Psychiatria Danubina, 2012; Vol. 24, Suppl. 3, pp 311–315 *Conference paper*

IS ACUTE AND TRANSIENT PSYCHOTIC DISORDER (ATPD) MINI SCHIZOPHRENIA? THE EVIDENCE FROM PHENOMENOLOGY AND EPIDEMIOLOGY

Saeed Farooq

Staffordshire University, Black Country partnership NHS Foundation Trust, Wolverhampton, UK

SUMMARY

Acute and transient psychotic disorders (ATPD) first appeared in ICD-10 but classification of acute psychosis has a long historical tradition. The prevalence rate of these disorders varies from 3.9 to 9.6 per 100,000 populations. Systematic clinical information that would provide definitive guidance on the classification of acute psychotic disorders is not yet available. Moreover there is no evidence available to guide the treatment of these disorders. In absence of the reliable epidemiological information the ATPD is treated as a form of 'mini schizophrenia' as if the disorder is an attenuated form of schizophrenia. A systematic review of the literature on acute and transient psychosis was conducted and all studies on epidemiology and treatment of acute and transient psychosis were identified. The existing evidence suggested that ATPD has little relationship with schizophrenia. ATPD is diagnostically unstable over time. Various estimates suggest that about 1/3 of patients with baseline ATPD retained their diagnosis over 3-12 years, the most frequent re-diagnosis being bipolar disorder and not schizophrenia. There are important differences in the epidemiology of this disorder from schizophrenia. These include gender distribution (ATPD has preponderance of females while equal gender distribution is one of the most established finding in epidemiology of schizophrenia) and much better premorbid level of functioning and social interactions. Other distinguishing features include the age at onset (onset throughout adult life, but usually between the 30- 50 years), development, and duration of symptoms (ATPD have an acute or even abrupt onset and the onset is only rarely precipitated by acute severe stress) and usually a favourable outcome, in spite of the fact that they are frequently recurrent. Literature on the subject is scanty and has serious methodological limitations. Treating ATPD has serious long term implications for the care of those suffering from ATPD. Long term treatments with antipsychotics which can induce metabolic disorders and reduce life expectancy, amongst many other side effects mean that we have to reconsider our approach to the diagnosis of ATPD seriously. Treating the acute and transient psychosis as a mini schizophrenia is seriously hindering research and clinical practice. I will review the epidemiology and phenomenology of acute and transient psychotic disorder, the current gaps in knowledge and its effects on our clinical practice in the light of systematic review of the evidence.

Key words: *acute and transient psychotic disorder - mini schizophrenia - classification*

* * * * *

INTRODUCTION

Acute and transient psychotic disorders (ATPD) first appeared in ICD-10 but classification of acute psychosis has a long historical tradition. In fact, it can be argued that different forms of acute psychosis are perhaps most well known psychotic disorders. Psychiatrists from all over the world recognise these, as is evident in different names the disorders have received over the century. These include the Germans (cycloid disorders), the French (bouffe´e de´lirante), the Scandinavians (psychogenic and reactive psychoses) and the Swiss (emotional psychoses), only to mention European traditions (Marneros 2006). However, the evidence about the classification, epidemiology and most importantly treatment of these disorders is sparse. It can be argued that this is perhaps a defence mechanism, as these disorders seriously challenge our notions of classifications of psychosis based on Kraepelinian dichotomy! But I will not be drawn into that and will argue that this issue is not just an academic debate but has serious clinical implications.

In this lecture, I will revise the rules for establishing validity of the diagnosis in psychiatry. This will be followed by an overview of the literature on ATPD and its clinical implications. My aim is not to delve into the controversies of the diagnostic validity of the category or its present classification, which could be subject of whole day symposium rather than a lecture! I will only remind you of the art of diagnosis which is central to our craft and the fact that debates about classification are not merely theoretical exercise.

In order to systematically review the subject, major data bases such as Medline, PsychInfo and Ebsco were searched systematically using following search terms: The Polymorphic psychotic disorder, Bouffe´e de´lirante, Cycloid psychosis, Reactive psychosis, Brief psychotic disorder, Transient psychosis, Remitting psychosis (full details available from the author). After excluding the papers which did not appear relevant to the ATPD and brief psychotic disorders 305 papers were selected for further examination. Finally, after reading the abstracts, 47 papers were selected for full text reading. The main objective was to examine the relationship of this diagnostic category with schizophrenia and systematically review the evidence for intervention used for the treatment of ATPD.

DIAGNOSTIC RULES IN PSYCHIATRY

Diagnosis is a central task in Medicine which determines our approach to treatment and to define prognosis. In psychiatry, the rules for considering diagnosis as valid

entity were defined by Robin & Guz (1970). They considered that for a valid diagnosis, it must have a specific clinical description which could be supported by laboratory studies; it could be separated from other entities based on clinical features and on follow up the diagnosis remains stable. There should also be familial aggregation of similar cases in the families. The lack of evidence in these fields for most psychiatric diagnosis means that over the years the scheme has been modified. The validity of diagnostic entity is now mostly based on the existence of separate antecedent, concurrent and predictive validators given below:

Antecedent

- Demographic factors;
- Premorbid personality;
- Precipitating factors;
- Family studies.

Concurrent

- Physiological;
- Neuropsychological;
- Neurophysiological;
- Neuroimaging;
- Biological;
- Genetics.

Predictive

- Course and outcome;
- Response to treatment.

THE CLASSIFICATION AND DEFINITION OF ATPD

Prior to ICD-10 there was no separate nosology for acute psychosis as a group and it was subsumed under the broad category of schizophrenia. Increasing evidence about the acute psychosis being distinct group of psychotic disorders from schizophrenia led to the inclusion of concept of acute psychosis as a separate nosological entity in ICD-10, listed under the heading of F20-29, which is the group for schizophrenia, schizotypal. and delusional disorders. The ICD-10 acknowledged that the ssystematic clinical information that would provide definitive guidance on the classification of acute psychotic disorders is not available, The key features of the disorder include following (Table 1):

a. An acute onset (within 2 weeks) as the defining feature of the whole group;
b. The presence of typical syndromes;
c. The presence of associated acute stress.

Complete recovery usually occurs within 2 to 3 months, often within a few weeks or even days, and only a small proportion of patients with these disorders develop persistent and disabling states.

According to ICD-10, the ATPD group (F23) consists of 6 disorders including acute schizophrenia-like psychotic disorder (Table 2). The first two disorders have polymorphic features, which mean a rapidly changing and variable state. The rest have no polymorphic features or are characterized by a more stable state.

Table 1. Key features of ATPD according to ICD 10 **(**WHO 1992)

The order of priority given for ATPD
1. Onset
▪ acute onset (within 2 weeks)
▪ or abrupt onset (within 48 hours)
2. Presence of typical syndromes
▪ polymorphic (rapidly changing, variable state)
▪ typical schizophrenic symptoms
3. Presence of associated acute stress (Bereavement, unexpected loss of partner or job, marriage, psychological trauma of combat, terrorism, torture)

Table 2. Subtypes of ATPD (WHO 1992)

F23.0	Acute polymorphic psychotic disorder without symptoms of schizophrenia
F23.1	Acute polymorphic psychotic disorder with symptoms of schizophrenia
F23.2	Acute schizophrenia-like psychotic disorder
F23.3	Other acute predominantly delusional psychotic disorders
F23.8	Other acute and transient psychotic disorders
F23.9	Acute and transient psychotic disorders, unspecified

AN OVERVIEW OF THE EPIDEMIOLOGY OF ATPD

The characteristic symptoms of ATPD include varied delusions, perplexity, hallucinations, confusion, disorganization of thought processes, less intense and few negative symptoms and mood instability (Marneros et al. 2002, Marneros et al. 2003). This disorder has acute onset of psychotic symptoms within 2 weeks without a prodrome. The symptoms are markedly variable, changing from day to day or even from hour to hour. The duration of symptoms usually does not exceed more than 3 months and the course is characterized by recovery within a few weeks, and longer periods of remission.

The prevalence of ATPD varies from 3.9-9.6 per 100,000 population (Singh et al. 2004, Castagnini et al. 2008). The disorder has preponderance of females; with female to male ratio of almost 2: 1 (Varma et al. 1996, Singh et al. 2004, Susser & Wanderling 1994). The most common age of onset is early adulthood and is same for males and females (Susser & Wanderling 1994). The evidence for familial psychiatric morbidity is rather conflicting. Das et al. (1999) reported increased incidence ATPD in first degree relatives of patients suffering from ATPD while Marneros & Pillmann (2004) found that relatives of those suffering from ATPD did not have increased chance of presenting with psychotic disorders.

Presence of acute stress was considered important for the diagnosis of acute psychosis as is evident in terms such as ‘reactive psychoses’, ‘psychogenic psychoses’ and ‘hysterical psychoses’, the precursors of

the ATPD concept. Recent evidence is conflicting. There seems to be little evidence for stress as a precipitant in developed countries (Castagnini et al. 2008; Jager et al. 2003; Jorgensen et al. 1996; Marneros & Pillmann 2004, Singh et al. 2004). However life events and 'social and cultural factors' are reported to be associated with acute psychosis in developing countries (Sajith et al. 2002, Guinness 1992, Malhotra & Malhotra 2003, Manschreck & Petri 1978). Collins et al. (1996, 1999) found that history of fever or stress related to adherence to traditional roles is associated with acute onset non-affective psychosis (onset < 1 week) in developing country context. It can be concluded that stress often precipitates the onset of acute psychosis but this is not necessary for diagnosis.

In absence of biological validators of the diagnosis, the course of illness remains an important criterion for the diagnostic validity of the concept. Castagnini & Berrios (2009) reviewed European literature and included 13 studies with total of 884 cases. The follow-up periods ranged from 1 to 15 years. They found low diagnostic stability with more than 50% of ATPD cases changing diagnosis to another diagnostic category from schizophrenia or other psychosis, or to affective disorders (Castagnini et al. 2008, Jorgensen et al. 1997, Marneros & Pillmann 2004, Singh et al. 2004, Jager et al. 2007, Chang et al. 2009).

Many studies report high recurrence rates (Jager et al. 2003, 2004, 2007, Jorgensen et al. 1997, Marneros & Pillmann 2004, Singh et al. 2004). For example Jager et al. (2007) report recurrence rates of 58-77%. However, literature from developing countries generally reports higher diagnostic stability (Okasha et al. 1993, Sajith et al. 2002, Thangadurai et al. 2006). Sajith et al. found that 33 patients from their sample of 45 retained diagnosis of ATPD at 3-year follow-up (Sajith et al. 2002). Similar higher diagnostic stability is reported for non affective psychosis (Alaghband-Rad et al. 2006, Susser et al. 1998, Mojtabai et al. 2003). Very abrupt onset (<48hours) and short duration of illness (<1 month) seemed to predict better stability of diagnosis and lower recurrence rate.

The long term outcome is reported to be much better than schizophrenia. Susser et al. (1998) found that the long term prognosis of acute brief psychosis was excellent and remarkably homogenous, with only one out of seventeen subjects developing a chronic psychotic illness at 12-year follow-up. Interestingly, none of the seventeen cases developed an affective syndrome. This course of illness is not confirmed by other studies but the overall outcome is better compared to that reported for schizophrenia (Amin et al. 1999, Singh et al. 2004).

In summary, the overview of the epidemiology of acute and transient psychotic disorder suggests that the disorder is characterized by:

- Having an acute or even abrupt onset usually within 2 weeks;
- Rapidly changing and variable mental state;
- Hallucinations or delusions of different type which usually change in either content or intensity from day to day or within the same day;
- Mainly affecting females;
- With possible onset throughout adult life, but usually between the ages of 30 - 50;
- The onset of which can be associated with acute severe stress;
- With a very short psychotic period, usually three months;
- Usually with a favourable outcome, in spite of the fact that they are frequently recurrent;
- Somewhat different epidemiology and course in developing and developed countries context.

This overview of epidemiology of ATPD shows that it is wrong to assume that acute and transient psychotic disorder is somehow rudimentary or attenuated form of schizophrenia. These are distinct form of psychosis with acute and florid onset, polymorphous symptomatology, are usually short lived and have much better outcome. The controversies around the nomenclature (ATPD or Brief reactive psychosis) or the existence of subtypes should not distract us from the fact these are different form of psychosis and not a just rudimentary form of schizophrenia.

A somewhat scientifically less accurate analogy should help to clarify this point. Rheumatic fever is an inflammatory disease that occurs following Streptococcus infection. Acute rheumatic fever commonly appears in children between the ages of 6 and 15 and afflicts large number of patients especially in developing countries. Significant proportion of these individuals develops chronic rheumatic heart disease as a result of inflammatory process but this is only a very small proportion of those suffering from rheumatic fever. Although both disorders are related clinically, biochemically and pathologically; these have distinct course, treatments and outcome. Importantly, antibiotics have no role in the treatment of the rheumatic heart disease.

The outcome of ATPD has been shown to be more favourable in people suffering from ATPD compared to schizophrenia. One of the well known epidemiological findings in schizophrenia is that the incidence and prevalence of schizophrenia is same in men and women (Saha et al. 2005). However, ATPD is consistently reported to be more common in females between early and middle adulthood, while schizophrenia is more frequent in younger males (Thorup et al. 2007). The prevalence of ATPD is quite variable, and the disorder has greater frequency in developing countries (Susser et al. 1994). No excess of schizophrenia can be found relatives of patients with ATPD (Das et al. 1999). The premorbid level of functioning and premorbid social interactions is much better in patients suffering from ATPD than those reported for patients suffering from schizophrenia. The mode of onset, development, duration and phenomenology, as well as structure of symptomatology is also significantly different in patients with ATPD (Suda et al. 2005).

IMPLICATIONS FOR TREATMENT AND RESEARCH

The diagnostic and classification uncertainties surrounding the ATPD have implications for the long term treatment. The inadequate epidemiological evidence for classification and diagnosis is reflected in the lack of evidence for the treatment. On literature search, only three trials were identified which addressed the treatment for ATPD. One trial is single arm study of olanzapine in paediatric patients (Agarwal & Sitholey 2006). The total sample in other trials in adult population comprises of 75 patients. One trial compared risperidone with haloperidol (Chaudhuri et al. 2000) and other trials compared low and high dose haloperidol (Khanna 1997). In the later trial there was no significant difference in low (5 mg) and high dose (20 mg) haloperidol in achieving symptomatic improvement in 4 weeks period. The study by Chauhduri et al (2000) did not find significant difference between haloperidol and risperidone in a six week study.

Major guidelines such as National Institute of Health and Clinical Excellence (NICE, United Kingdom) guidelines do not even mention acute psychosis as a separate diagnostic category requiring different management. I searched the guidelines using the term acute psychosis, instead of ATPD, as it can be argued that the latter is controversial diagnostic entity with doubtful validity. Interestingly the word 'psychosis' appears in 41 page guidelines only 4 times, and only in relation to first episode and substance abuse (NICE 2009).

In absence of any guidance and evidence, it can be concluded that these disorders are either not being classified properly or the treatment is lumped with other disorders. One authority on the subject suggested that 'patients with ATPD have a favourable response to drug treatment, but are usually prescribed antipsychotic medications for long periods to prevent recurrences (Castagnini & Berrios 2009). This reinforces the impression from clinical practice, that the ATPD is perhaps being treated as a form of 'mini schizophrenia' as if the disorder is an attenuated form of schizophrenia.

The following questions require evidence and scientific approach for the proper treatment of these disorders:

1. What is most suitable therapeutic agent for the treatment of ATPD?

   Antipsychotics are currently used but there is no evidence base for this. There is substantial evidence that a significant proportion of those presenting with ATPD are classified as suffering from bipolar affective disorders on long term follow up.
2. What is the duration of the treatment required? When should antipsychotics be stopped after an initial episode?
3. Does the side effects/efficacy ratio with newer antipsychotics justify long term treatment for ATPD?

The last two questions are very important. Considering that most ATPD occur at a young age and the fact that the definition of ATPD includes 'transient' duration, the treatment with atypical antipsychotics may produce serious long term effects over a longer period. The long term treatments with antipsychotics which can induce metabolic disorders and reduce life expectancy amongst many other side effects mean that the debate about the diagnosis and treatment of ATPD is not merely an academic debate.

THE WAY FORWARD

The present classification of the ATPD is cumbersome and is seriously hindering research and practice. The classification of ATPD in different subtypes lacks empirical evidence and is not useful in clinical practice. The Working Group on the Classification of Psychosis has realized this and the classification of ATPD in the draft of ICD-11 will be addressing this. There is urgent need for evidence for the most appropriate treatment of acute and transient psychotic disorders. This is only possible if the ATPD is dealt as diagnostic construct and is not considered as a 'mini schizophrenia'.

Acknowledgements

The efforts of my colleagues, Prof. Jonathan Burns and Prof. Pichet Udomratn, members of WHO Working Group on Classification of Psychosis in ICD-11 and who contributed to literature search, are gratefully acknowledged.

Disclaimer

The author is member of the Working Group on Classification of Psychosis. The views expressed in this lecture are those of the author and in no way reflect the position of the working group or the WHO.

Conflict of interest: None to declare.

REFERENCES

1. *Agarwal V, Sitholey P. A preliminary open trial of olanzapine in paediatric acute and transient psychotic disorders. Indian Journal of Psychiatry 2006; 48:43-6.*
2. *Alaghband-Rad J, Boroumand M, Amini H, Sharifi V, Omid A, Davari-Ashtiani R. Non-affective acute remitting psychosis: a preliminary report from Iran. Acta Psychiatr Scand 2006; 113:96-101.*
3. *Amin S, Singh SP, Brewin J, Jones PB, Medley I, Harrison G. Diagnostic stability of first-episode psychosis. Comparison of ICD-10 and DSM-III-R systems. Br J Psychiatry 1999; 175:537-43.*
4. *Castagnini A, Bertelsen A, Berrios GE. Incidence and diagnostic stability of ICD-10 acute and transient psychotic disorders. Compr Psychiatry 2008; 49:255-61.*
5. *Castagnini A, Berrios GE. Acute and transient psychotic disorders (ICD-10 F 23): a review from a European perspective. Eur Arch Psychiatry Clin Neurosci 2009; 259:433-43.*

6. *Chang WC, Pang SLK, Chung DWS, Chan SSM. 5-year stability of ICD-10 diagnoses among Chinese patients presented with first-episode psychosis in Hong Kong. Schizophrenia Research 2009; 115:351-357.*
7. *Chaudhuri BP; Bhagabati D; Medhi D. Risperidone versus haloperidol in acute and transient psychotic disorder. Indian Journal of Psychiatry 2000; 42:280-90.*
8. *Collins PY, Wig NN, Day R, Varma VK, Malhotra S, Misra AK, Schanzer B, Susser E. Psychosocial and biological aspects of acute brief psychoses in three developing country sites. Psychiatric Quarterly 1996; 67:177-193.*
9. *Collins PY, Varma VK, Wig NN, Mojtabai R, Day R, Susser E. Fever and acute brief psychosis in urban and rural settings in north India. British Journal of Psychiatry 1999; 174:520-4.*
10. *Das SK, Malhotra S, Basu D. Family study of acute and transient psychotic disorders: comparison with schizophrenia. Social Psychiatry and Psychiatric Epidemiology 1999; 34:328-32.*
11. *Guiness EA. Brief reactive psychosis and the major functional psychoses: descriptive case studies in Africa. British Journal of Psychiatry 1992; 160(supp. 16):24-41.*
12. *Jager MDM, Hintermayr M, Bottlender R, Strauss A, Moller HJ. Course and outcome of first-admitted patients with acute and transient psychotic disorders (ICD-10: F23). Focus on relapses and social adjustment. Eur Arch Psychiatry Clin Neurosci 2003; 253:209-15.*
13. *Jager MDM, Bottlender R, Strauss A, Moller HJ. Klassifikation der funktionellen psychosen: Die bedeutung der ICD-10-diagnosen (forschungskriterien) fur die vorhersage des langzeitverlaufes. Fortschr Neurol Psychiatr 2004; 72:70-8.*
14. *Jager M, Riedel M, Moller HJ. Acute and transient psychotic disorders (ICD-10: F23). Empirical data and implications for therapy. Nervenarzt 2007; 78:745-52.*
15. *Jorgensen P, Bennedsen B, Christensen J, Hyllested A. Acute and transient psychotic disorder: comorbidity with personality disorder. Acta Psychiatr Scand 1996; 94:460-4.*
16. *Jorgensen P, Bennedsen B, Christensen J, Hyllested A. Acute and transient psychotic disorder: a 1-year follow-up study. Acta Psychiatr Scand 1997; 96:150-4.*
17. *Khanna A.Lal N..Dalal PK,Khalid A & Trivedi JK. Treatment of acute and transient psychotic disorders with low and high doses of oral haloperidol. Indian J. Psychiatry 1997; 39:136-42.*
18. *Malhotra S, Malhotra S. Acute and transient psychotic disorders: comparison with schizophrenia. Curr Psychiatry Rep 2003; 5:178-86.*
19. *Manschreck TC, Petri M. The atypical psychoses. Cult Med Psychiatry 1978; 2:233-68.*
20. *Marneros A, Pillman F. Acute and transient psychoses. Cambridge University Press, Cambridge, 2004.*
21. *Marneros A, Pillmann F, Haring A, Balzuweit S, Bloink R. The relation of acute and transient psychotic disorder (ICD-10 F23) to bipolar schizoaffective disorder. J Psychiatr Res 2002; 6:165-71.*
22. *Marneros A, Pillmann F, Haring A, Balzuweit S, Bloink R. What is schizophrenic in acute and transient psychotic disorder? Schizophrenia Bulletin 2003; 29:311-23.*
23. *Marneros A. Beyond the Kraepelinian dichotomy: acute and transient psychotic disorders and the necessity for clinical differentiation. British Journal of Psychiatry 2006; 189:1-2.*
24. *Mojtabai R, Susser E, Bromet EJ. Clinical characteristics, 4-year course and DSM-IV classification of patients with non affective acute remitting psychosis. Am J Psychiatry 2003; 160:2108-15.*
25. *NICE Schizophrenia: Core Interventions in the Treatment and Management of Schizophrenia in Adults in Primary and Secondary Care. NICE clinical guideline 82; 2009. Available at www.nice.org.uk/CG82.*
26. *Robins E, Guze SB. Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. American Journal of Psychiatry 1970; 126:107-11.*
27. *Saha S, Chant D, Welham J, McGrath J. Systematic Review of the Prevalence of Schizophrenia. PLoS Med 2005A;2:e141.*
28. *Sajith SG, Chandrasekaran R, Sadanandan Unni KE, Sahai A. Acute polymorphic psychotic disorder: diagnostic stability over 3 years. Acta Psychiatr Scand 2002; 105:104-109.*
29. *Singh SP, Burns T, Amin S, Jones PB, Harrison G. Acute and transient psychotic disorders: precursors, epidemiology, course and outcome. Br J Psychiatry 2004;185:452-9.*
30. *Suda K, Hayashi N, Hiraga M. Predicting features of later development of schizophrenia among patients with acute and transient psychotic disorder. Psychiatry Clin Neurosci 2005; 59:146-50.*
31. *Susser E, Wanderling J. Epidemiology of nonaffective acute remitting psychosis vs schizophrenia. Sex and socio-cultural setting. Arch Gen Psychiatry 1994; 51:294–301.*
32. *Susser ES, Fennig S, Jandorf L, Amador X, Bromet E. Epidemiology, diagnosis, and course of brief psychoses. Am J Psychiatry 1995; 152:1743–8.*
33. *Susser ES, Varma VK, Mattoo SK, Finnerty M, Mojtabai R, Tripathi BM, et al. Long-term course of acute brief psychosis in a developing country setting. Br J Psychiatry 1998; 173:226–30.*
34. *Thangadurai P, Gopalakrishnan R, Kurian S, Jacob KS. Diagnostic stability and status of acute and transient psychotic disorders. Br J Psychiatry 2006; 188:293.*
35. *Thorup A, Waltorf BL, Pedersen CB, Mortensen PB, Nordentoft M. Young males have a higher risk of developing schizophrenia: a Danish register study. Psychol Med 2007; 37:479-84.*
36. *Varma VK, Malhotra S, Yoo ES, Jiloha RC, Finnerty MT, Susser E. Course and outcome of acute non-organic psychotic states in India. Psychiatric Quarterly 1996; 67:195-207.*

Correspondence:

Dr. Saeed Farooq
Visiting Professor Staffordshire University & Consultant Psychiatrist
Black Country partnership NHS Foundation Trust
Wolverhampton, UK
E-mail: sfarooqlrh@yahoo.com