

Antipsychotic treatment of primary delusional parasitosis

Systematic review

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Background Little is known about the treatment of delusional parasitosis with typical and atypical antipsychotics.

Aims To evaluate the effectiveness of typical and atypical antipsychotics in primary delusional parasitosis (delusional disorder, somatic type).

Method A systematic review was conducted.

Results No randomised trials were found and hence we collected the best evidence from 16 other trials and case reports, separating primary from other forms of delusional parasitosis. Studies using typical antipsychotics showed partial or full remission in between 60 and 100% of patients. Analysis of selected patients with primary delusional parasitosis showed that typical and atypical antipsychotics were effective in the majority, but that remission rates did not differ significantly between typical and atypical antipsychotics.

Conclusions In the absence of controlled trials there is limited evidence that antipsychotics are effective in primary delusional parasitosis. Rigorous studies are needed to evaluate their effectiveness and to compare typical and atypical antipsychotics directly.

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Delusional parasitosis is characterised by the fixed belief that one is infested with parasites or small living creatures although there is no medical evidence for this (Arnold, 2000; Freudenmann, 2002). Patients usually complain about itching that they ascribe to the presence of animals in or under the skin. The belief is usually held with delusional intensity but the severity of the delusional intensity can vary. The annual prevalence of delusional parasitosis is estimated at 80 cases per million inhabitants, with a yearly incidence of 20 per million (Trabert, 1997).

History

It is usually said that delusional parasitosis was first described by Thibierge in 1894 and Perrin in 1896. However, according to Trabert's comprehensive historical literature search (Trabert, 1993, 1997), the clinical picture was first mentioned by Robert Willan in 1799 and Johann Heinrich Jördens in 1801. According to our research neither author suspected a psychiatric aetiology. Moreover, Musalek (1991) discovered a patient with delusions of *intestinal* parasitosis (*Enterozoewahn*) in an article from 1843 (Charcellay, 1843).

Pathogenesis

Delusional parasitosis is a non-specific syndrome rather than a single disorder. It can occur as a delusional disorder, meeting ICD-10 criteria for persistent delusional disorder (World Health Organization, 1993) and DSM-IV-TR criteria for delusional disorder, somatic type (American Psychiatric Association, 2000). This is what clinicians usually mean when they refer to 'delusional parasitosis', although it accounts only for about 40% of all patients with such symptoms (Trabert, 1995). We will call this type of delusional parasitosis 'primary delusional parasitosis' following Ganner & Lorenzi's (1975) concept of '*reiner Dermatozoewahn*' (German '*rein*'=

primary or pure). The diagnosis of primary delusional parasitosis can be made only after real infection or other underlying medical or psychiatric conditions have been excluded, because delusional parasitosis can be associated with several physical illnesses, psychiatric disorders or intoxications (Magnan & Saury, 1889; Ekblom, 1938; Huber, 1957; Berrios, 1985; Freyne & Wrigley, 1994; Freudenmann, 2002). Delusional parasitosis can also occur as a *folie à deux* or *folie à trois* (shared psychotic disorder; Trabert, 1995) as well as by proxy (Nel *et al*, 2001). Delusional parasitosis syndromes can thus be classified according to their pathogenesis (Appendix 1).

Clinical management

The clinical management of patients with delusional parasitosis is a challenge, as patients are often reluctant to engage in a meaningful therapeutic relationship because of their somatic concept of the illness. Thus they seek help from general practitioners, dermatologists or pest control companies but refuse psychiatric referral or therapy. Usually, it is difficult to obtain informed consent to treat patients with delusional parasitosis with antipsychotics. Therefore experienced clinicians tell their patients that the antipsychotics are effective 'against the itch' or the 'problems with the pests' in order not to have to lie. A few practical guidelines have been proposed (Musalek, 1991; Driscoll *et al*, 1993; Winsten, 1997; Freudenmann, 2002).

Another approach to achieve a better therapeutic relationship was developed in the late 1980s. Specialised out-patient clinics were located in *dermatology* clinics to acknowledge the patients' non-psychiatric concept of their illness (Musalek & Kutzer, 1989; Musalek *et al*, 1989; Musalek, 1991; Trabert, 1993). However, even these 'low threshold' settings have often failed to allow the establishment of a sufficient therapeutic alliance. Trabert's study in Homburg, Germany stated that 20 of 35 patients (57%) were seen for less than 3 months (Trabert, 1993). Despite all these efforts, many patients lose faith in professional medicine and resort to dangerous self-therapies such as excessive skin cleaning with chemicals or pesticides (Freudenmann, 2002).

Antipsychotic treatment

For adequate treatment of delusional parasitosis it is necessary to differentiate

between the different forms (Berrios, 1985; Freudenmann & Schönfeldt-Lecuona, 2005). Although antipsychotics provide the main treatment for primary delusional parasitosis, they are used only symptomatically for delusional parasitosis secondary to somatic diseases, which mainly requires adequate therapy of the underlying disorder. Even in recent years, many sources recommended the use of the typical antipsychotic pimozide in delusional parasitosis (Driscoll *et al.*, 1993; van Vloten, 2003), although pimozide is no longer a first-line antipsychotic because of concerns about drug safety (high risk of extrapyramidal symptoms, longer QTc interval and drug–drug interactions (Food and Drug Administration, 1996; National Institute for Clinical Excellence, 2002; Benkert & Hippus, 2005).

Several case reports have indicated the beneficial effects of *atypical* antipsychotics in primary delusional parasitosis, but evidence for these is still limited to risperidone (Gallucci & Beard, 1995; Freyne *et al.*, 1999; Moretti & Varga, 2000), quetiapine (Kim *et al.*, 2003), olanzapine (Le & Gonski, 2003) and amisulpride (Lepping *et al.*, 2005).

Although it is often stated that there is a lack of randomised controlled trials of the use of antipsychotics (including pimozide) in delusional parasitosis (Driscoll *et al.*, 1993; Trabert, 1995; Freudenmann & Schönfeldt-Lecuona, 2005), we know of no systematic review on this topic. Moreover, no antipsychotic is licensed for the treatment of delusional parasitosis. We therefore undertook the first systematic review of the effectiveness of typical and atypical antipsychotic treatment for primary delusional parasitosis (meeting ICD–10 F22.0 criteria for persistent delusional disorder or DSM–IV–TR criteria for delusional disorder of somatic type) in order to determine whether: *typical* antipsychotics are effective in treating primary delusional parasitosis and are more effective than placebo; *atypical* antipsychotics are effective in treating primary delusional parasitosis and more effective than placebo; atypical antipsychotics are more or less effective than typical antipsychotics.

METHODS

Search strategy

Our first priority was to discover randomised controlled trials that addressed the study questions. We tried to identify all

available works on delusional parasitosis published in English, German, French, Spanish, Portuguese, Italian, Dutch or Hungarian before December 2005. A comprehensive search of EMBASE, Medline, PsycInfo, PsycLit and Psyn dex was performed using the search terms ‘delusion(s) of parasitosis’, ‘delusional parasitosis’, ‘delusion(s) of infestation’, ‘*parasitosis*’, ‘monosymptomatic hypochondriacal psychosis’, ‘parasitophob*’, ‘entomophob*’, ‘acarophob*’, ‘Dermatozoenwahn’, and ‘Ekbohm’s syndrome’ (discarding papers on the ‘burning feet syndrome’ which has also been labelled with this eponym). We checked the reference lists of identified articles. We searched the internet using Google, and textbooks of psychiatry, theses, unlisted journals and conference proceedings by hand. We wrote to pharmaceutical companies producing substances often used to treat delusional parasitosis and known authorities in the field of delusional parasitosis (e.g. Wolfgang Trabert, Emden, Germany, and Marc Bourgeois, Bordeaux, France) to identify unpublished data on the use of antipsychotics in delusional parasitosis. We searched for continuing trials via two websites – ClinicalTrials (<http://www.clinicaltrials.gov>) and Current Controlled Trials (<http://www.controlled-trials.com>).

Assessment of literature

P.L. and R.W.F. independently assessed whether all retrieved works dealt with delusional parasitosis in general or primary delusional parasitosis, and whether the intervention consisted of typical or atypical antipsychotics. We also assessed whether any of these were randomised controlled trials.

In the absence of randomised controlled trials we planned to gather sound evidence from other studies meeting defined inclusion criteria (see Appendix 2). In particular we sought well-designed quasi-experimental and observational studies relevant to our research questions. We included all open studies with either prospective design or more than 30 patients. We then summarised in structured form the main findings of the 16 studies meeting these minimal criteria (Table DS1, data supplement to online version of this paper). We assigned individual outcomes between three main categories: no effect (0); partial remission (i.e. some response) (1) and full remission (2). To strengthen our

conclusions we also tried to separate primary delusional parasitosis from secondary delusional parasitosis.

P.L. and R.W.F. also selected all case reports containing information on diagnosis of primary delusional parasitosis, gender, age, antipsychotic medication used and dose, and clinical outcome on the same 3-point scale after 4 weeks or more. In this way we applied Trabert’s case-based meta-analysis which is designed for uncommon syndromes that cannot be studied in a traditional randomised controlled trial (Trabert, 1995). We also separated patients treated with typical and atypical antipsychotics. Although this approach is subject to publication bias because it considers only published cases, we aimed to increase comparability between studies. To judge the success of this strategy we tested whether clinical outcomes differed significantly between studies.

RESULTS

Literature search

We identified a total of 368 works on delusional parasitosis in general, including poster presentations, in December 2005 (Fig. 1). We found most on Medline ($n=191$), and in review articles and the comprehensive theses of Musalek (1991) and Trabert (1993). At least half were not in English – most of these were in German, but some were in Italian and French. The full bibliography can be obtained from the authors on request.

Before the psychopharmacological era, which began with the discovery of chlorpromazine in 1952, only 31 works on delusional parasitosis were retrieved. The majority ($n=223$) were published between 1952 and the launch of risperidone in about 1990. The remainder ($n=114$) were published after 1990, but many of these did not examine the use of atypical antipsychotics.

Absence of randomised controlled trials

Our systematic search found *no* randomised controlled trials on the effects of typical or atypical antipsychotics in either primary or other delusional parasitosis. When accessed in December 2005, the Clinical Trials (<http://www.clinicaltrials.gov>) and Current Controlled Trials (<http://www.controlled-trials.com>) websites gave no indication of unpublished or current

Table 1 Summary of 92 case reports of the treatment of primary delusional parasitosis with typical antipsychotics¹

Antipsychotic	Dosage	n	Outcome			
			Full remission	Partial remission	No effect	Non-adherence
Pimozide	1–12 mg/day	53	24	26		3
Trifluoperazine	2–15 mg/day	7	3	3	1	
Haloperidol	1–10 mg/day	6	4	2		
Chlorpromazine	150–300 mg/day	4		2	2	
Perfenazine	4–12 mg/day	3	1	2		
Sulpiride	50–150 mg/day	2	2			
Perithiazine	5 mg/day	1	1			
Thioridazine	75 mg/day	1	1			
Depots						
Fluphenazine	7.5–25 mg	10	7	3		
Flupenthixol	2–20 mg	5	4		1	

1. See Table DS2 in data supplement to online version of this paper for further details.

randomised controlled trials. Our evaluation of the literature therefore relied on results from other studies.

Effect of typical antipsychotics

Table DS1 (see data supplement to online version of this paper) summarises the 16 quasi-experimental or observational studies which primarily used typical antipsychotics and met our inclusion criteria (Frithz, 1979; Hamann & Avnstor, 1982; Munro, 1982; Lyell, 1983; Ungvari, 1983, 1984; Ungvari & Vladar, 1984, 1986; Lindskov & Baadsgaard, 1985; Bourgeois, *et al*, 1986; Reilly & Batchelor, 1986; Musalek, *et al*, 1989; Paholpak, 1990; Trabert, 1993, 1995; Srinivasan *et al*, 1994; Zomer *et al*, 1998; Bhatia *et al*, 2000). The studies showed aggregate partial and full remission rates between 60 and 100% after treatment with typical antipsychotics. Unfortunately, the majority were not limited to primary delusional parasitosis. Nevertheless they suggest a generally good outcome for primary and other forms of delusional parasitosis whenever continuous antipsychotic treatment can be established.

In primary delusional parasitosis, aggregate partial and full remission rates with pimozide ranged from 67% ($n=66$; Lyell, 1983) through 89% ($n=9$; Munro, 1982) to 100% ($n=10$; Ungvari & Vladar, 1984, 1986), $n=18$; Ungvari, 1983, 1984). In mixed samples with primary and other forms of delusional parasitosis, aggregate

partial and full remission rates with pimozide were similar and varied from 61% ($n=33$; Zomer *et al*, 1998), through 87% ($n=52$; Bhatia *et al*, 2000) to 91% ($n=11$; Hamann & Avnstor, 1982). A high rate of side-effects such as sedation, extrapyramidal symptoms and depression was noted in several studies using pimozide (38%; Ungvari, 1983, 1984 and 73%; Hamann & Avnstor, 1982).

The only two placebo-controlled trials in delusional parasitosis both used pimozide (Hamann & Avnstor, 1982; Ungvari & Vladar, 1984, 1986). However, they are limited by a lack of randomised allocation to the treatment groups and small samples ($n=10$ or 11 respectively). Only Ungvari & Vladar (1984, 1986) treated patients with primary delusional parasitosis.

Studies not specific for particular antipsychotics demonstrated aggregate partial and full remission rates between 82% ($n=35$, not only primary delusional parasitosis, Trabert, 1993) and 89% ($n=19$, only primary delusional parasitosis, but some patients were treated with electroconvulsive therapy; Srinivasan *et al*, 1994).

The only study that investigated traditional depot antipsychotics found an aggregate response and remission rate of 93%, even in patients that could not be treated with oral medication (Frithz, 1979).

The sample consisted only of patients with primary delusional parasitosis ($n=15$). Another study using haloperidol reported a 100% response rate (but no full

remissions) (Paholpak, 1990); nine of ten patients in this study had primary delusional parasitosis.

Across the different typical antipsychotics used, an effect of antipsychotic medication in delusional parasitosis was noted after about 3–6 weeks (Hamann & Avnstor, 1982; Trabert, 1995). Studies came to different conclusions as to whether or not it is necessary to continue antipsychotics after successful acute therapy.

Symptoms of delusional parasitosis that were associated with major depression could be treated successfully with antidepressants (Musalek *et al*, 1989; Trabert, 1993; Bhatia *et al*, 2000).

One small study indicated that electroconvulsive therapy might be effective in patients with primary delusional parasitosis (Srinivasan *et al*, 1994).

A survey of British dermatologists suggested that combining psychopharmacological and dermatological treatments (local and systemic) is superior to single therapeutic approaches. Of particular note is that therapy without psychotropic medication was ineffective (Reilly & Batchelor, 1986).

We abstracted data from case series and case reports on 92 patients with primary delusional parasitosis treated with typical antipsychotics who met our selection criteria – (see Table DS2 (data supplement to online version of this paper) (Riding & Munro, 1975; Gould & Gragg, 1976; Munro, 1978a,b, 1982; Frithz, 1979; Avnstor *et al*, 1980; Ungvari, 1984; Berrios,

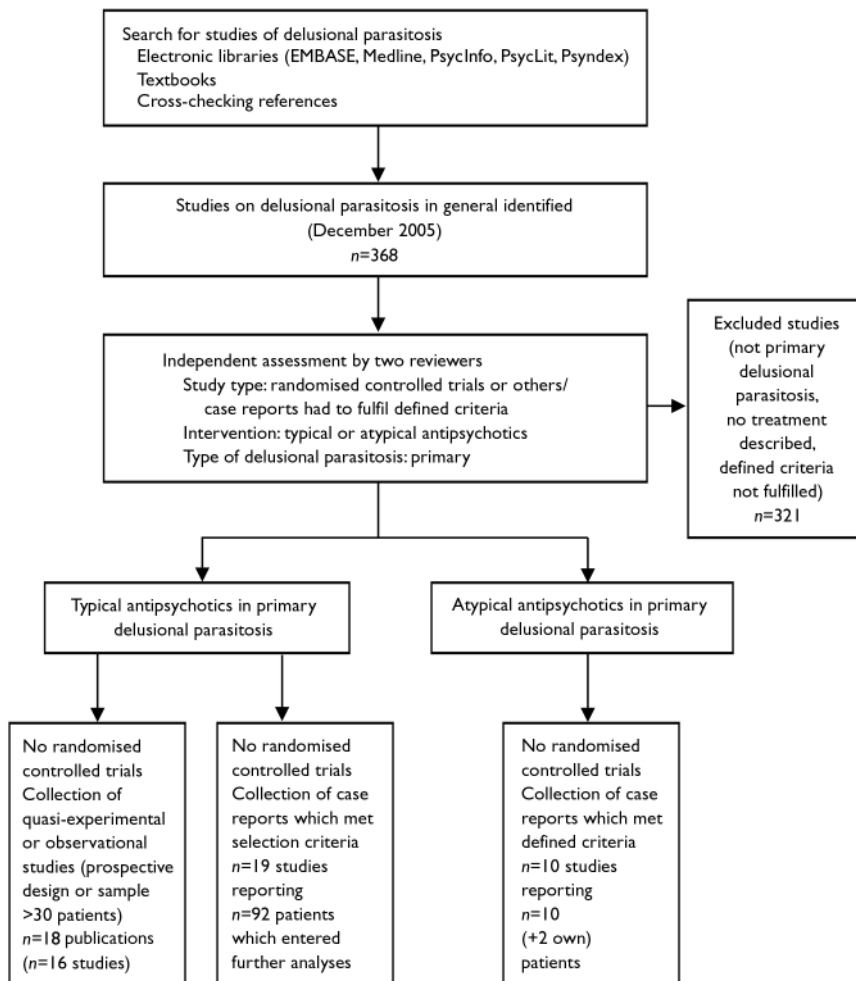


Fig. 1 Method used for identification and selection of studies of delusional parasitosis.

1985; Andrews *et al*, 1986; Sheppard *et al*, 1986; Ungvari & Vldar, 1986; May & Terpenning, 1991; Srinivasan *et al*, 1994; Chiu *et al*, 1996; Rasanen *et al*, 1997; Kim *et al*, 2003; Takahashi *et al*, 2003).

Table 1 shows that the majority were treated with pimozide, whereas for other typical antipsychotics only small numbers have been reported. The majority of these patients with primary delusional parasitosis were effectively treated with typical antipsychotics. Pimozide was helpful for 50 of 53 patients (94%), with 24 (45%) achieving full remission. Trifluoperazine and haloperidol appeared to be similarly effective, as did fluphenazine and flupenthixol depot.

Effect of atypical antipsychotics

We were able to identify only 12 case reports on atypical antipsychotics that met our selection criteria (Table 2). Although atypical antipsychotics were effective for

the majority of patients with primary delusional parasitosis only three patients achieved full remission. All six patients for whom risperidone was prescribed, achieved full (four) or partial (two) remission; the dosages used ranged from 1 to 8 mg per day.

Effect of typical v. atypical antipsychotics

The five main studies of patients with primary delusional parasitosis treated with typical antipsychotics report very heterogeneous outcomes (Table 3), suggesting that the studies themselves are very heterogeneous, for example in their inclusion and exclusion criteria (selection bias) or in their definitions of partial and full remission (measurement bias), or that there is publication bias. Furthermore, the eight studies of patients with secondary delusional parasitosis treated with typical antipsychotics reported heterogeneous outcomes. This reduces the value of comparing studies

reporting the use of typical primary antipsychotics in secondary delusional parasitosis. However, there was a large difference between the failure rate of 5% in primary delusional parasitosis and that of at least 26% in secondary delusional parasitosis ($\chi^2=18.2$, d.f.=2, $P<0.001$). It follows that studies of secondary delusional parasitosis have nothing to contribute to the issue of the most effective treatment for primary delusional parasitosis.

The heterogeneity in the reported outcome of patients with primary delusional parasitosis treated with typical antipsychotics reduces the value of comparison with reports of atypical antipsychotics. Although the difference is not statistically significant ($\chi^2=2.6$, d.f.=2), we cannot conclude that typical and atypical antipsychotics are equally effective because of the innate biases already identified.

DISCUSSION

This is the first systematic review of the effectiveness of typical and atypical antipsychotics in the treatment of delusional parasitosis. Our review was based on 368 published works and covered almost twice as many papers as the 193 covered by the most comprehensive review published to date (Trabert, 1993). In contrast to previous review articles (e.g. Aw *et al*, 2004; Bourgeois & Nguyen-Lan, 1986; Driscoll *et al*, 1993; Freudemann, 2002; Lynch, 1993; Slaughter *et al*, 1998; Wykoff, 1987; Zanol *et al*, 1998), our review focuses on primary delusional parasitosis. We separated this important form of delusional parasitosis (delusional disorder of somatic type) from symptomatic forms of delusional parasitosis ('secondary delusional parasitosis') which cover different nosological entities and require other forms of therapy that focus on the underlying illness. As we were unable to show homogeneity in the outcomes of primary and secondary delusional parasitosis, we did not review other studies examining the effect of antipsychotic medication in other types of ICD-10 F22.0 disorders, which also differ clinically from delusional parasitosis.

Our systematic review identified no randomised controlled trials of the efficacy of typical and atypical antipsychotics in primary delusional parasitosis, probably because the disorder is rare and it is difficult to recruit patients, obtain informed consent, and achieve sufficient adherence

Table 2 Summary of 12 case reports of the treatment of primary delusional parasitosis with atypical antipsychotics

Reference	Case no. in paper	Age, years	Gender	Treatment	Dosage, mg	Outcome on atypical antipsychotics
Gallucci & Beard (1995)	1	72	F	Risperidone	1–6	Partial remission
Slaughter <i>et al</i> (1998)	3	32	F	Olanzapine (+ nefazodone)	5–20	Non-adherence
Freyne <i>et al</i> (1999)	1	81	M	Risperidone	0.5–1.0	Full remission
Kim <i>et al</i> (2003)	1	33	M	Risperidone	1–3	Partial remission
Kim <i>et al</i> (2003)	2	55	F	Quetiapine, then pimozide	Up to 800 3–4	Partial remission (quetiapine), Full remission (pimozide)
Aw <i>et al</i> (2004)	5	66	F	Quetiapine + steroids + antihistamines	12.5	Inestimable – multiple drugs
Aw <i>et al</i> (2004)	8	90	F	Quetiapine then risperidone	12.5 1.5	No effect reported (quetiapine) partial remission (risperidone)
Pacan <i>et al</i> (2004)	1	56	M	Olanzapine then risperidone	10–20 4–8	No effect (olanzapine), partial remission (risperidone)
Pacan <i>et al</i> (2004)	2	54	F	Risperidone (later + sertraline + diazepam)	1–3	Full remission
Lepping <i>et al</i> (2005)		32	F	Venlafaxine XR + olanzapine then amisulpride	150–225 5 800	No effect Full remission (amisulpride)
Freudenmann <i>et al</i> (2007)		77	F	Olanzapine	2.5–7.5	Partial remission
Own unpublished patient		67	F	Amisulpride	50–400	Partial remission

to medication throughout a clinical trial because of their poor insight (Gould & Gragg, 1976; Munro, 1982; Ungvari & Vladar, 1986; Freudenmann & Schönfeldt-Lecuona, 2005). It is difficult to establish a good therapeutic alliance with these patients even in highly specialised settings (Trabert, 1993). Because of a lack of randomised controlled trials all our suggestions for therapy need to be interpreted cautiously. Nevertheless we are keen to provide clinicians with the current best evidence.

Use of typical antipsychotics

Our findings show that primary delusional parasitosis can be effectively treated with typical antipsychotics. Outcome is generally good, although this conclusion is limited by a possible publication bias. We confirm Trabert's finding that the introduction of typical antipsychotics has substantially improved remission rates (Trabert, 1995). Although the better studies have so far used pimozide (Hamann & Avnstorp, 1982; Ungvari & Vladar, 1984, 1986), the evidence for its efficacy is weak by today's standards. The level of evidence for its use in primary delusional parasitosis is IIa according to the criteria of the Agency for Health Care Policy and Research (1992), whereas other typical antipsychotics such as haloperidol have only level III evidence. Pimozide should not be used in patients with a high

cardiac risk, together with other substances that prolong the QTc interval (Food and Drug Administration, 1996), or in elderly patients with delusional parasitosis.

Another important treatment in primary delusional parasitosis is the intramuscular application of traditional depot antipsychotics (Frithz, 1979), because the main problem in clinical management is to convince patients to take oral medication regularly. Injection may be more consistent with patients' (false) somatic concept of their illness and require less cooperation than oral medication. If the patient agrees to a first depot injection, the delusion may well remit at least partially and further antipsychotic treatment will be accepted. As the only study of this approach (Frithz, 1979) has only 15 patients, larger samples are needed.

Use of typical antipsychotics

Our systematic review revealed only 12 usable case reports of the use of atypical antipsychotics in primary delusional parasitosis. These provide limited evidence that primary delusional parasitosis can be treated effectively with these drugs. To our knowledge, this is the first complete collection of patients with primary delusional parasitosis treated with atypical antipsychotics, whereas many patients with secondary forms of delusional parasitosis have been reported in recent years (e.g. De Leon *et al*, 1997; Safer *et al*, 1997;

Kumbier & Kornhuber, 2002; Freudenmann, 2003; Le & Gonski, 2003; Scheinfeld, 2003; Wenning *et al*, 2003). Thus the evidence for the use of atypical antipsychotics in delusional parasitosis is even weaker than for typical antipsychotics.

Most case reports are available for risperidone, whereas we are not aware of reports on the use of clozapine, ziprasidone or aripiprazole in primary delusional parasitosis. Amisulpride might be a good alternative given that its selective D₂/D₃-antidopaminergic action resembles that of typical antipsychotics without the same high probability of side-effects (Freudenmann & Lepping, 2006; Lepping *et al*, 2006). Its lack of anticholinergic and adrenergic effects is particularly useful in elderly patients or patients with a higher cardiovascular risk profile. Risperidone microspheres for intramuscular injection provide a potentially interesting new treatment for delusional parasitosis, as this is the only atypical antipsychotic in depot form, but this recommendation is entirely theoretical since there are no reports of the use of risperidone microspheres in delusional parasitosis at present.

Other treatment options

An alternative to these pharmacological strategies is electroconvulsive therapy. The use of electroconvulsive therapy in a patient with delusional parasitosis was first

Table 3 Outcome of treatment of delusional parasitosis with antipsychotics

Outcome study	No effect, refusal, etc., n (%)	Partial remission, n (%)	Full remission, n (%)	Total, n
<i>Atypical antipsychotics</i>	2 (17)	7 (58)	3 (25)	12
Primary delusional parasitosis (five studies) ¹				
<i>Typical antipsychotics</i>	7 (8)	40 (43)	45 (49)	92
Primary delusional parasitosis				
Frithz (1979)	1	3	11	15
Munro (1982)	1	5	3	9
Ungvari (1984)	0	7	12	19
Ungvari & Vladar (1986)	0	10	0	10
Srinivasan <i>et al</i> (1994)	2	4	5	11
14 studies with ≤ 4 patients	3	11	14	28
Mixed delusional parasitosis outcome on 3-point scale ^{2,3}	43 (26)	50 (30)	73 (44)	166
Lindskov & Baadsgaard (1985)	0	4	10	14
Musalek <i>et al</i> (1989)	12	5	17	34
Trabert (1993)	6	18	9	33
Zomer <i>et al</i> (1998)	19	7	7	33
Bhatia <i>et al</i> (2000)	6	16	30	52
Mixed delusional parasitosis: binary outcome ³	27 (29)	67 (71)		94
Hamann & Avnstorp (1982)	1	10		11
Lyell (1983)	16	44		60
Reilly & Batchelor (1986)	10	13		23

1. $\chi^2 = 22.1$, d.f.=8, $P < 0.01$.

2. Test for homogeneity of studies with outcome on 3-point scale $\chi^2 = 43.5$ d.f.=8, $P < 0.001$.

3. Outcome dichotomised, i.e. partial and full remission combined. Test for homogeneity of all studies of mixed delusional parasitosis, $\chi^2 = 34.6$, d.f.=7, $P < 0.001$.

described by Harbauer in 1949 and has since occasionally been reported (Baumer, 1951; Bers & Conrad, 1954; Hopkinson, 1970). Srinivasan *et al* (1994) reported effectiveness in primary delusional parasitosis in a small sample. Electroconvulsive therapy might be a useful option in cooperative refractory patients when antipsychotics are contraindicated or problematic (e.g. in the elderly).

Synthesis

The very heterogeneous outcomes reported by the five main studies of treating primary delusional parasitosis with typical antipsychotics (see Table 3) suggest that the studies themselves suffer from some or all of selection bias, measurement bias and publication bias. Together with these flaws the paucity of evidence on treating primary delusional parasitosis with atypical antipsychotics undermines any comparison of typical and atypical antipsychotics. Despite weaker evidence for the effectiveness of atypical antipsychotics in treating delusional

parasitosis in comparison with pimozide, the use of atypical antipsychotics might improve side-effects, and thus adherence and patient outcome.

It is important to strengthen this weak evidence in the future. We limited our selection of case series and case reports of delusional parasitosis to those including a minimum data-set for each recruited patient (age, gender, the nature and timing of diagnosis, the name and dose of medication, and the nature and timing of remission on a 3-point scale; Appendix 2).

Implications

Our systematic review generated weak evidence that antipsychotics are effective in treating primary delusional parasitosis. However, in view of the limited evidence, this recommendation is tentative and needs caution in implementation. Since the introduction of atypical antipsychotics, pimozide is no longer the treatment of choice for reasons of drug safety, even though it has the best evidence of effectiveness in

treating primary delusional parasitosis. It is important to improve this evidence through rigorous, ideally randomised, studies which compare typical antipsychotics and atypical antipsychotics directly.

APPENDICES

Appendix I: Aetiological classification of delusional parasitosis

(I) Primary delusional parasitosis: delusional disorder.

Primary delusion according to Berrios (1985), first described by Huber (1957); diagnosis: persistent delusional disorder (ICD-10 F22.0); delusional disorder, somatic type (DSM-IV-TR 297.1)
Special form: as a shared psychotic disorder (ICD-10 F24, DSM-IV-TR 297.3)

(II) Secondary forms of delusional parasitosis: secondary to another condition.

(a) *Concomitant psychotic symptom in another psychiatric disorder:*

- (1) Schizophrenia or other psychotic disorders; diagnosis according to underlying psychotic disorder (ICD-10 F2x, DSM-IV-TR 295, etc).
- (2) Major depressive disorder with psychotic symptoms or mania; diagnosis according to underlying affective disorder (ICD-10 F3x, DSM-IV-TR 296, etc).
- (3) Dementia; diagnosis ICD-10 F00-03, DSM-IV-TR 290, 294.

(b) *Delusional parasitosis based on other brain pathologies ('macroscopic') or general medical condition:*

- (1) Brain disorders not mentioned in ICD-10 F0 (e.g. brain neoplasm/infection, stroke); 'organic damage with secondary delusions' according to Berrios (1985), first described by Ekblom (1938).
- (2) Somatic illness with pruritus or paraesthesia (e.g. diabetes mellitus with neuropathic pain, uraemia, jaundice, cancer); 'paraesthesia or other somatic pathological sensations with secondary delusions' according to Berrios (1985); diagnosis: organic hallucinosis or organic delusional disorder (ICD-10 F06.0 or F06.2), psychotic disorder due to . . . [indicate the general medical condition] with delusions (DSM-IV-TR 293.81) or with hallucinations (293.82) or persistent delusional disorder (ICD-10 F22.0); delusional disorder, somatic type (DSM-IV-TR 297.1), when delusional parasitosis is not the direct physiological consequence of the somatic illness.

(c) *Delusional parasitosis as a substance-induced 'toxic' psychosis:*

Substance-induced 'paraesthesia or other somatic pathological sensations with secondary delusions' according to Berrios (1985), first described by Magnan & Saury in 1889 for cocaine addicts ('*signe de Magnan*');

- (1) Owing to psychotropic substance, e.g. cocaine, amphetamines; diagnosis: acute intoxication, psychotic disorder, predominantly delusional (ICD-10 F1x.51) or predominantly hallucinatory (ICD-10 F1x.52); substance-induced psychotic

disorder, with hallucinations (DSM–IV–TR 292.11), with delusions (292.12).

- (2) Owing to non-psychotropic substances, e.g. antibiotics, steroids, non-steroidal anti-inflammatory drugs; diagnosis: organic hallucinosis or organic delusional disorder (ICD–10 F06.0 or F06.2), DSM–IV–TR codes see 1.

Appendix 2: Proposed minimum information required for case series and case reports of primary delusional parasitosis

Case report criteria

- (1) Diagnosis including confirmation date
- (2) Gender of patient
- (3) Age of patient
- (4) Medication used with dosage
- (5) Outcome on 3-point scale: (0) no remission, (1) partial remission, (2) full remission
- (6) Length of follow-up (at least 4 weeks after date of diagnosis).

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