HAEMODIALYSIS IN SCHIZOPHRENIA: 
A DOUBLE BLIND STUDY – PRELIMINARY REPORT

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Summary

The therapeutic effects of haemodialysis were evaluated in schizophrenic patients using a double blind procedure. Twelve patients were diagnosed as acute schizophrenics according to Feighner's criteria for psychopathology. After obtaining informed consent, the patients were randomly assigned to active haemodialysis (AD) or sham dialysis (SD). An 8 days 'drug washout period' was followed by AD or SD treatment of 4 weeks (two 5 hours sessions per week) and psychopathological evaluations were performed regularly in a blind fashion using the Brief Psychiatry Rating Scale (BPRS) and the Comprehensive Psychopathological Rating Scale (CPRS). Nine of the 12 patients were improved by both extracorporeal procedures with or without active dialysis. No significant difference appeared however between both groups in the rate and degree of improvement of nuclear symptoms of schizophrenia. Nevertheless, AD was significantly more efficient in relieving affective symptomatology, suggesting the potential involvement of some endogenous dialysable substance(s) in the pathogenesis of mood disturbances in schizophrenia.

Introduction

Partial improvement of schizophrenia by haemodialysis was first reported by Thölen et al in 1960 [1]. More recently, Cade and Wagemaker [2,3] showed haemodialysis to be beneficial in 75% of 25 schizophrenic patients. Other reports have since cast doubt on these results arguing that schizophrenic improvement using haemodialysis [4,5,6,7,8], haemoperfusion [9] or haemofiltration [10] was not greater than the rate of spontaneous remission of the illness. Since none of the above studies used proper controlled procedure, it was imperative to evaluate the effect of haemodialysis in schizophrenia according to a double blind controlled design.
Methods

From December 1978 to May 1979, 12 patients diagnosed as schizophrenic according to Feighner's criteria [11] were ascertained for the present study, after obtaining informed consent from the patients and/or relatives. All drugs were withdrawn for at least 8 days. All the patients were maintained free of drugs throughout the study. Out of these 12 patients, 7 were then assigned to active dialysis (AD), 5 to sham dialysis (SD). The randomisation was established by the nephrologist, the psychiatrists remaining blind throughout the investigation. Haemodialysis was performed twice weekly for 4 weeks, each session lasting 5 hours.

Blood access for AD as well as SD was obtained by catheterising a femoral vein. A single needle dialysis system was used by means of an arterial and venous pumps system [12]. AD was performed using a blood flow of 250ml/min, a CD-3500 dialyser (cellulose acetate, 0.9m²) and a single pass dialysate at a flow rate of 500ml/min. SD was performed with a blood flow of 100ml/min, a CD-0.6 dialyser (regenerated cellulose, 0.6m²) and a reduced volume of dialysate (150ml) circulating in a closed circuit, so as to maintain a constant blood temperature. The experimental situation was so designed as to keep the patient 'blind' as to the type of procedure.

An extensive psychopathological evaluation was performed before, during and after the dialysis programme using the Brief Psychiatric Rating Scale (BPRS) [13] and the Comprehensive Psychopathological Rating Scale (CPRS) [14]. Moreover, nuclear symptoms of schizophrenia [15] were analysed separately from the CPRS and from the BPRS.

Statistical analysis was performed using the analysis of variance and also the $x^2$ test.

Results

Patients on AD ($n = 7$) and on SD ($n = 5$) did not differ significantly ($p > 0.05$) for the following variables: age (mean: 32.5 years), sex, duration of illness (mean: 6.5 years), duration of the present episode (mean: 2.3 years), schizophrenic heredity as well as a previous response to antipsychotic drugs. The incidence of typical schizophrenic symptoms such as Schneider's first rank symptoms (auditory hallucinations, thought withdrawal, etc.) [16], autism, paranoid and other delusions, thought disturbances and catatonia was similar in both groups ($0.22 \leq p \leq 0.42$).

As illustrated in Figure 1, blood urea levels decreased significantly ($p < 0.01$) after AD while it was not modified by the SD procedure.

Before dialysis the baseline scores for BPRS and CPRS were not significantly ($p < 0.05$) different between the 2 groups.

Figure 2 indicates that BPRS score significantly ($0.01 < p < 0.05$) improved after active treatment but not following sham procedure ($p > 0.05$) as confirmed by significant improvement in $\Delta$-scores in AD as compared to SD ($0.01 < p < 0.05$).

CPRS scores (Figure 3) were significantly reduced by AD ($0.05 < p < 0.01$) and
not (p >0.05) by SD, despite apparent improvement in 4 out of the 5 patients of this group. However, a significant difference between both groups could not be observed when considering the Δ-scores for CPRS (p >0.05).

The analysis of nuclear symptoms of schizophrenia (Figure 4) for BPRS and CPRS demonstrated apparent improvement in 6/7 patients in AD and in 3-4/5 patients in SD. Furthermore clinical improvement, as measured by the Δ-scores on both sub-scales, did not differ significantly in AD and SD groups (p >0.05).

For the non schizophrenic items (Figure 4) CPRS did not yield any significant difference (p >0.05) in Δ-scores between AD and SD, while BPRS provided discrimination between AD and SD: i.e. patients treated with AD demonstrated significant clinical improvement as compared to SD patients (p <0.05).

Discussion

The results of our double blind study indicate that in a sample of 12 schizophrenic patients, nuclear symptoms of schizophrenia were improved in 75% of the patients. This rate of remission is strikingly similar to that reported by Cade and Wagemaker [2,3] in their open study. However, in our study improvement of schizophrenic symptoms occurred in 5 out of 7 patients in active dialysis and in 3 out of 5 patients in sham dialysis. Moreover the degree of improvement was not different in both groups. Thus, the improvement of nuclear symptoms of schizophrenia in our patients is apparently not linked to a dialysable compound. Nevertheless, the high improvement rate (75%) observed in these patients treated with extracorporeal circulation, with or without dialysis, cannot be
Figure 2. Changes in Brief Psychiatric Rating Scale (BPRS) scores during active and sham dialysis.

explained solely by spontaneous remission the rate of which is considered not to exceed 14% [17]. Using a double blind procedure to evaluate the extent of placebo effect in experimental therapeutic trials, our observations do indeed stress the importance of such a placebo effect in the response to dialysis in schizophrenia. Nevertheless, the involvement of putative factors resulting from blood transport through plastic tubing cannot be excluded.

More intriguing is the significantly greater improvement of non-schizophrenic symptoms in patients treated with active dialysis as compared to those treated.
by sham dialysis. The symptoms which seem to be relieved by haemodialysis are of an affective nature, such as mood disturbances (in particular depressive feelings) and psychomotor retardation. Improvement in mood disturbances in schizophrenic patients treated with haemodialysis could thus be related to clearance of some dialysable endogenous substance(s) such as hypothetical neuropeptide(s) with a mood-depressing activity.

Acknowledgment

The skilful assistance of the nursing and technical staff of our Dialysis Unit and of our Psychiatric ward is gratefully acknowledged.
Figure 4. Changes in schizophrenic and non-schizophrenic items from BPRS and CPRS scores in active and sham dialysis

References

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Open Discussion

SPLENDIANI (L’Aquila) Could I ask what kind of membrane you are using, because we think that the poly-acrylonitrile membranes are better than cuprophan. After the treatment what drug do you use?

VANHERweghem We use, for active dialysis, cellulose acetate membrane which also has a relatively high permeability. To the second question, patients were maintained free of drugs. After the dialysis programme we will open the study: if the patient was on active dialysis and if he has improved and wishes to continue the treatment, we will do so. If the patient was on sham dialysis we intend to move him to active dialysis.