Analysis of the Therapeutic Effect of Sulpiride on Individual Symptoms of so-called Major Depression

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The aim of the study was analysis of therapeutic effects of sulpiride in individual symptoms of endogenous depressive syndrome, an attempt of general assessment of the therapeutic effectiveness of sulpiride in endogenous depression, comparison of therapeutic effects of sulpiride in mild, medium and severe depressions. Sulpiride is a good, effective drug in the treatment of endogenous depression. Its effect after administration is very rapid and the drug is relatively save – it produces few mild complications, frequently including galactorrhoea and amenorrhoea in women. Most of benzamide derivatives exert a rather selective effect on dopaminergic transmission in mesolimbic structures, demonstrate a high affinity to D2 receptors and, to a lower extent, to D1 receptors, and some newer benzamide derivatives also to 5-HT2 and 5-HT1A receptors. Pharmacologically, sulpiride is a selective dopaminergic receptor, namely a D2 and D3 receptor antagonist. Sulpiride selectively blocks the above-mentioned types of dopaminergic receptors. It is an exceptionally hydrophilic drug and not lipophilic as most drugs of this type are. It causes no strong extrapyramidal symptoms which could result from D2 receptor blockade in the corpus striatum and which are the equivalent of catalepsia in animals.

Key words: sulpiride, major depression, therapeutic effects, depression intensity, galactorrhoea, amenorrhoea

INTRODUCTION

Sulpiride, an atypical (1–4) neuroleptic from the group of benzamides, exerts antiautistic, stimulating effects. It has also a positive influence on productive symptoms of psychosis. It shows antidepressant activity. Analysis of many papers on sulpiride action encouraged the author to use this drug in the treatment of endogenous depression. Sulpiride has been unpopular among psychiatrists in the treatment of endogenous depressive syndromes. Nevertheless, numerous reports demonstrate the beneficial effects of this drug in endogenous depression. Here are some of them (4):

1. One of Polish authors (5) stressed in one table a strong antidepressant effect of sulpiride. The author wrote that the drug is indicated in affective diseases.

2. Benkert O, Holsboer F (7) used sulpiride in endogenous depressions in 150 mg daily doses. According to these authors, low sulpiride doses exert an antidepressant effect in both severe depression and in its milder forms.

3. The drug exerts an evident antidepressant effect (4).

4. Standish-Barry HM et al (6) compared the effects of sulpiride and amitriptyline in patients with the diagnosis of major depression. Sulpiride demonstrated an antidepressant effect equivalent to that of amitriptyline. The assessments were performed after 4, 6 and 12 weeks of treatment. The Hamilton scale and the Wakefiled depression self-assessment scale were used. Only in the 24th week of treatment amitriptyline showed a statistically significant advantage over sulpiride (6).

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5. Bocchetta A et al observed patients with bipolar affective disease treated with lithium preparations, in whom a recurrence of "major depression" developed. The effects of L-sulpiride and amitriptyline were compared. It was found that the antidepressant effect of L-sulpiride was equivalent to that of amitriptyline in the 4th week of treatment. For the assessment, the Hamilton Depression Scale was used. In a sulpiride study, it was demonstrated that the onset of antidepressant action of sulpiride was more rapid than that of amitriptyline. A significant improvement after sulpiride was demonstrated in the first week of the treatment. This included somatization of anxiety, depressive mood, feeling of guilt, activity and impairment of ability to work (7, 8).

6. The drug was used in the treatment of depression developing in the course of affective diseases (4).

7. Among patients with endogenous depression, suicidal tendencies frequently predominate (9). Therefore, in view of patient's life safety, a drug is needed with a rapid onset of therapeutic action and at the same time less toxic in high doses. Many tricyclic antidepressants exhibit their antidepressant effects only after 2–4 weeks of treatment (4). Sulpiride, on the other hand, exerts an antidepressant effect more rapidly than the mentioned drugs. A significant improvement after sulpiride used to be demonstrated after one week of treatment (7, 8).

8. Depressive syndrome, particularly in young people, is frequently an initial stage of the schizophrenic process. Administration in such cases of tricyclic antidepressants could release the productive symptoms of schizophrenic psychosis. Sulpiride, however, would exert here a therapeutic effect, since it is effective in productive symptoms (9). Antipsychotic properties of sulpiride have been confirmed in (10). Some authors regard it as the most potent antiautistic drug of all neuroleptics (4).

The author of the current paper used sulpiride in endogenous depression with productive symptoms with a good therapeutic effect on the latter.

9. It is commonly known that sulpiride is a therapeutically effective drug in gastroduodenal ulcer, ulcerative colitis, headaches and vertigo (Mničre's disease, migraines) (2, 11).

These diseases were diagnosed in many patients who came to the author with endogenous depression symptoms, therefore the choice of sulpiride seemed to be most appropriate.

10. Besides that, the drug has been commonly used in neuroses, in lower doses as an anxiolytic, and also in the treatment of drug addiction in early abstinence phase, in the treatment of alcoholism, in schizophrenia with depressed mood manifestations (4). Sulpiride is a drug with relatively minor adverse effects. It has been regarded by some psychiatrists as the safest neuroleptic (5).

Sulpiride has been introduced to treatment of psychoses in 1968 (12). Generally speaking, it belongs to psychotropic drugs (13), more precisely to the group of neuroleptics of a cyclic structure (3, 4). It is an atypical new-generation neuroleptic with unique pharmacological properties and a very wide spectrum of clinical use (11), belonging to the group of benzamide derivatives (4).

Benzamide derivatives administered in intramuscular injections are rapidly absorbed and after 10 to 20 minutes reach their peak concentrations in blood. When administered orally they reach the peak concentration in blood within 1–2 hours (4).

Some authors believe that sulpiride after oral administration reaches the maximal blood concentration after 2–4 hours (2).

Shinkuma D et al. suggest that taking food and the size of meal before sulpiride administration significantly influence gastrointestinal absorption of the preparation. The total amount of sulpiride excreted with urine during 48 hours was reduced by 30% if the drug was taken with food. The drug was taken in the form of coated tablets in the total dose of 100 mg by 13 healthy male volunteers (14). The same authors studied the bioavailability of sulpiride administered to healthy volunteers in the form of 100 mg tablets coated with polyvinyl acetal diethylamine acetate which is insoluble at pH above 4–5. Sulpiride was administered together with sodium bicarbonate, cimetidine, natural orange juice or diluted hydrochloric acid. The biological availability was determined on the basis of the total amount of unchanged drug excreted with urine within 48 hours. A decrease of the bioavailability was observed if the drug was taken together with sodium bicarbonate or cimetidine, as compared to administration of sulpiride alone. An increase of the bioavailability occurred with simultaneous administration of orange juice or diluted hydrochloric acid. The results suggested that the bioavailability of sulpiride administered in the above-mentioned coated tablets was influenced by the pH of gastric contents and food or beverages taken, which changed the pH of gastric contents. Therefore, these authors studied in detail the relationship between sulpiride bioavailabilty and the pH of gastric contents. The above-mentioned sulpiride 100 mg tablets were given to healthy volunteers. The biological availability was assessed by the total amount of unchanged drug excreted with urine within 48 hours. The fasting bioavailability varied significantly in individual volunteers due to differences in gastric contents acidity. The influence of meal was also varying among the study subjects, being lowest in persons with a

high acidity and higher in subjects with a low acidity of gastric contents. When the coated tablets were administered during induced achlorhydria, the fasting bioavailability was very low and no differences were observed between the subjects studied. After taking a meal the bioavailability increased sixfold, probably due to a high mobility of gastrointestinal contents, as both the baseline and meal-stimulated hydrochloric acid secretion in the stomach was very low under conditions of provoked achlorhydria (14–16). Sulpiride bioavailability was not exceeding 30% because of a rather poor absorption from the gastrointestinal tract. Drug absorption from capsules was better than from tablets (2).

THE MECHANISM OF ACTION

Most benzamide derivatives exert a rather selective effect on dopaminergic transmission in mesolimbic structures, demonstrate a high affinity to D2 receptors and a lower one to D1 receptors, and some newer benzamide derivatives also to 5-HT2 and 5-HT1A receptors (4).

Pharmacologically, sulpiride is a selective dopaminergic receptor, namely a D2 and D3 receptor antagonist.

Sulpiride selectively blocks the above-mentioned types of dopaminergic receptors. It is an exceptionally hydrophilic drug and not lipophilic as most drugs of this type are. It causes no strong extrapyramidal symptoms which could result from D2 receptor blockade in the corpus striatum and which are the equivalent of catalepsia in animals (11).

The receptor studies demonstrated a particular affinity of sulpiride to D2 receptors in limbic structures (2).

This affinity was determined according to the following scale:

– sulpiride affinity to D1 receptors (+)
– sulpiride affinity to D2 receptors (++++)
– sulpiride affinity to a1 receptors (+)
– sulpiride affinity to 5-HT2 receptors (+/0).

Sulpiride, selectively blocking D2 and D3 receptors, causes a slight activation of D1 dopaminergic receptors which, in contrast to D2 and D3 receptors, positively correlate with adenyl cyclase, can exert beneficial effects in cases of neurosis or depression and can control the so-called negative symptoms of schizophrenia (11).

The effect of sulpiride was also studied on the location of the EEG signal source in the frequency domain. EEG signal was recorded in 19 leads with shut eyes before and 1, 15, 30, 45 and 60 minutes after intravenous administration of the drug. The location of the source of beta waves was significantly shifted upwards and forwards, particularly within one minute after drug administration (17).

We also assessed the effect of sulpiride on EEG record. It was most evident two to four hours after drug administration. The EEG profile was characterized by a relative increase of slow-wave (delta and theta) activity and a decrease of alpha (and beta) wave presence (18). Other authors interpreted their results as demonstrating the lack or a minimal sulpiride influence on the results of tests used for determination of the vigilance level and degree of autonomous system stimulation (19).

Nahoum C R et al studied the effect of sulpiride on prolactin secretion in humans. The rate of prolactin secretion was studied after sulpiride administration to 30 ovulating women. A highly statistically significant correlation was observed between the area under the curve and the level of this hormone 30 minutes after sulpiride administration (20).

Other authors noted that sulpiride therapy was associated with a significantly higher increase of plasma prolactin level (10). The stimulating effect of sulpiride was also studied on prolactine secretion in the late phase of puerperium. Forty-one lactating women were studied. They were followed up for 90 days after labour. Twenty women were given sulpiride and 21 received placebo.

In the placebo group, prolactin concentration elevation after breast feeding decreased significantly and 90 days after labour it was parctically absent (21).

Other authors in their studies noted that the prolactin level demonstrated a significant increase (maximal value after 30 minutes) after sulpiride administration. Twenty-four hours later the prolactin level was still higher in relation to the baseline value and failed to react to administration of sulpiride + placebo and sulpiride + TRH (22).

Generally speaking, sulpiride is a neuroleptic with mainly antiautistic, stimulating, and antidepressant actions (4, 5, 7, 8, 23), antipsychotic (10), and, in lower doses, anxiolytic effects (23). Some authors believe that it is the most potent antiautistic drug out among neuroleptics. It exerts a positive effect on the productive symptoms of psychosis, although weaker than that of some other neuroleptics (4).

The clinical effect of sulpiride was determined according to the following scoring scale: 4 – very strong effect, 3 – strong effect, 2 – medium effect, 1 – weak effect, 0 – no effect, ? – lacking or contradictory data.

According to this scale, sulpiride was evaluated as follows:

A – sedative effect – ?
B – effect on productive symptoms – 1
C – antiautistic effect – 3

D – stimulating effect – 3
E – antidepressant effect – 2.

STUDY AIMS

The aims of the study were as follows:

1. An attempt of general assessment of therapeutic effectiveness of sulpiride in endogenous depression.
2. Analysis of therapeutic effects of sulpiride in individual symptoms of endogenous depressive syndrome.
3. Comparison of therapeutic effects of sulpiride in mild, medium and severe depressions.
4. Determination of the influence of demographic factors on the intensity of sulpiride therapeutic effect.

MATERIALS AND METHODS

Clinical material

Sulpiride was administered to outpatients in the Public Health Care Institution, Warszawa–Żoliborz, and to patients discharged from the Department of Neurosurgery, Central University Teaching Hospital in Warsaw, 128 Szaserów st. The drug was given to 100 patients. For the studies, only persons with the diagnosis of endogenous depressive syndrome were included. These were persons in whom endogenous syndrome developed for the first, second or third time. The patients were chosen with endogenous depressive syndrome of not precisely determined aetiology (first episode). In the case of a greater number of episodes it was established that the patients had a unipolar affective disease.

Patients were qualified only if they had no history of manic episode. The study subjects were taking sulpiride and were systematically monitored for six weeks. The drug was administered in a dose from 50 mg to 600 mg daily, only orally, always in the form of 50 mg capsules. All the subjects studied met the criteria of endogenous depressive syndrome according to DSM III and DSM IV classifications. During visits, the patients' clinical status, i.e. mental and somatic conditions were assessed. Basic laboratory blood and urine analyses, ECG, EEG and chest radiogram were also performed. All patients were always received and treated by the same doctor, the author of the paper. The observations were noted in patients' case records.

Methods

The data for the studies were collected from the case records of patients from the study and control groups. In each record, family history was presented and the clinical status (mental and somatic) of the patients was described many times during successive visits, on the basis of medical examination. The results of laboratory blood and urine analyses, ECG and EEG records and chest radiogram were also noted. Each patient was examined in detail, at the beginning and end of the 6-week monitoring period, using the 24-point Hamilton Depression Assessment Scale and Beck Depression Self-Assessment Inventory and Montgomery–Asberg Scale.

These tests have no normal value range and are not standardized. Therefore they cannot be used for depression intensity assessment. They can be, however, definitely useful for the assessment of therapeutic effectiveness of drugs used in endogenous depression treatment. These tests served for the evaluation of clinical improvement in individual patients.

The author evaluated the therapeutic effect on the basis of clinical examination of the patients and also by CGI, Hamilton scale, Beck Depression Self-Assessment Inventory and Montgomery–Asberg scale.

Depression intensity was assessed by the author on the basis of clinical examination according to ICD-10 (The ICD-10 Classification of Mental and Behavioural Disorders), Clinical Descriptions and diagnostic guidelines), World Health Organization, Geneva 1992).

Statistical methods

The basic method of statistical analysis was comparison of several groups of patients. The significance of differences among the groups with respect to one feature was tested by analysis of variance. The significance of the p value was calculated on the basis of F statistics with several degrees of freedom designated as df Effect and df Error.

For a number of features of low values the so-called contingency tables were calculated. Frequently, these tables are the basis for calculating the per cent values important for arriving to a definite conclusion. In some cases, the contingency tables allow calculation of a statistical significance (p) resulting from a given statistical test or correlation coefficient.

This was done, e.g., when individual questions in the Hamilton and Beck tests were compared in order to check whether the results obtained after treatment were significantly lower than those before treatment. For this purpose, Student's t test was used for dependent variables (23).

The significance of the relationship between these questions and therapeutic results was studied using the Kendall tau correlation coefficient (24).

The reliability of Hamilton and Beck tests was also studied. It was important in the first place for

the characteristics of our study material. Therefore, the Pearson coefficients of correlation between individual questions and the total result of the test were calculated. Also, the Cronbach alpha coefficients were calculated to characterise the degree of agreement of test questions (25).

When two groups were compared, Student's t test was applied. The statistical analysis of per cent values was done by the chi-square statistical method (26).

RESULTS AND DISCUSSION

A relationship between therapeutic effects and differences of results in Hamilton and Becks scales was studied before and after treatment. The results are presented in Tables 1 and 2.

Table 1. **Assessment of results of depression treatment with sulpiride in the Hamilton scale**

Difference in Hamilton scale	Therapeutic effects
0–5	25% poor, 75% lack of improvement
5–10	100% poor
10–15	30% significant improvement, 40% medium improvement, 30% poor improvement
15–20	3% complete cure, 70% significant improvement, 20% medium improvement, 7% poor improvement
20–30	10% complete cure, 70% significant improvement, 20% medium improvement
Over 30	50% complete cure, 30% significant improvement, 20% medium improvement

Table 2. **Assessment of results of depression treatment with sulpiride in the Beck scale**

Difference in Beck scale	Therapeutic effects
0–5	25% poor, 75% lack of improvement
5–10	10% medium improvement, 90% poor improvement
10–15	40% significant improvement, 30% medium improvement, 30% poor improvement
15–20	70% significant improvement, 25% medium improvement, 5% poor improvement
20–30	15% complete cure, 65% significant improvement, 20% medium improvement
Over 30	50% complete cure, 50% significant improvement

A relationship was studied between therapeutic effects and the percentage of improvement in a joint assessment by Hamilton and Beck tests after treatment in relation to the assessment before treatment. The results are presented in Tables 3 and 4.

Table 3. **Relationship between therapeutic effects of sulpiride in depression and the percentage of improvement in Hamilton test**

Difference (%) between results in Hamilton test before and after treatment	Therapeutic effects				
	1	2	3	4	5
0–10	0	0	0	2	8
10–40	0	0	0	9	0
40–60	0	0	7	6	0
60–70	0	7	10	0	0
70–90	0	36	4	0	0
Over 90	6	5	0	0	0

Table 4. **Relationship between the therapeutic effects of sulpiride in depression and the percentage of improvement in the Beck test**

Difference (%) between results in Beck test before and after treatment	Therapeutic effects				
	1	2	3	4	5
0–10	0	0	0	2	8
10–40	0	0	0	12	0
40–60	0	1	5	3	0
60–70	0	7	13	0	0
70–90	0	38	3	0	0
Over 90	6	2	0	0	0

Effects of treatment:
1. Complete, persistent remission
2. Significant improvement
3. Medium improvement
4. Poor improvement
5. No improvement.

Analysing the reduction of depression symptoms in the Hamilton scale, sulpiride proved to be a definitely effective drug in 68% of patients. These were patients in whom the reduction of symptoms in the Hamilton scale was over 60%.

A complete, persistent remission was obtained in six patients, significant improvement in 48 patients, medium improvement in 28 subjects, poor

improvement in 17 cases, and no improvement in eight patients.

Out of 100 patients treated with sulpiride in the group studied according to CGI scale, 54 subjects returned to normal life and occupational functioning, six of them obtained 1 point in CGI scale, and 48 obtained a CGI score of 2 points. (CGI scale: 1 point – regression of symptoms, 2 points – significant improvement, 3 points – slight improvement, 4 points – no change).

A relationship was studied between the baseline results in the Hamilton scale before treatment and the differences of the results were assessed before and after treatment, both as differences of the absolute values and percentage of improvement. The results are presented in Tables 5 and 6.

The definitely best therapeutic effects were achieved in patients who had baseline results in the Hamilton scale below 25 points.

A relationship was studied between the baseline results in the Beck scale before treatment, and the differences of the results before and after treatment were assessed, both as differences of absolute values and percentage of improvement. The results are presented in Tables 7 and 8.

Table 5. **Relationship between baseline results before treatment and the differences of data before and after treatment in the Hamilton scale**

Hamilton scale before treatment	Absoulte difference of total scores					
	0–5	6–10	11–15	16–20	21–30	31 and more
Up to 20	1	0	0	5	2	0
21–25	4	2	7	21	14	0
26–30	1	3	4	2	9	0
31–35	0	1	1	3	5	1
36 and more	4	0	1	1	3	5

Table 6. **Rrelationship between baseline results before treatment and differences of data before and after treatment in the Hamilton scale**

Hamilton scale before treatment	Difference (% of improvement of total score)					
	0–10	11–40	41–60	61–70	71–90	91 and more
Up to 20	1	0	1	8	3	3
21–25	4	2	2	7	19	4
26–30	1	4	4	0	9	1
31–35	0	2	4	1	5	1
36 and more	4	1	2	1	4	2

Table 7. **Relationship between baseline results before treatment and differences of data before and after treatment in the Beck scale**

Beck scale before treatment	Absolute difference of total scores					
	0–5	6–10	11–15	16–20	21–30	31 and more
Up to 20	1	0	10	8	1	0
21	0	1	6	6	1	0
21–25	0	0	0	13	6	0
26–30	3	1	5	0	3	0
31–35	1	5	1	3	8	1
36 and more	5	1	0	2	3	5

Table 8. **Relationship between baseline results before treatment and differences of data before and after treatment in the Beck scale**

Beck scale before treatment	Difference (% of improvement of total score)					
	0–10	11–40	41–60	61–70	71–90	91 and more
Up to 20	1	0	1	8	9	1
21	0	0	2	5	6	1
21–25	0	0	0	4	12	3
26–30	3	5	1	0	3	0
31–35	1	6	3	2	7	0
36 and more	5	1	2	1	4	3

The definitely best therapeutic effects were achieved in patients who had baseline results in the Beck scale below 25 points.

Attention should be paid to the fact that the tables show rather evident limits of the H and B test data before treatment and of adequately high ratios of differences of data before and after treatment.

The final effects of treatment are strongly determined by the baseline summarized results of Hamilton and Beck tests. The result of 25 points seems to be a significant borderline value for both tests.

The borderline of 60% improvement is known from earlier considerations as indicating significant improvement.

Evidently better therapeutic effects were obtained in patients who scored 25 points or less in the Hamilton scale before treatment.

Similarly, evidently better therapeutic effects were obtained in patients who scored 25 points or less in the Beck scale before treatment.

Depression intensity

A great improvement was achieved in the study group treated with sulpiride for depressions with a mild and medium intensity of symptoms. On the other hand, sulpiride therapy in severe depressions with a high intensity of symptoms gave only a poor or medium improvement.

The above conclusions of the author are not in full agreement with the studies by Benkert O and Holsboer F (7). These authors administered sulpiride in a 150 mg daily dose to 11 patients with endogenous depression. Sulpiride turned effective in severe depression and also in its milder forms.

The author observed a group of 100 patients in whom sulpiride significantly improved the depressive mood. This action was most effective in patients with a medium lowered mood.

The antidepressant effects of sulpiride were confirmed by studies of many authors (2, 4, 5–8, 11, 23, 27). However, these studies involved smaller groups of patients. Bocchetta A et al studied only 30 patients (8), Kato K two persons (23), and Standish-Barry HM et al 36 subjects (6). In the group studied, about 50% of patients had a feeling of guilt associated with delusions of guilt. Sulpiride fairly effectively controlled this symptom, particularly in patients who had a medium-grade feeling of guilt. Bocchetta et al studied 30 self-accusing patients in whom sulpiride produced a significant improvement.

In the group studied, about 50% of patients had suicidal ideation and tendencies. Sulpiride almost completely eliminated the actual risk of suicidal attempt. It showed an outstanding effect in patients with intensive suicidal compulsions. The author found no studies on this problem in literature.

About 80% of patients complained of insomnia. Sulpiride proved to be a particularly useful drug in all types of insomnia. They included difficulties in falling asleep, shallow and intermittent sleep and early awakening with impossibility or difficulty of falling asleep again. The author found no studies on this problem in literature.

In the study group, patients with feeling of significant fatigue, inability to work and with significantly decreased activity accounted for about 85%. Sulpiride exerted very favourable effects in patients with a medium intensity of this symptom. Patients with psychomotor sluggishness, from its mild forms to stupor, accounted for about 45%. Sulpiride exerted an evidently favourable effect in slight and evident forms of sluggishness. In the literature, quite a number of authors confirmed the stimulating effect of sulpiride and such its features as increasing the psychomotor drive as well as activity and ability to work (4, 5, 7, 8). Benkert O and Holsboer F studied in this aspect only 11 patients (7) and Bocchetta et al 30 subjects (8).

In the study group, restlessness with motor agitation was observed in about 40% of patients, while nervoussness and irritation were present in 98% of cases. Sulpiride most effectively controlled restlessness of medium intensity. The drug even potentiated the nervousness of slight intensity.

No less than 98% of patients developed mental symptoms of anxiety. Sulpiride proved fairly effective in extreme and medium anxiety, but was found ineffective in mild forms of anxiety. Many authors confirmed the anxiolytic effect of the drug (5, 6, 8, 11, 23). Standish-Barry et al studied 36 patients and found that the anxiolytic effect of sulpiride was equivalent to that of amitriptyline.

In our study group, as many as 88% of patients had somatic manifestations of fear. Sulpiride exerted here an evidently beneficial effect in medium and significant levels of the above-mentioned complaints. The drug exacerbated the mild form of anxiety. In literature, Bocchetta et al studied somatization of fear in 30 patients with endogenous depression. These authors observed a significant improvement as soon as after one week of treatment.

In our study group, 75% of patients showed reduced appetite or complete loss of appetite. Sulpiride exerted best effects in patients with the complete lack of appetite and slightly less good in patients with moderately decreased appetite. The author found no studies on this problem in the literature.

Our study group included 89% of patients with systemic somatic manifestations of endogenous depression. Sulpiride proved particularly effective in the treatment of patients with a significant intensity of these symptoms and signs. In patients with a moderate intensity of the manifestations, the therapeutic effect of the drug was satisfactory. In literature, some authors assessed the effectiveness of the drug in headache and vertigo (2, 27).

Lanemark M and Olesen J studied a total number of 37 patients treated with sulpiride and, in another time period, with paroxetine. Their detailed analysis demonstrated better improvement in persistent headache after sulpiride as compared to paroxetine.

In our study group, 77% of patients had decreased libido. Sulpiride improved potency in patients with its extreme and medium decrease. The drug proved ineffective in patients with a mild decrease of potency. The author found no reports on this problem in the literature.

In our study group, 58% of patients had hypochondriac symptoms. Sulpiride exerted a most favourable effect in hypochondria of medium and

extreme intensity. Best effects were obtained in the treatment of hypochondriac delusions and slightly less good in the treatment of hypochondriac attitudes. In the literature, some authors stressed a slightly antiproductive effect of the drug (4, 5).

Our group of patients included about 30% of emaciated subjects with cachexia. Sulpiride in a great majority of cases caused body weight gain. The above effect was confirmed in the literature by Wojciech Kostowski (2).

Among our patients 50% had a decreased or no criticism towards depression as a disease. Sulpiride was very good in restoring criticism in patients with its complete loss. The drug proved slightly less useful in the treatment of patients with partial reduction of criticism. The author found no related reports in the literature.

Fifty-six percent of our patients demonstrated circadian fluctuations of general feeling. Sulpiride was most effective in patients with the highest intensity of the symptom and also in those who were feeling worst in morning hours, which is pathognomonic of endogenous depression. The author failed to find reports on this problem in the literature.

About 40% of our patients showed depersonalization, derealization and a negative opinion about their own appearance. Sulpiride proved particularly effective in the treatment of the above-mentioned symptoms of high intensity. The effect of the drug was barely satisfactory in cases of medium intensity of the symptoms. The author found no respective data in the literature.

In our group, 39% of patients had delusions of persecution and delusion of reference from depression group. Delusions of guilt and punishment developed in 16% of patients. Sulpiride turned out to be an evidently effective drug in these cases. In the literature, some authors confirmed the antiproductive and antipsychotic effects of the drug (4, 5, 10).

Bocchetta et al (8) effectively treated the depressive feeling of guilt. In our group, 70% of patients had anancastic symptoms. Sulpiride proved particularly effective in the treatment of obsessions of high intensity. On the other hand, the drug exerted almost no therapeutic effect on obsessions of medium intensity. The author found no data on this problem in the literature.

The feeling of helplessness and hopelessness was reported by over 90% of our patients. Sulpiride proved evidently effective in the treatment of medium and severe forms of these symptoms. The author found no reports on this problem in the literature.

Our group included 62% of patients with typical depressive delusions. Sulpiride was found here to be particularly therapeutically effective. Some authors confirmed the antiproductive effects of the drug (4, 5).

Patients with inferiority feeling, self-accusation accounted for 59% of our study group. Sulpiride rather effectively increased the level of assertiveness and decreased the feeling of guilt. Bocchetta et al treated 30 depressive patients with a great feeling of guilt with sulpiride and obtained fairly good effects (8).

As many as 92% of patients in our group were rather pessimistic about their future. Sulpiride proved very effective in patients with the borderline and medium intensity of the symptom. On the other hand, it was completely useless and even exerted unfavourable effects in the patients who regarded their future as black but in a mild degree. The author found no studies on this problem in the literature.

Our study group included 69% of patients who felt guilty for their negligence while performing various activities. Sulpiride was here relatively therapeutically effective but less effective than other drugs, *e.g.*, clomipramine. Bocchetta et al effectively treated with sulpiride a group of 30 patients with a significant feeling of guilt during endogenous depression (8).

In our study group, 100% of patients were not satisfied with their work. In the patients with a severe and medium intensity of this symptom, sulpiride proved therapeutically very effective. On the other hand, the drug was completely useless in the patients with a mild intensity of the symptom and even exerted a slight unfavourable effect. No reports on this problem were found in the literature.

No less than 100% of patients in our group had a feeling of dissatisfaction with their own personality. In the most severe and medium forms of this symptom, sulpiride exerted a very favourable therapeutic effect. In the mild form of the symptom the therapeutic effect of sulpiride was slight. The author found no reports on this problem in literature.

In the group studied, 74% of patients demonstrated evident tearfulness. Sulpiride failed here to exert a good therapeutic effect. After the treatment, quite a large part of the patients who previously were relieving their emotions by weeping could not weep any more. The author found no studies on this problem.

Of our patients, 88% isolated themselves from other people and lost interest in the environment. Sulpiride rather evidently helped to renew old contacts with friends and acquaintances, but only in patients with a high and medium intensity of this symptom. In patients who only slightly isolated themselves from the environment, the drug exerted even

unfavourable effects, potentiating the tendencies for separating themselves. The author found no related reports in the literature.

In the study group, 86% of patients had difficulties in decision-making. Sulpiride proved very effective therapeutically in the patients with great difficulties in decision-making. The effect of the drug was slightly less good in patients unable to make any decision and was even unfavourable in patients with minor problems in decision making. The author failed to find reports on this problem in the literature.

Many authors analysed the adverse effects of sulpiride (1, 2, 4, 28, 29, 30). The drug has been occasionally reported to evoke extrapyramidal symptoms, including tardive dyskinesia. The drug exerts no or only weak parkinsonian and cataleptic effects. A single case of malignant postneuroleptic syndrome with acute renal failure with myoglobinuria was described after discontinuation of sulpiride and maprotiline therapy.

Sulpiride as a stimulating drug can cause sleep disturbances. This usually occurs when the drug is administered in evening hours. In some patients the drug may cause excessive sedation and somnolence. It may also upregulate the arterial blood pressure. The drug may induce hormonal disturbances such as gynaecomastia, amenorrhoea, galactorrhoea. Quite frequently body weight gain is observed. During administration of the drug, the hepatic function and blood morphotic pattern should be monitored. The drug may exert a negative effect on the ability to drive vehicles and operate machinery.

In the study group, only part of adverse effects was in agreement with the reports of the abovementioned authors. Amenorrhoea was found in 37% of the menstruating women. In 9% of women galactorrhoea occurred. In 7% of patients body weight gain was observed. The rest adverse effects were found sporadically: 2–3% of patients were complaining of abdominal pain, decrease of potency, physical weakness, isolated extrasystoles and intensification of fears. In three subjects the following manifestations were noted:

in one patient constipation, nausea, lack of appetite, dyspepsia of hepatic origin, breast enlargement, daytime somnolence were observed;

in another patient supraventricular tachycardia, stupefaction, vertigo, palpebral tremor, paraesthesiae were noted;

in the third subject verbal agrression, violent active aggression with strong psychomotor agitation, auditory hallucinations, trismus occurred.

In summary, it should be stated that the current study confirmed the effectiveness of sulpiride as an antidepressant.

CONCLUSIONS

1. Sulpiride is a good, effective drug in the treatment of endogenous depression. Its onset of action after administration is very rapid and the drug is relatively safe – it produces few mild complications, frequently including galactorrhoea and amenorrhoea in women.

2. The general results in Hamilton and Beck tests very strongly correlate with depression intensity and therapeutic effects. Only part of detailed assessments of patient's status included in the questions in the Hamilton and Beck scales are related to depression intensity and therapeutic effects; the others occur with an equal incidence on various levels of depression intensity and with various therapeutic effects.

3. The treatment of endogenous depression can be regarded as effective if the general result of Hamilton or/and Beck tests has improved by at least 60%. Treatment is effective usually in the case when the summarized score in the Hamilton and Beck scales before treatment is 25 points or lower.

Received 20 January 2003
Accepted 29 may 2003

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