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What treatments do patients with panic disorder and agoraphobia get?

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Abstract In a retrospective study 100 patients with DSM-III-R/ICD-10 panic disorder and agoraphobia (PDA) were interviewed about the psychopharmacological, psychological and 'alternative' treatments they had received in the course of their illness. Patients gave global statements about how satisfied they were with the various treatments they had experienced. Many patients received treatments that have never been investigated under controlled conditions. The most common drug treatments, in descending order, were: 48% benzodiazepines, 42% tricyclic antidepressants, 32% herbal preparations, 29% neuroleptics, 7% selective serotonin reuptake inhibitors and 6% beta blockers. Of the drug prescriptions, 63% were according to international standards. Of the neuroleptics, two-thirds (63.3%) were prescribed by nonpsychiatric physicians, and only one-third by psychiatrists (33.3%). Tricyclic antidepressants were prescribed more often by psychiatrists (64.7%) than by non-psychiatrists (31.4%). Among psychological treatments, autogenic training (43% of the patients) and psychodynamic therapy (33%) were used far more frequently than behavioural/cognitive therapy (20%). These results confirm the underutilisation of available effective treatments for panic disorder (e.g. tricyclic antidepressants or behavioural therapy) and the overutilisation of treatments without proven efficacy (e.g. herbal preparations or autogenic training). Patients were most satisfied with treatments that have been proven effective in controlled studies. Among drug treatments, benzodiazepines, selective serotonin inhibitors and tricyclic antidepressants were favoured (mean on a 0–4 scale indicating effectiveness: 2.6, 2.6 and 2.4). Neuroleptics (1.4), beta-blockers (1.0) and herbal preparations (0.9) were not rated highly effective by the patients. Among psychological treatments, patients were more satisfied with behavioural/cognitive therapy (2.6) than with psychodynamic therapies (1.5). Satisfaction with autogenic training was very low (1.0). Results have to be interpreted very carefully, because many factors could not be controlled in the study: proper recollection of the applied treatments, adequate duration and dosage of the drugs, compliance of drug intake, availability of psychological treatments, adequate duration of psychological treatments, qualification level of therapists, treatment combinations and other factors. The results may have been influenced by the fact that most respondents were recruited from an outpatient anxiety-disorders unit.

Key words Panic disorder · Agoraphobia · Drug treatment · Psychological treatment

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Introduction

Many studies have shown the efficacy of certain pharmacological and psychological treatments in panic disorder and agoraphobia (PDA). Only the results of studies involving a control group should be considered when judging the efficacy of a treatment. Most authors agree that a high placebo response rate is common in panic disorder (Rosenberg et al. 1991; see Clark et al. 1994 for an alternative view). Among the drugs that have reliably proven effective against PDA in many controlled studies are benzodiazepines, such as alprazolam (Ballenger et al. 1988), tricyclic antidepressants, such as imipramine (CNCPS 1992) or clomipramine (Johnston et al. 1988), irreversible MAO inhibitors, such as phenelzine (Sheehan et al. 1980), and selective serotonin reuptake inhibitors, such as fluvoxamine (Black et al. 1993). For other drugs proof of efficacy is less consistent. Efficacy of neuroleptics in anxiety neuroses has been shown in many older studies in the 1970s and 1980s (e.g. Laakmann et al. 1988), but few studies have used patient samples comparable with the DSM-III and DSM-III-R definitions of panic disorder. It remains unclear whether treatment with beta-blockers, such as propranolol, is as effective as standard treatments (Munjack et al. 1989; Ravaris et al. 1991). For herbal preparations (e.g. Piper methysticum and Hypericum perfora-

tum), no controlled studies pertinent to anxiety disorders have been published.

Among psychological treatments, cognitive/behavioural therapies have consistently shown efficacy in PDA (Barlow 1994; Clark 1994)). Within the group of behaviourally orientated therapies, techniques that use in vivo exposure to feared situations have shown the best results (Marks 1987; Grawe et al. 1994). Efficacy was also proven for cognitive therapy that focusses directly on panic attacks (Clark 1994). The only study investigating psychodynamic treatment of panic disorder is a study comparing a combination of psychodynamic therapy and exposure with pure psychodynamic therapy. The combination was found to be superior (Hoffart and Martinsen 1990). Presently, the efficacy of psychodynamic treatment in panic disorder is regarded as unproven (National Institute of Health 1991). Hypnosis has been shown to be effective in two of four existing anxiety studies (Marks et al. 1968; Grawe et al. 1994), but studies involving DSM-defined panic-disorder patients are lacking. In Germany 'autogenic training', a self-applied relaxation technique, is very common. No controlled studies on the treatment of PDA with autogenic training exist. Psychotherapy research showed that results with autogenic training in other psychological disorders were insufficient (Grawe et al. 1994). Progressive relaxation was found to be less effective than exposure therapy (Marks et al. 1983) Biofeedback methods were found to be effective in two of three control comparisons conducted with anxiety patients (not defined by DSM), but the effects seemed to be unspecific (Grawe et al. 1994).

Controlled comparisons of pharmacological with psychological treatments of PDA are rare. Superiority of psychological treatments was found in two studies (Marks et al. 1983, 1993). Superiority of drug treatment was found in two studies (Klein et al. 1987, Black et al. 1993). No difference was found between drugs and psychological therapy in three studies (Telch et al. 1985; Mavissakalian and Michelson 1986a; Klosko et al. 1990).

In one follow-up study comparing drugs and exposure therapy (Marks et al. 1993), exposure was more effective after treatment termination than alprazolam. In two studies no difference was found between drug and psychological therapy upon follow-up (Marks et al. 1983; Mavissakalian and Michelson 1986b). In order to obtain a survey of pharmacological and psychological methods applied in patients with PDA, a field study was conducted by interviewing PDA patients to find out which therapy methods had been applied and what experiences the patients had had with these methods.

Subjects and methods

Patients fulfiling criteria of DSM-III-R and DSM-IV Panic Disorder and/or Agoraphobia (300.21, 300.01 and 300.22) or ICD-10 Agoraphobia and/or Panic Disorder (F40.00, F40.01 and F41.0) were included in the study. Patients had either a current episode of PDA or were in a state of remission. Severity of PDA was measured with the Hamilton Anxiety Scale (HAMA; Hamilton 1969) and the Panic and Agoraphobia Scale (P & A; Bandelow 1995). The mean HAMA score was 23.93 (± 10.29) and the mean P & A score was 23.38 (± 9.99) in the psychiatrist-rated version and 22.96 (± 10.89) in the self-rating. The mean duration of PDA was 4.75 years (SD 5.5 years). Most subjects ($n = 90$) had been clients of the outpatient anxiety-disorders unit at the University of Göttingen and were contacted by mail to participate in the investigation. Ten subjects were hospitalised because of PDA at the time in two psychiatric clinics and two departments for inpatient psychotherapy. Of 207 patients who were contacted, 100 agreed to participate, 83 did not participate and 24 had moved and were not traceable.

Patients were interviewed in person with a structured interview concerning the whole range of pharmacological and psychological treatments they had received for PDA in their illness history. Acute panic-attack treatments with parenteral, sublingual or oral benzodiazepines were not analysed because of low case number. Patients with comorbid conditions requiring neuroleptics were not included in the study. Only treatments that were well remembered by the patients were analysed. Drug treatments that were given either in a subclinical dose or not long enough to be effective were excluded. For tricyclic antidepressants, selective serotonin inhibitors (SSRIs) and monoamine oxidase inhibitors (MAOIs) only treatments with a minimum duration of 4 weeks' continuous intake were evaluated. For benzodiazepines, neuroleptics and herbal preparations a minimum-intake duration of 1 week was required. Of 241 drug treatments reported by the patients, 28 were not evaluable because of these criteria. For outpatient psychological treatments a minimum treatment duration of 8 weeks was necessary for inclusion. For inpatient treatment in a psychotherapy unit a minimum duration of 4 weeks was required. Five psychological treatments out of 103 had to be excluded because of insufficient duration.

Patients stated that it usually took a long time from the first onset of symptoms until the adequate diagnosis 'PDA' was made by a physician (on average 3.76 years; SD 5.17 years). Patients had to indicate their satisfaction with a certain therapy by responding to the statement, 'This therapy has been very helpful against my fears' on a 5-point Likert scale (from 0 = 'not true' to 4 = 'true'). As the scale was assumed to be of ordinal rank level, the central tendency ("mean") of these answers was taken as a "satisfaction index". Central tendencies were compared with Mann-Whitney's U test. Statistical analyses were performed with the Statistical Analysis System (SAS 6.08), SAS Institute, Heidelberg.

Finally, 54 patients who had received both drugs (not including herbal preparations) and psychological treatment in the course of their illness had to indicate which kind of treatment had helped most in the course of their illness. Only one answer was possible to this question.

Results

Application of treatments

Table 1 shows the percentages of patients who received particular treatment modalities at least once in the course of their illness. Four percent of patients had received no treatment at all before the interview.

Table 1 Application of different treatment modalities and satisfaction index

Treatment modality	Application (%)	Satisfaction	
		Mean	SD
Drugs	88	2.6	1.1
Individual psychotherapy	58	1.8	1.1
Relaxation techniques	54	1.2	1.1
Inpatient treatment	38	2.0	1.5
Group psychotherapy	28	1.3	1.1
"Alternative treatments"	7	2.1	1.2

Table 2 Percentage of patients having received a certain drug in the course of panic disorder and agoraphobia (PDA) treatment (< 5%: each of the drugs in the cell was used in less than 5%)

Group	(%)	Substance	(%)
Benzodiazepines	48	Diazepam	21
		Lorazepam	13
		Bromazepam	11
		Alprazolam	10
		Chlordiazepoxide, clobazam, clonazepam, dipotassiumchlorazepate, flurazepam, nitrazepam, oxazepam, prazepam	each < 5
Tricyclic antidepressants	42	Doxepine	18
		Imipramine	10
		Trimipramine	7
		Amitriptyline	7
		Clomipramine	5
		Opipramol, dibenzipine	each < 5
Herbal preparations	32	Rad. Valerianae + Hypericum perforatum	29
		Piper methysticum, homoeopathic agents	each < 5
Neuroleptics	29	Fluspirilene	18
		Promethazine	5
		Levomepromazine, perazine, sulpiride, haloperidol	each < 5
Selective serotonin-reuptake inhibitors	7	Fluoxetine, fluvoxamine, paroxetine	each < 5
Beta-blockers	6	Atenolol, propranolol	each < 5
Tetracyclic antidepressants	3	Maprotiline, mianserine	each < 5
MAO inhibitors	2	Tranylcypromin	2

Table 3 Prescription of drugs by different physicians (in percent)

	No. prescriptions	Psychiatrists (%)	Nonpsychiatrists (%)	No. prescription (%)	Unknown (%)
Benzodiazepines	77	40.2	57.1	–	2.6
Tricyclic antidepressants	51	64.7	31.4	–	3.9
Neuroleptics	30	33.3	63.3	–	3.3
Herbal preparations	37	10.8	54.9	35.1	0.0
Total	195	40.0	50.7	6.7	2.6

Table 4 Psychological therapies: frequency of application in percent

Psychological treatment	%
Autogenic training	43
Psychodynamic therapy	33
Unknown	28
Cognitive/behavioural therapy	20
Biofeedback	6
Progressive relaxation	6
Hypnosis	4

Drugs

Of the patients, 88% had had experiences with drug therapy for PDA. Altogether 213 drug treatments were evaluated. Table 2 shows the percentage of patients who received a certain drug at least once in the course of their illness at an adequate dosage and for a sufficient length of time.

In Table 3 the frequency of prescriptions of the drugs by either psychiatrists or nonpsychiatrists (general practitioners or other physicians) is given. Herbal preparations can be bought by the patients without prescription.

Psychological therapies

In Table 4 the frequency of application of nondrug therapies is shown. Psychological therapies were divided into psychodynamic therapies (psychoanalysis or depth psychology), cognitive/behavioural therapies, hypnosis and relaxation techniques (autogenic training, progressive relaxation and biofeedback). A large number of patients could not indicate the specification or 'school' of psychological therapy applied to them. All of these patients confirmed that they were talking to the therapist in a sitting position

without performing special behavioural techniques such as imagination or in vivo exposure.

Individual group therapy

Taking all psychotherapeutic treatments together, individual psychotherapy was applied in 58% of patients, and 28% had experienced group psychotherapy.

Inpatient treatment

Of the patients, 38% were treated as inpatients at least once during the course of their illness. Eighteen percent had been patients in an acute psychiatric ward for crisis intervention because of their anxiety disorder. Twenty-six percent had been clients of departments for inpatient psychotherapy because of PDA. Of these, 24% were treated in a psychoanalytically oriented clinic and 2% in a clinic for behavioural/cognitive therapy.

Alternative treatments

Of the patients, 7% were treated with so-called alternative treatments. Among these therapies yoga, "dynamic meditation according to Bhagwan", "Bach flower remedies" and "quacks" were named.

Satisfaction with treatments

Drugs

In Fig. 1 the satisfaction with the different drugs applied as rated by the patients is shown. Benzodiazepines, SSRIs and tricyclic antidepressants were the most favoured psychopharmacological drugs. The SSRIs were only used in 7% so that the results may not be representative. Neuroleptics were not rated very highly, and herbal preparations were assessed as practically ineffective. In Table 5 the significant comparisons among drug therapies are given. Tetracyclic antidepressants and irreversible MAO inhibitors were only used very rarely and therefore were not considered in this rating.

Psychological therapies

Behavioural/cognitive therapies were the preferred methods among the nondrug treatments of PDA (Fig. 2). Satisfaction with behavioural/cognitive therapy differed significantly from psychodynamic therapy ($P < 0.005$; Mann-Whitney's $U = 171$; Bonferoni correction), "unknown" psychotherapy ($P < 0.005$; $U = 141$) and autogenic training ($P < 0.0001$; $U = 158$). Other comparisons between these treatments were not significant. Hypnosis (not shown in the figure) achieved a score of 2.5 (SD 1.0). Because of low case number (4), this score may not be representative.

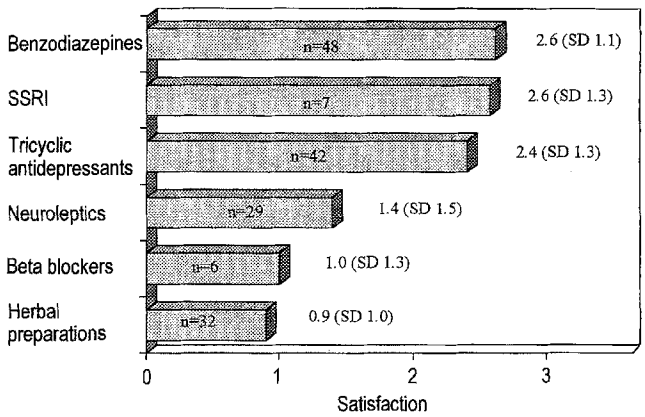

Fig. 1 Mean satisfaction with drug therapy indicated on a 5-point scale (from 0 = 'not at all helpful' to 4 = 'very helpful'). SSRI selective serotonin reuptake inhibitors

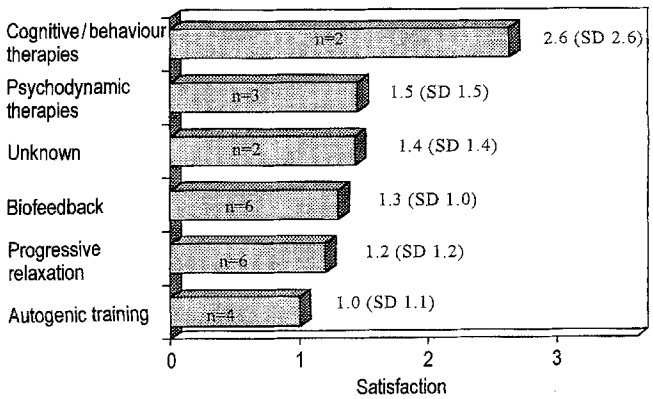

Fig. 2 Mean satisfaction with psychological therapies, indicated on a 5-point scale (from 0 = 'not at all helpful' to 4 = 'very helpful')

Individual vs group therapy

Patients were more satisfied with individual therapy (1.8, SD 1.1) than with group psychotherapy (1.3, SD 1.1). The

Table 5 Significance of comparisons between different medications (Mann-Whitney's U test; Bonferoni correction) (*SSRI* selective serotonin reuptake inhibitors; *TCA* tricyclic antidepressants)

	SSRI	TCA	Neuroleptics	Herbal preparations
Benzodiazepines	NS	NS	$P < 0.001$ ($U = 167$)	$P < 0.0001$ ($U = 214$)
SSRI		NS	NS	$P < 0.005$ ($U = 35$)
Tricyclic antidepressants			$P < 0.005$ ($U = 381$)	$P < 0.0001$ ($U = 248$)
Neuroleptics				NS

difference is significant ($P = 0.05$; $U = 606$). Inpatient group therapy was judged less effective (0.9, SD 0.9) than outpatient group therapy (2.1, SD 1.3). The difference is significant ($P < 0.05$; $U = 371$).

Inpatient treatment

The 'satisfaction index' of inpatient treatment in an acute psychiatric ward was 2.3 (SD 1.4), but there was a large difference between the university department of psychiatry (2.8, SD 1.3) and other psychiatric clinics (1.0, SD 1.3). The satisfaction with special clinics for inpatient psychotherapy was markedly less (1.6, SD 1.5). Of these, treatment in psychodynamically orientated clinics achieved a score of 1.6 (SD 1.5). The only two patients (2%) treated in a behaviourally oriented clinic named a score of 2.0.

Alternative treatments

"Alternative" treatments achieved an overall 'satisfaction score' of 2.1 (SD 1.2).

Treatments mostly favoured in comparison

In Table 1 the mean satisfaction scores for the main treatment groups are given. Mean satisfaction with drug therapy (herbal preparations not included) was markedly better than with individual or group psychotherapy. This is mostly due to low satisfaction in the psychodynamic and "unknown" psychological therapy group. Psychodynamic therapy (Fig. 2) was rated significantly less effective than treatment with benzodiazepines ($P < 0.0001$; $U = 385$) or tricyclic antidepressants ($P < 0.005$; $U = 402$; see Fig. 1). Cognitive/behavioural treatment did not differ from benzodiazepines or tricyclic antidepressants. All 100 patients were included in this comparison.

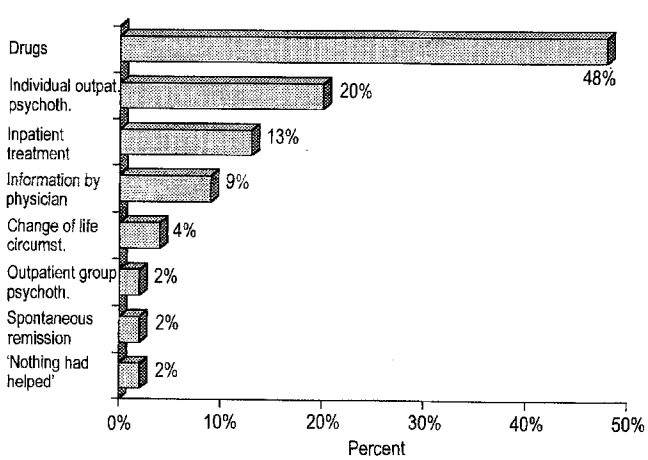

Fig. 3 Factor that helped most in patients who had experienced both drug treatment and psychological therapy ($n = 54$). Only one choice was possible

Patients who had received both drugs and psychological therapy ($n = 54$), and were able to compare both modalities, were asked which factor contributed most to the improvement of their disorder. In this rating, only one nomination was possible. The following reasons were named (Fig. 3): drug therapy, individual outpatient therapy, inpatient treatment (including both acute psychiatric wards and psychosomatic clinics), information by a physician about the nature of PDA, changes in life circumstances (e.g. marriage or other positive changes), outpatient group psychotherapy and spontaneous remission. Of patients, 2% indicated that nothing had helped. Herbal preparations were not included in the 'drugs' group.

Discussion

Application of Treatments

Panic Disorder and agoraphobia (PDA) were introduced as diagnostic entities in the DSM-III in 1980. However, the official classification system in Germany is still ICD-9 (World Health Organization 1978), in which panic disorder has not yet been introduced. Many physicians and psychologists working in primary care are not familiar with the DSM-III-R classification. They use a great variety of different and inhomogeneous diagnostic descriptions for patients with anxiety attacks and agoraphobic fears instead, such as "anxiety neurosis" or "vegetative dysfunction". The variety of descriptions is also reflected by the variety of different treatment plans. Almost all existing psychopharmacological agents are being prescribed to patients with PDA, and a great variety of non-drug treatments are applied.

The results of the present investigation show underutilisation of available effective drug treatments for PDA (e.g. tricyclic antidepressants and serotonin reuptake inhibitors) and overutilisation of treatments without proven efficacy (e.g. herbal preparations). Benzodiazepines, which may cause withdrawal reactions in some patients (see Salzmann, 1993; Shader and Greenblatt 1993), but show good anxiolytic properties and a low side effect profile, were used most frequently. In almost one-third of the patients neuroleptics were used, although these drugs have not been advocated for PDA in recent years (National Institute of Health 1991). This pattern differs largely from the recommendations given by the international literature concerning drug therapy of PDA, which favour tricyclic antidepressants, SSRIs and benzodiazepines. Of 213 evaluable drug treatments, only 135 (63%) were treatments with recommended drugs (benzodiazepines, tricyclics and SSRIs). Psychiatrists showed a more adequate prescription profile than nonpsychiatrists: Most antidepressants were prescribed by psychiatrists. Most benzodiazepines, neuroleptics and herbal preparations were prescribed by nonpsychiatrists. Of the herbal preparations, one-third were bought by the patients without prescription.

In a comparable study by Goisman et al. (1994) a different prescribing pattern was shown in U.S. patients: Sub-

jects in this investigation received more benzodiazepines (65%), fewer tricyclics (26%), markedly fewer neuroleptics (2%) and far more new antidepressants (22%) than our German sample. The use of herbal preparations was not reported in this paper. Swinson et al. in Canada (1992) found that only 15% of patients with panic disorder received the tricyclic antidepressant imipramine and 13% alprazolam.

Looking at psychological treatments, underutilisation of effective treatment modalities is even more evident. Of the patients, one-third had been treated with psychodynamic therapy. Only 20% of patients had ever received cognitive/behavioural therapy (CBT) in their case history, although controlled studies clearly favour this kind of therapy over psychodynamic therapy and other psychological treatment methods including autogenic training. A large group of patients (28%) could not name the type of psychological therapy they had received. Many patients (43%) applied autogenic training, a method with unproven efficacy in PDA. Of 98 evaluable psychological therapies, only 22 (22%) therapies were CBT.

The underutilisation of treatments with proven efficiacy have also been shown in other countries. Swinson et al. in Canada (1992) found that only 11% of their panic patients received cognitive/behavioural therapy. Authors in the U.S. reported that only 15–18% of PDA patients received behavioural therapy (Breier et al. 1986; Aronson et al. 1987; Taylor et al. 1989). In a recent U.S. study by Goisman et al. (1994), psychodynamic therapy was found to be applied in 37%, behavioural therapy in 16%, cognitive therapy in 18% and relaxation in 13%. Information campaigns seem to be necessary to improve the level of knowledge about recommended treatments for PDA.

Satisfaction with treatments

Patients experienced the most significant improvement of anxiety with benzodiazepines, selective serotonin reuptake inhibitors and tricyclic antidepressants. Neuroleptics were only considered as poorly effective. Beta-blockers and herbal preparations were rated as virtually ineffective. The high rating for the SSRIs should be interpreted cautiously, because they were used in only 7 cases.

The judgement of efficacy of the different psychological methods significantly favours behavioural/cognitive therapy over psychodynamic therapy. The least effective psychotherapies – from the standpoint of the patients – were the ones in which the name of the applied method was unknown to the patient. Relaxation techniques, such as autogenic training, biofeedback and progressive relaxation, were not considered effective. Patients clearly prefer individual therapies over group therapy. Inpatients treated in psychosomatic clinics seem not to be very convinced of the benefit of this treatment. One of the consistent findings in psychotherapy research is that exposure to feared situations is an important factor for treatment success (Marks 1987). When inpatient treatment facilitates avoidance of feared situations, a significant reduction in phobic avoidance cannot be expected. Patients hospitalised in acute psychiatric departments experienced greater improvement in their opinion. This may be due to the fact that patients were also treated with drugs in these departments, but it may also be possible that these clinics admitted the most severely ill patients who may show a more significant change in psychopathology in a shorter time. When patients who had received both drug and psychological treatment in the course of their illness were asked which treatment modality was most successful in improving anxiety symptoms, psychopharmacological drugs were significantly favoured over psychological therapy. Forty-eight percent said that drugs were most effective. Only 20% of these patients found individual psychotherapy to be superior.

To our knowledge, only one comparable opinion poll has been conducted among agoraphobic patients (Norton et al. 1983). Of a total of 9 patients, only 4 had experienced psychological therapy before.

The results of this retrospective analysis have to be interpreted carefully. Many factors that could lead to a distortion of the picture were not controlled in the study: proper recollection of applied therapies by the patients, adequate duration and dosage of the drugs, compliance of drug intake, availability of psychological treatments, adequate duration of psychological treatments, qualification level of therapists, assessment problems arising from combined treatments and many other factors. Moreover, most of the interviewed persons were patients of an acute psychiatric outpatient unit, where patients might have come with the expectation of receiving drug therapy, rather than psychological treatment. This could bias the results in favour of drug therapy. The results might have turned out differently if the survey had been conducted mainly among clients of a pure psychotherapy unit.

Another reason why the results should be interpreted with caution is the fact that patients do not have the same possibility to judge the risk/benefit ratio of a treatment as the physicians or psychologists do. Long-term effects, such as possible addiction to benzodiazepines, may not have been taken into consideration when appraising the anxiolytic properties of these drugs. On the other hand, the survey revealed that patients appreciated precisely those treatment methods that have been shown to be effective in controlled studies.

These results should not be generalised to psychiatric conditions other than PDA. This study cannot be taken as a replacement for controlled clinical trials. Its aim was to obtain an overview of the application of treatment methods in PDA and the views of the patients concerning this field, in order to generate hypotheses for future controlled trials.

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