic renal failure (63.3%), while only 36.7% had acute on chronic renal failure.

The above-mentioned findings were consistent with other international studies, which have also shown deficits on sustained attention, mental processing speed, and memory for both immediate and delayed recall, language ability, and intelligence.[2,9-11] As the assessment was done just after one hemodialysis, the differences were found to be significant. However, the findings should be interpreted with caution due to the small sample size.

The current study shows a positive correlation between cognitive functions and renal failure, which can help in understanding a lot more about the pathophysiology. Better understanding of pathophysiology and targeting specific cognitive deficits that correlate with the effect of hemodialysis on cognitive function can probably improve the overall functional outcome. Future work
is needed in the Indian population, in view of the increasing number of renal failure patients. A large sample-based study might provide further interesting details.

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