Adverse effects of phenothiazines in chronic schizophrenic patients

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Abstract

A high dose of phenothiazines may develop extrapyramidal reaction and they may interact with other drugs leading to different adverse effects. This study was conducted to show the possible adverse effects of a combination of drugs from the phenothiazine family. A case series from psychiatric unit were collected during the period from the 1st of September 1997 to the end of December 1998. The study included 1060 chronic schizophrenic patients receiving combined phenothiazine therapy. The results revealed that the adverse effects in 145 (13.7%) patients. The most common adverse effects were drowsiness 5.9%, anticholinergic effects 2.6% and hypertension 2%. Other less common effects were extrapyramidal 1.2%, dermatological 1%, weight gain 0.9%. The study concludes that many adverse effects of phenothiazines were revealed and drowsiness with other anticholinergic effects was more dominant.

Key words: Schizophrenia, Phenothiazines, Adverse effects.

Introduction

Phenothiazines have a wide range of pharmacological actions and are used therapeutically mainly as psycho sedatives and anti histamines, but also as antiemetics and antipruritics [1]. These largely used drugs especially at the mental hospitals, do however, cause several kinds of side effects [2]. They all have strong antiadrenergic and weaker anticholinergic effects and thus cause faintness, palpitation, nasal stuffiness, dry mouth, slight constipation and inhibition of ejaculation[3].

After high doses, the patients may develop extrapyramidal reactions with bizarre motor effects that may simulate Parkinson`s disease [4]. Interaction with other drugs should be remembered, particularly the potentiative effect on sedatives and alcohol [5]. The most dangerous side effects of phenothiazines are those resulting from hypersensitivity reactions, particularly blood dyscrasias, obstructive jaundice and dermatological reactions [6]. In the present study, the adverse effects of phenothiazines in schizophrenic patients were reported.

Patients and Methods

This study was conducted on 1060 chronic schizophrenic patients attending psychiatric department at Ibn-Sena General Hospital in Mosul. The duration of illness ranges between 3-30 years, and the duration of treatment ranges between 3mounths to 10 years. The patients were not asked specifically about possible listed side effects, but were merely asked for any problem or difficulty with the drug [7]. Any complaint was discussed with the patient and examined clinically and if it appeared to be drug related, the case was reported as drug adverse effect.

Results

The adverse effects were reported in 145 patients (75 males and 70 females) out of 1060 patients with a proportion of 13.7%. The most common adverse effects were drowsiness 5.9%, anticholinergic effects 2.6% and hypotension 2%. Other less common adverse effects were extrapyramidal 1.2%, dermatological 1%, weight gain 0.9% Tardive dyskinesia 0.8% endocrine effects 0.7% and lastly impotence 0.5% Table (1).

Discussion

The present study showed that phenothiazines cause drowsiness which is a common complication of many drugs, particularly psychotropic drugs. It has been claimed that three quarters of patients on phenothiazines experience some degree of drowsiness [8]. Such a reaction is to a large extent dose dependent.

Phenothiazines have anticholinergic activity which is sufficient to cause dryness of mouth [8]. This reaction is usually due to competition with acetylcholine released at the parasympathetic effectors junction. Bassuk and Schoonover [9] pointed out that most psychoactive drugs, particularly the tricyclic antidepressants and the phenothiazines have significant anticholinergic properties commonly resulting in dryness of the mouth and occasionally contributing to carious destruction of the teeth.

Orthostatic hypertension is the most frequent cardiovascular effect of neuroleptic drugs (10). It is more common with the aliphatic and piperidine phenothiazines and unusual with the other neuroleptic drugs except when given intramuscularly, this action is usually due to α-adrenoceptor blocking action of phenothiazines (2).

The anticholinergic and α-adrenoceptor antagonist activity of phenothiazines can cause impotence and ejaculatory dysfunction (11). Thioridazine is the drug most frequently reported to cause impotence and this is consistent with the greater peripheral autonomic activity of the piperidine group (12).

In this study, a number of patients were reported to have extrapyramidal symptoms which are related to parkinsonism and akathisia. Pseudoparkinsonism is probably the most common drug induced disorders of involuntary movement and almost all of the phenothiazines have been associated with the production of parkinsonism which has also been induced by the butyrophenones such as haloperidol (8).

Extrapyramidal syndrome has been estimated to occur in about 39% of patients receiving phenothiazines and this represents a most important complication of the treatment (13). The other neurological disorders caused by phenothiazines include tradive dyskinasia and this disorder appeared in eight patients in the present study. Tradive dyskinasia is a late appearing effect which looks like an extrapyramidal effect but in most aspects is exactly opposite in terms of etiology and responsiveness to treatment (3). The adverse effects related to endocrine system resulted from the suppression of prolactin inhibitory factor in the median eminence of the hypothalamus by neuroleptic drugs allowing secretion of prolactin from the anterior pituitary (2). Margolis et al reported gynecomastia in three patients while they are taking phenothiazine. A cause and effect relationship is suggested by the regression of symptoms when the drug was discontinued and the reappearance of symptoms on a second course of treatment (14).

Neuroleptic drugs can also influence body weight as appeared in the present study where 10 patients have increase in body weight as a result of chronic use of phenothiazines. The mechanism of neuroleptic drug induced body weight change is unknown but an alteration of hypothalamic monitoring of plasma glucose, pathological glucose tolerance and carbohydrates craving have been postulated (15).

In the present study, six patients showed skin eruption appeared as maculopapular rash on the face, neck, upper chest and extremities. Other six patients showed skin pigmentation changes. The dermatological reactions to phenothiazines are multiple and may be divided into two categories; the first one is allergic reactions such as urticaria, maculopapular eruptions and non-thrombocytopenic purpura. The second is photosensitivity (16). Pigmentary effects on the skin and the eye occur with high dose-long term phenothiazine therapy (3). In conclusion, the study revealed different adverse effects of the phenothiazines drugs; the most common effects were drowsiness, anticholinergic effects and hypotension.

References

1. Davis JM, Casper R. Antipsychotic drugs. Clinical pharmacology and therapeutic use. Drugs 1977; 14:260-82.

2. Laurence DR, Bennett PN, Brown MJ. Meuroleptics In: Clinical Pharmacology. Eight edition. Churchill Livingstone 1997:337.

3. Stimmel GL. Shizophrenia In: Clinical pharmacy and therapeutics. Herfindal ET, Hirschman JL (eds) Third edition. Williams and Wilkins 1948: 744-60.

4. Donlon PT, Stenson RL. Neuroleptic induced extrapyramidal symptoms Dis Nerv Syst. 1976; 37: 629-35.

5. Hollister LE. Antipsychotic agents. In: Basic and clinical pharmacology. BG Kafzung (ed) 1995: 43-5.

6. Swett. Outpatient Phenothiazine use and bone marrow depression. Arch Gen Psychiat 1975; 32: 1416-8.

7. Huskisson E, Wojtulewski JA. Measurement of side effects of drugs. Br Med J 1974; 2: 698-99.

8. Davies DM. Psychiatric disorder. In: Textbook of adverse drug reactions. Third edition. Oxford University Press 1987:552.

9. Bassuk E, Schoonover S. Rampant dental caries in the treatment of depression. J Clin Psychiat 1978; 39: 163.

10. Stimmel B. Cardiovascular effects of mood altering drugs. New York: Raven Press 1979: 117-31.

11. Mitchell LE, Popkin MK. Antipssychotic drug therapy and sexual dysfunction in men. Am J Psych 1982; 139: 633.

12. Kotin J, Wibert DE, Verburg D, Soldinger SM. Thioridazine and sexual dysfunction. Am J Psych 1976; 133:82.

13. Ayd FJ. A survey of drug induced extrapyramidal reactions. JAMA 1961; 175:1054-60.

14. Margolis JB, Gross CG. Gynecomastia during phenothiazines therapy. JAMA 1967; 199: 942-4.

15. Doss FW. The effect of antipsychotic drugs on body weight: A retrospective review. J Clin Psychit 1979; 40: 528-30.

16. Almeyda J. Cutaneous side effects of phenothiazines. Br J Derm 1997; 84: 605-7.

Table (1): The distribution of adverse effects reported in study sample.

Adverse effects	Number of patients	Percentage from 145 patients	Percentage from 1060 patients	Drug
Drowsiness	62	42.8	5.9	Th, Ch & Tr
Anticholinergic:	28	19.3	2.6	Th, Ch & Tr
• Dry mouth	16	11	1.5	Th, Ch & Tr
• Constipation	10	6.9	0.9	Th, Ch & Tr
• Blurred vision	5	3.5	0.5	Th & Ch
• Palpitation	4	2.8	0.4	Th & Ch
Hypotension	21	14.5	2	Th, Ch & Tr
Extrapyramidal	13	9	1.2	
• Parkinsonism	8	5.5	0.8	Ch & Tr
• Akathisia	5	3.5	0.5	Ch & Tr
Dermatological	11	7.6	1	
• Maculopapular rash	6	4.1	0.6	Th, Ch & Tr
• Skin pigmentation	6	4.1	0.6	Th & Ch
Weight gain	10	6.9	0.9	Th, Ch & Tr
Tardive dyskinesia	8	5.5	0.8	Ch & Tr
Endocrine	7	4.8	0.7	
• Galactorrhoea	3	2.1	0.3	Th & Ch
• Gynecomastia	4	2.8	0.4	Th, Ch & Tr
Impotence	5	3.5	0.5	Th & Ch