Alcohol-induced psychotic disorder: brain perfusion and psychopathology – before and after anti-psychotic treatment

Gerhard P Jordaan[1], James M Warwick[2], Daan G Nel[3],
Richard Hewlett[4], Robin Emsley[1]

[1] Department of Psychiatry, [2]Department of Nuclear Medicine, [3] Centre for Statistical Consultation, [4]Department of Anatomical Pathology, University of Stellenbosch, Tygerberg 7505, Cape Town, South Africa

BACKGROUND

Alcohol-induced psychotic disorder (AIPD) is a rare complication of alcohol abuse. The pathogenesis and treatment of AIPD are still unclear. No standard pharmacological treatment for AIPD has yet been determined. Alcohol abstinence and antipsychotic treatment have been associated with good outcome in case series and reports (Soyka, 2007). Aliyev and Aliyev (2008) reported efficacy with valproate compared with placebo. Brain imaging changes in relation to treatment response have also not been studied except for case reports.

AIM

The aim of this study was to prospectively investigate the effect of anti-psychotic treatment (haloperidol) on psychopathology and rCBF (SPECT) in patients with AIPD.

METHODS

Twenty patients with AIPD were assessed by the Positive and Negative Syndrome Scale (PANSS) and single photon emission computed tomography (SPECT; n=19) before and after 6-weeks of open-label treatment with a fixed dose of haloperidol (5mg/day). Firstly pre- and post-treatment PANSS scores were compared and a paired t-test was used to detect changes in regional cerebral blood flow (rCBF) in AIPD patients following pharmacotherapy. Finally correlations were sought between changes in rCBF and changes in PANSS scores resulting from treatment.

RESULTS

Improvement noted on the PANSS total, positive and general subscale scores is consistent with previous reports indicating that AIPD symptoms are generably reversible. Anti-psychotic treatment was associated with a good outcome and limited the need for ongoing treatment. As is the case with schizophrenia, most improvement was observed in positive and general psychopathology symptoms, while negative symptoms were more persistent. Post-treatment increased rCBF to the left caudate and left frontal lobe was noted. Changes in frontal, temporal, parietal, thalamic and cerebellar rCBF showed significant negative correlations with the degree of symptom improvement on the negative and general PANSS subscales, suggesting dysfunction of these areas in AIPD.

CONCLUSION

Significant post-therapy improvement was demonstrated on the positive, general and total scales of the PANSS. Assessment of rCBF before and after treatment with haloperidol in AIPD was associated with post-treatment increased rCBF to specific areas of the left frontal lobes and left basal ganglia (caudate).We were unable to distinguish between therapeutic effects of haloperidol and the possible improvement accomplished by abstinence from alcohol and postulate that both mechanisms were simultaneously operative. Psychopathological and rCBF findings suggest reversible generalised cerebral dysfunction in AIPD.

AIPD psychopathology that significantly improved from baseline to 6 weeks:

PANSS	Mean [SD] baseline score (n = 20)	Mean [SD] score at 6 weeks (n = 20)	Paired t tests p value <0.01
PANSS Positive scale			
P1 – delusions	4.0 [1.30]	1.65 [0.75]	p<0.001
P3 – hallucinations	3.95 [1.10]	1.35 [0.67]	p<0.001
P4 – excitement	2.95 [1.05]	1.25 [0.55]	p<0.001
P6 – suspiciousness	4.20 [1.44]	1.50 [0.61]	p<0.001
P7 - hostility	2.35 [0.99]	1.25 [0.55]	p<0.001
Positive Total	19.85 [3.17]	9.10 [2.43]	p<0.001
PANSS Negative scale			
N2-emotional withdrawal	2.05 [0.94]	1.45 [0.69]	p<0.01
PANSS General scale			
G2 – anxiety	3.25 [0.85]	1.70 [0.92]	p<0.001
G4 – tension	2.60 [0.82]	1.45 [0.76]	p<0.01
G6 – depression	2.65 [1.46]	1.55 [0.83]	p<0.01
G9 - unusual thought content	3.00 [0.97]	1.25 [0.55]	p<0.001
G12 - lack of judgement	3.55 [1.00]	1.50 [0.76]	p<0.001
G14 - poor impulse control	2.40 [1.14]	1.15 [0.37]	p<0.01
G16 - active social avoidance	2.55 [1.19]	1.50 [0.69]	p<0.01
General Total	33.70 [6.71]	20.90 [4.22]	p<0.001
PANSS Total Score	67.10 [12.43]	40.85 [9.06]	p<0.001

Baseline to 6 weeks changes in rCBF (SPECT) in patients (n=19) with AIPD:

Cluster size (voxels)	MNI coordinates (x,y,z)	Brain region	p value = 0.001
Increase in rCBF post vs. pre therapy:			
54	-8,0,68	Suppementary Motor Area L	p<0.001
62	-12,16,12	Caudate L	p<0.001
38	-48,-20,20	Rolandic Operculum L	p<0.001

Main correlations between changes from baseline to 6 weeks in rCBF & PANSS:

Cluster size (voxels)	MNI coordinates (x,y,z)	Brain region	p value = 0.001
Change in PANSS negative subscale and negative correlation with rCBF changes:			
304	-28,-16,68	Frontal Pre-central L	p<0.001
77	36,-56,48	Parietal Angular R	p<0.001
18	-12,-60,-40	Cerebellum L	p<0.001
14	-56,-20,4	Temporal Sup L	p<0.001
Change in PANSS general subscale and negative correlation with rCBF changes:			
56	-8,-20,20	Thalamus L	p<0.001

REFERENCES

Soyka M, Täschner B, Clausius N. Neuroleptic treatment of alcohol hallucinosis : case series. Pharmacopsychiatry 2007;40:291-292.

Aliyev ZN, Aliyev NA. Valproate treatment of acute alcoholic hallucinosis: a double blind placebo-controlled study. Alcohol and Alcoholism 2008:43:456-459.

Jordaan GP, Nel D, Warwick JM, Hewlett RH, Emsley RA. Alcohol-Induced Psychotic Disorder: Brain perfusion and psychopathology – before and after anti-psychotic treatment. Metabolic Brain Disease 2012;27(1):67-77.

DISCLOSURE*: This study was supported by funding from the Harry Crossley Foundation and research assistance funds from the University of Stellenbosch, South Africa. It was published in Metabolic Brain Disease 2012;27(1):67-77. No potential conflict of interest is declared .*

P.3.d.041

Alcohol-induced psychotic disorder: brain perfusion and psychopathology - before and after anti-psychotic treatment

G.P. Jordaan[1], R.A. Emsley[1], J.M. Warwick[2], D. Nel[3], R. Hewlett[4]

[1]Faculty of Medicine and Health Sciences, Dept Psychiatry, Tygerberg, South Africa

[2]Faculty of Medicine and Health Sciences, Dept Nuclear Medicine, Tygerberg, South Africa

[3]Faculty of Medicine and Health Sciences, Centre for Research Development and Support, Tygerberg, South Africa

[4]Faculty of Medicine and Health Sciences, Dept Anatomical Pathology, Tygerberg, South Africa

Introduction: Alcohol-induced psychotic disorder (AIPD) also known as alcohol hallucinosis is a rare complication of alcohol abuse. The pathogenesis and treatment of AIPD are still unclear. Few prospective treatment studies are available but case reports generally suggest that antipsychotic treatment is effective. No standard pharmacological treatment for AIPD has yet been determined. Alcohol abstinence and antipsychotic treatment (that included haloperidol, risperidone, flupentixol and olanzapine) have been associated with good outcome in case series and reports (Soyka, 2008) Aliyev and Aliyev (2008) reported efficacy with valproate compared with placebo, although concerns were raised about the methodology of that study. Brain imaging changes in relation to treatment response have also not been studied except for case reports. The aim of this study was to prospectively investigate the effect of anti-psychotic treatment (haloperidol) on psychopathology and rCBF (SPECT) in patients with AIPD. We postulated that: (i) clinical and brain imaging variables of AIPD would normalize with anti-psychotic treatment and therefore (ii) demonstrate a possible correlation between clinical symptoms and neuroanatomical dysfunction.

Methods: Nineteen patients with AIPD were assessed by the Positive and Negative Syndrome Scale (PANSS) and single photon emission computed tomography (SPECT) before and after 6-weeks of open-label treatment with a fixed dose of haloperidol (5mg/day). Wilcoxon's matched pairs test (WILC) were used in all the analyses to assess pre- and post-treatment PANSS scores. Statistical analyses in this component of the study were performed with a significance level of 5% ($p<0.05$). Three study designs were employed. Firstly a paired t-test was used to detect changes in rCBF in AIPD patients following pharmacotherapy. Secondly correlations were sought between baseline rCBF and PANSS scores, and finally correlations were sought between changes in rCBF and changes in PANSS scores resulting from therapy. To adjust for multiple comparisons an uncorrected p-value of $p<0.001$ was chosen as a threshold for statistical significance. A spatial extent threshold of 10 voxels was also used at all times.

Results: The improvement noted on the PANSS total scale and positive and general subscale scores is consistent with previous reports indicating that the symptoms of AIPD are generably reversible. Anti-psychotic treatment was associated with a good outcome and limited the need for ongoing treatrment. As is the case with schizophrenia, most improvement was observed in positive and general psychopathology symptoms, while negative symptoms were more persistent. Post-treatment increased rCBF to the left caudate and left frontal lobe was noted. Changes in frontal, temporal, parietal, occipital, thalamic and cerebellar rCBF showed significant negative correlations with the degree of symptom improvement, suggesting dysfunction of these areas in AIPD.

Conclusion: Significant post-therapy improvement was demonstrated on the positive, general and total scales of the PANSS. Assessment of rCBF before and after treatment with haloperidol in AIPD was associated with post-treatment increased rCBF to specific areas of the left frontal lobes and left basal ganglia (caudate).We were unable to distinguish between therapeutic effects of haloperidol and the possible improvement accomplished by abstinence from alcohol and postulate that both mechanisms were simultaneously operative. Psychopathological and rCBF findings suggest reversible generalised cerebral dysfunction in AIPD.

1. Jordaan GP, Nel D, Warwick JM, Hewlett RH, Emsley RA (2012) Alcohol-Induced Psychotic Disorder: Brain perfusion and psychopathology – before and after anti-psychotic treatment. Metabolic Brain Disease 27(1):67–77.

2. Soyka, M., 2008. Pharmacological treatment of alcohol hallucinosis. Alcohol and Alcoholism 43(6), 719–720.

3. Aliyev, Z.N., Aliyev, N.A., 2008. Valproate treatment of acute alcoholic hallucinosis: a double blind placebo-controlled study. Alcohol and Alcoholism 43, 456–459.

Disclosure statement: I am the first author of this paper which has also been published in Metabolic Brain Disease, 27(1):67–77, 2012.

Citation: Eur Neuropsychopharmacol. 2014;24(Suppl 2):S546

Keywords

Alcoholism

Behavioural pharmacology

Brain imaging