ESTIMATION OF SERUM CREATINE KINASE ON TAKING ANTI PSYCHOTICS IN PSYCHIATRIC PATIENTS

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ABSTRACT

Creatine kinase (CK) is an enzyme with three isoforms BB/CK1, MB/CK2 and MM/CK3. Normal range is 22 to 198 U/L (units per liter). Serum creatine kinase (SCK) activity of the skeletal muscle form is sometimes moderately increased in psychiatric patient and may be massively increased as a result of muscle damage and serum creatine kinase activity increases in patients treated with antipsychotics drugs. Raised level of total creatine kinase has been detected in the serum of patients with psychiatric disorders. Different types of psychiatric disorders are present in the Indian population. Bipolar disorder, unipolar disorder, schizophrenia, attention deficit hyperactivity disorder, anxiety disorder, Patterns of belief, language use and perception of reality can become disordered (e.g., delusions, thought disorder, hallucinations). Antipsychotics also known as neuroleptics or major tranquilizers are a class of drugs used in the treatment of psychiatric disorders. There are two categories of antipsychotics: typical antipsychotics and atypical antipsychotics. This review is designed to estimate the serum creatnine kinase on taking antipsychotics in psychiatric patients and thus to find the type of antipsychotics having increased creatine kinase activity. The review shown that the estimation of serum creatine kinase on taking antipsychotics in psychiatric patients.

Keywords: serum creatine kinase, antipsychotics, psychiatric disorders, psychiatric patients.

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INTRODUCTION

A mental disorder, also called a mental illness or psychiatric disorder, is a disease that causes mild to severe disturbance in thoughts and /or behavior , resulting in an inability to cope with life‘s ordinary demands and routing (1). There are many different categories of mental disorder, and many different facets of human behavior and personality that can become disordered. They are Anxiety or fear, other affective (emotion/mood) processes can also become disordered, Bipolar disorder (also known as manic depression), major depression, Patterns of belief, language use and perception of reality can become disordered (e.g., delusions, thought disorder, hallucinations). Psychotic disorders in this domain include schizophrenia, and delusional disorder. Schizoaffective disorder is a category used for individuals showing aspects of both schizophrenia and affective disorders. (2)

Antipsychotics also known as neuroleptics or major tranquilizers, are a class of drugs used in the treatment of psychiatric disorders, most notably schizophrenia, but also in disorders such as bipolar disorder, delusional disorder and increasingly for certain nonpsychotic disorders. (3) Since the introduction of antipsychotic medication for the treatment of psychosis, a wide range of different types of drugs have been developed under this genre. The first generation of antipsychotic medication is known as the ‘typical antipsychotics’ and these were first discovered in the 1950s. Soon following their clinical use it was recognized that they caused extrapyramidal symptoms (EPS) in patients including Parkinsonism, tardive dyskinesia, akathisia and dystonia (Steck 1954). The severe side effects created a need for a new generation of these medications that would be more tolerable to the patient. Subsequently, second generations of antipsychotics were developed known as the ‘atypical antipsychotics’, the first of which was clozapine which was clinically introduced in the 1970s. (4)

There are two categories of antipsychotics: typical antipsychotics and atypical antipsychotics. Most antipsychotics are available only by prescription.

Typical antipsychotics: Chlorpromazine (Thorazine), Haloperidol (Haldol), Perphenazine (Trilafon), Thioridazine (Melleril), Thiothixene (Navane), Flupenthixol (Fluanxol) Trifluoperazine (Stelazine)

Atypical antipsychotics: Aripiprazole (Abilify) , Clozapine (Clozaril) , Olanzapine (Zyprexa) ,Paliperidone (Invega) , Quetiapine (Seroquel) , Risperidone (Risperdal) , Zotepine (Nipolept) ,Ziprasidone (Geodon).

Creatine kinase (CK) is an enzyme with three isoforms BB/CK1, MB/CK2 and MM/CK3. In a healthy adult, the CPK level in the blood serum varies with a number of factors (gender, race and activity), but normal range is 22 to 198 U/L (units per liter).(5) Higher amounts of serum CPK can indicate muscle damage from chronic disease or acute muscle injury. The skeletal muscle contains primarily MM; cardiac muscle contains primarily MB and MM. Brain tissue, GI system and genitourinary tract contain primarily BB(6). Normally, total CK levels are virtually 100% MM isoenzyme also that catalyzes the reversible trans phosphorylation of creatine by adenosine triphosphate, plays a key role in energy transport in cells and neurons. (7) Serum creatine kinase (SCK) activity of the skeletal muscle form is sometimes moderately increased in psychiatric patient and may be massively increased as a result of muscle damage and SCK increases in patients treated with antipsychotics drugs. (8) Raised level of total CK has been detected in the serum of patients with psychiatric disorders. Current scientific literature indicates that patients with psychotic disorders can also have increased creatine kinase activity. This phenomenon may result from increased motor activity, increased tension and intense muscular activity in catatonic conditions. (9)

METHODOLOGY

STUDY DESIGN : Prospective, experimental study

STUDY POPULATION: Patients reported to Department of psychiatry.

INCLUSION CRITERIA :

1. Psychiatric patients having schizophrenia, bipolar disorder, psychosis, and admitted in the inpatient department, Department of psychiatry.

2. Inpatients who give consent voluntarily to participate in the study.

3. Both male & female patients of all age groups.

EXCLUSION CRITERIA

1. Patients who are not wiling have to give consent for collection of residual blood.

2. Patients having other comorbidities.

3. Pregnant and breastfeeding women or women of child bearing potential

STUDY SETTING

Tertiary care setting, Department of psychiatry; Pushpagiri Medical College Hospital Thiruvalla.

Pushpagiri college of pharmacy , Thiruvalla.

SAMPLE SIZE OF THE STUDY: 60 psychiatric patients.

$\frac{(Z^2\ 1-\alpha/2)\ (1-p)\ p}{\zeta 2\ p}$ where p: Expected proportion

ζ: Relative precision

$1-\alpha/2$: Desired confidence level

STUDY PERIOD : 6 months

BRIEF PROCEDURE OF THE STUDY

A Prospective experimental study is going to be conducted in Department of psychiatry in Pushpagiri Medical College Hospital on the topic "ESTIMATION OF SERUM CREATINE KINASE ON TAKING ANTIPSYCHOTICS IN PSYCHIATRIC PATIENTS". Informed consent of the patients will be taken before the study. Patient data collection form will be used for recording the demographic details of the patients. It is a 6 months study in which patients are recruited based on inclusion & exclusion criteria. About 50 patients have to be selected for the follow up study. For the determination of creatine kinase, residual blood will be collected from laboratory and determined by using semiautomatic analyzer in the Pushpagiri College of Pharmacy.

Medication adherence of the patient will be evaluated by using MARS Scale.(Medication Adherence Rating Scale)

Procedure to find out creatine kinase

- Preparation of working reagent: Add 1ml of 2CK-NAC to one bottle of 1 CK-NAC. Mix to dissolve use after 10 minutes.
- Pipette out 1ml of working reagent and add 0.05ml of sample.

- Mix immediately and read first absorbance of test at 120 seconds
- Second, third and fourth absorbance at an interval of 30 seconds at 340 nm.
- Read the CK in semiautomatic analyzer.

RESULTS AND DISCUSSION

Table-1: DISTRIBUTION OF PATIENT BASED ON AGE

Age		Olanzapine	Risperidone	Clozapine	Total
Below 35	Count	11	4	7	22
	% of Total	18.3%	6.7%	11.7%	36.7%
35 - 55	Count	6	8	10	24
	% of Total	10.0%	13.3%	16.7%	40.0%
Above 55	Count	3	8	3	14
	% of Total	5.0%	13.3%	5.0%	23.3%
Total	Count	20	20	20	60
	% of Total	33.3%	33.3%	33.3%	100.0%

Fig-1 : DISTRIBUTION OF PATIENT BASED ON AGE

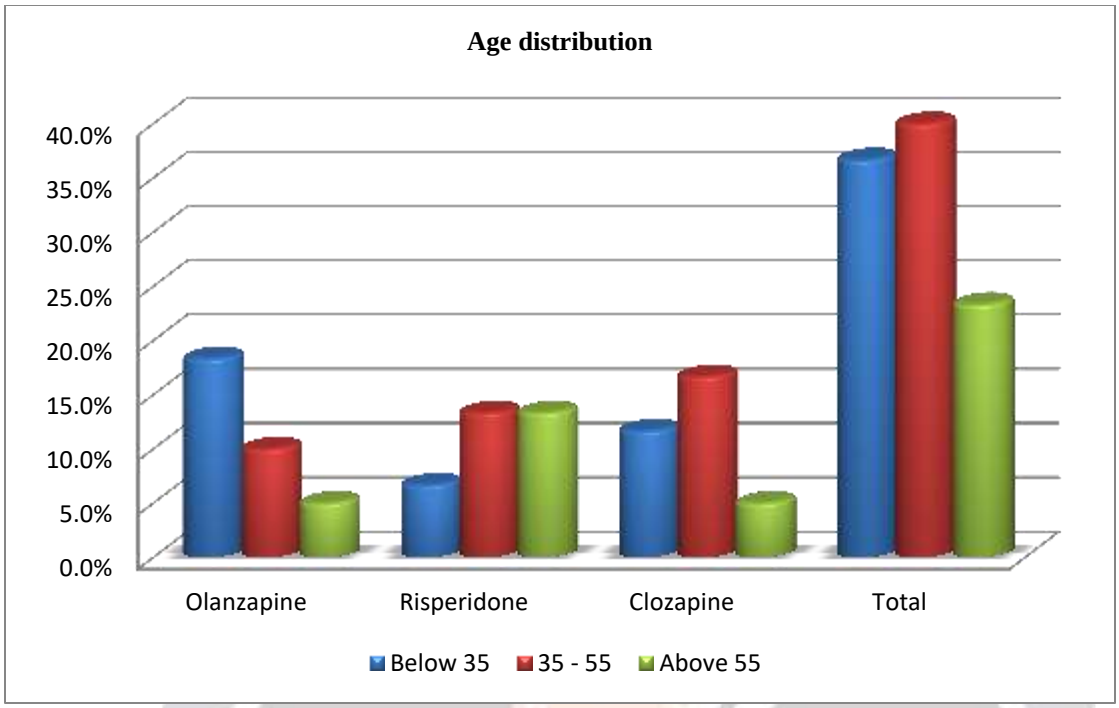


Table -2 : DISTRIBUTION OF PATIENT BASED ON GENDER

Sex		Olanzapine	Risperidone	Clozapine	Total
Female	Count	15	12	8	35
	% of Total	25.0%	20.0%	13.3%	58.3%
Male	Count	5	8	12	25
	% of Total	8.3%	13.3%	20.0%	41.7%
Total	**Count**	**20**	**20**	**20**	**60**
	% of Total	**33.3%**	**33.3%**	**33.3%**	**100.0%**

Figure- 2 : DISTRIBUTION OF PATIENT BASED ON GENDER

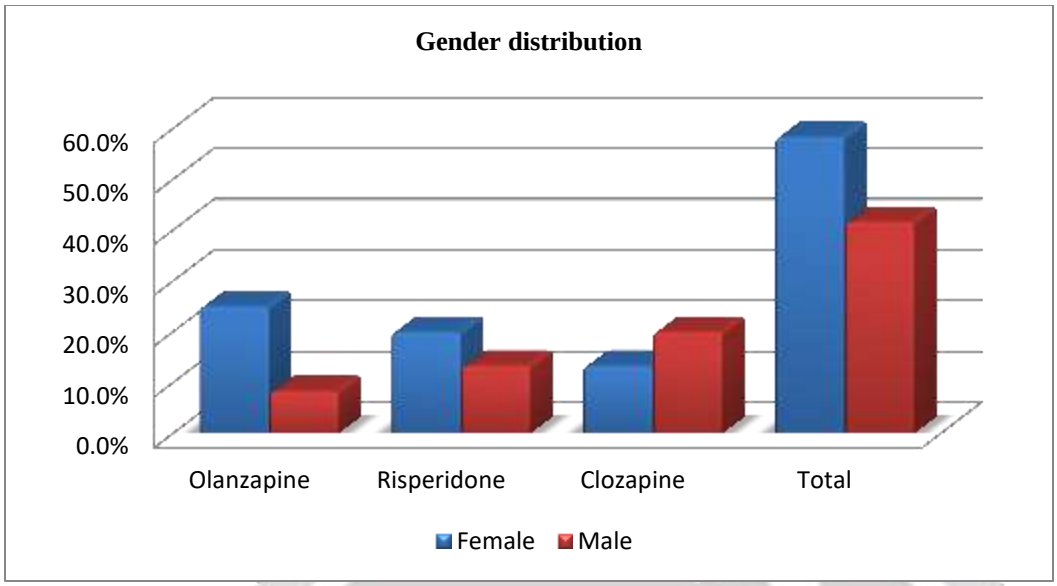


Table-3: DISTRIBUTION OF PATIENT BASED ON MEDICATION ADHERANCE

MEDICATION ADHERANCE	Before			After		
	Olanzapine	**Risperidone**	**Clozapine**	**Olanzapine**	**Risperidone**	**Clozapine**
Yes	2	4	3	8	9	8
	3.3%	6.7%	5.0%	13.3%	15.0%	13.3%
No	18	16	17	12	11	12
	30.0%	26.7%	28.3%	20.0%	18.3%	20.0%
Total	20	20	20	20	20	20
	33.3%	33.3%	33.3%	33.3%	33.3%	33.3%
P value		***0.137***			***0.934***	

Figure-3 : DISTRIBUTION OF PATIENT BASED ON MEDICATION ADHERANCE

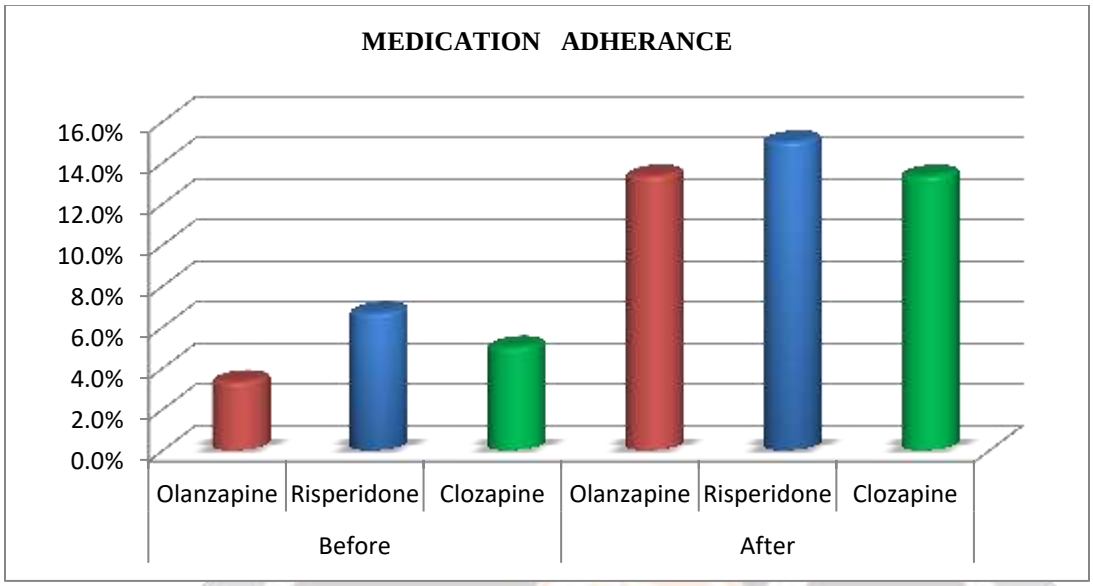


Table-4 :EFFECT OF SERUM CREATINE KINASE ON OLANZEPINE

CREATINE KINASE	Mean	SD	Mean difference	95% confidence interval of difference	Paired t value	P value
First week	147.00	87.39	529.15	293.29 - 765.01	4.696	P<0.001
After 2 weeks	676.15	536.88				

Figure-4 : EFFECT OF SERUM CREATINE KINASE ON OLANZAPINE

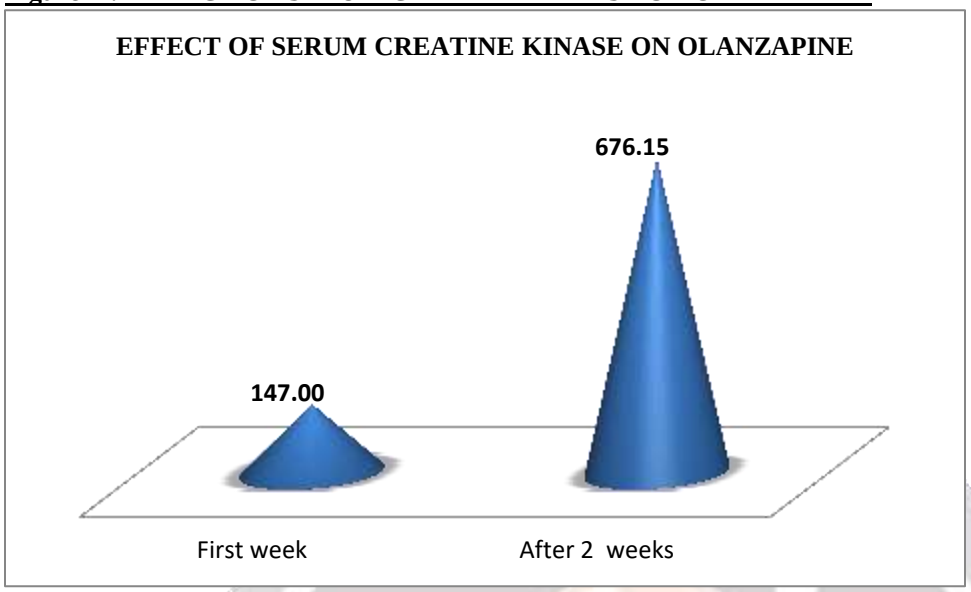


Table-5: EFFECT OF SERUM CREATINE KINASE ON RISPERIDONE

CREATINE KINASE	Mean	SD	Mean difference	95% confidence interval of difference	Paired t value	P value
First week	138.01	71.54	531.89	318.04 - 745.74	5.206	P<0.001
After 2 weeks	669.90	494.08				

Figure-5 : EFFECT OF SERUM CREATINE KINASE ON RISPERIDONE

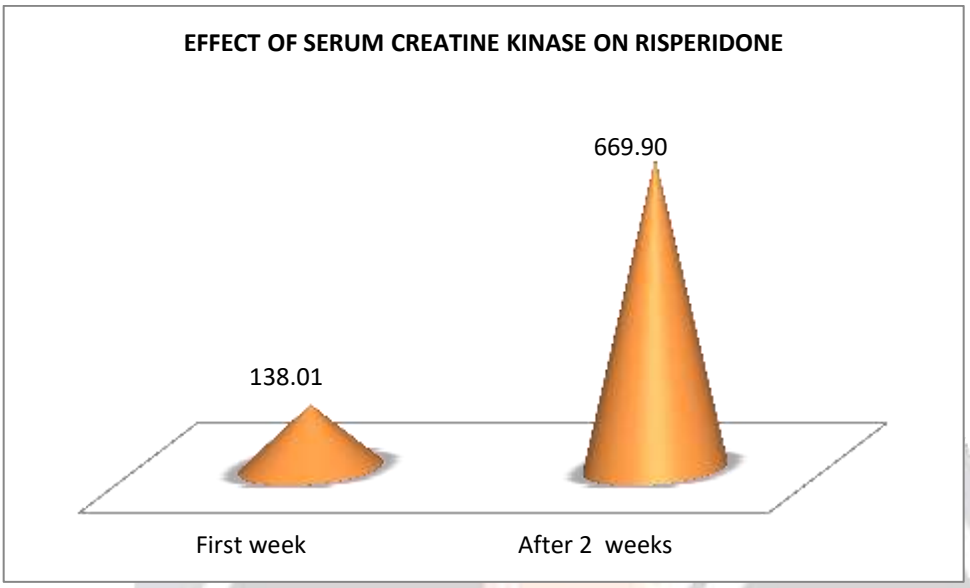
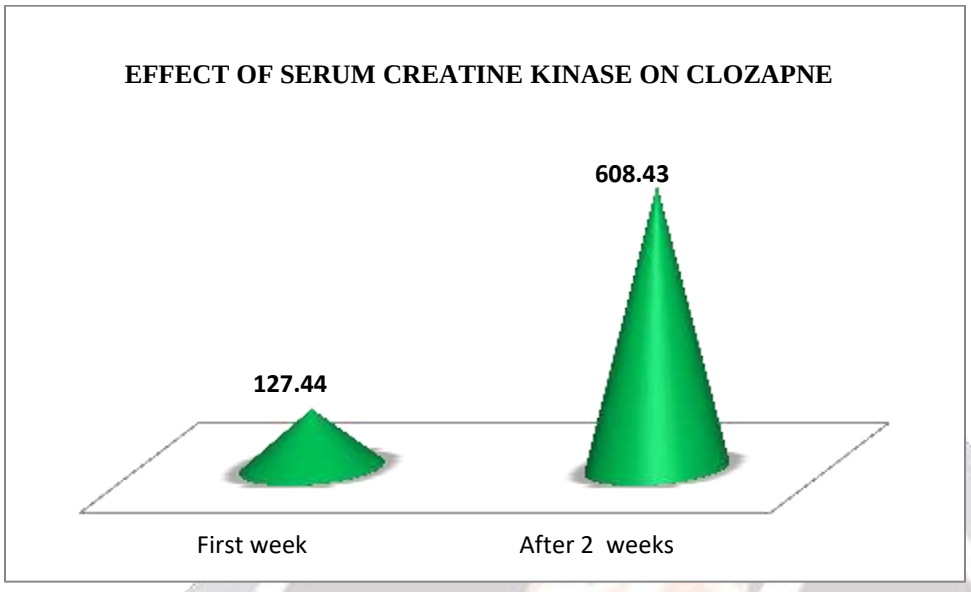


Table – 6 : EFFECT OF SERUM CREATINE KINASE ON CLOZAPINE

CREATINE KINASE	Mean	SD	Mean difference	95% confidence interval of difference	Paired t value	P value
First week	127.44	53.39	480.99	266.98 - 694.99	4.704	P<0.001
After 2 weeks	608.43	107.20				

Figure-6 : EFFECT OF SERUM CREATINE KINASE ON CLOZAPINE



DISCUSSION

PATIENT DEMOGRAPHIC DETAILS

AGE

In this study , total study population falls in the age group 35-55

GENDER

In this study, majority of patient on taking olanzepine were females 25% followed by males 8.3%. In Risperdone 20% female & 13.3 % male patients. In clozapine 13.3% females & 20% male patients

EFFECT OF CREATINE KINASE ON OLANZEPINE

Mean value of creatine kinase after drug use is 676.15 & p value <0.001 which is significant . Since p value <0.001 , the creatine kinase level significantly increased.

EFFECT OF SERUM CREATINE KINASE ON RISPERIDONE

Mean value of creatine kinase after drug use is 669.9& p value <0.001 which is significant . Since p value <0.001 , the creatine kinase level significantly increased.

EFFECT OF SERUM CREATINE KINASE ON CLOZAPINE

Mean value of creatine kinase after drug use is 608.43 & p value <0.001 which is significant . Since p value <0.001 , the creatine kinase level significantly increased.

MEDICATION ADHERANCE

In this study, before counseling medication adherence p value is 0.137 and after counseling medication adherence p value is 0.934 . 75 % become adherent.

CONCLUSION

A mental disorder, also called a mental illness or psychiatric disorder, is a diagnosis by a mental health professional of a behavioral or mental pattern that may cause suffering or a poor ability to function in life. Antipsychotics also known as neuroleptics or major tranquilizers, are a class of medication primarily used to manage psychosis (including delusions, hallucinations, paranoia or disordered thought), principally in schizophrenia and bipolar disorder. Serum creatine kinase (SCK) activity of the skeletal muscle form is sometimes moderately increased in psychiatric patient and may be massively increased as a result of muscle damage and SCK increases in patients treated with antipsychotics drugs. Medication adherence was increased after patient counseling.

Thus, pharmacist has an important role in monitoring serum creatine kinase in patients taking antipsychotics. Regular monitoring of serum creatine kinase in psychiatric patient is required.

- In this study , pointed out the effect of biomarker in psychiatric patients.
- The majority of the patients were found to have elevation in serum creatine kinase after the administration of olanzapine
- Majority of the study population belongs to the age group 35-55
- Medication adherence was increased after counseling.

REFERENCE

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (5th ed.). Arlington: American Psychiatric Publishing. pp. 101–05. ISBN 978-089042)

2. Katschnig, Heinz "Are psychiatrists an endangered species? Observations on internal and external challenges to the profession". World Psychiatry. (2010). 9 (1): 21–8. doi:10.1002/j.2051-5545.2010.tb00257.

3. King, Caroline; Voruganti etal "What's in a name? The evolution of the nomenclature of antipsychotic drugs". Journal of Psychiatry and Neuroscience. (2002-05-01) 27 (3): 168–175.

4. Leucht S, Corves C, Arbter D, Engel RR, Li C, Davis JM "Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis.". Lancet. January (2009). 373 (9657): 31–41. doi:10.1016/S0140-6736(08)61764-X.

5. Michael L. Bishop, et.al "Clinical chemistry: principles, procedures, correlations." Philadelphia: Lippincott Williams & Wilkins. (2004). p. 243. ISBN 978-0-7817-4611-3. OCLC 56446391

6. Nanji AA. Serum creatine kinase isoenzymes: A review. Muscle Nerve 1983; 6:83-90.

7. Andres RH etal. " Functions and effects of creatine in the nervous system". Brain Res Bull. 2008: 76 (4): 329 -43

8. Bengzon A, etal: "Some changes in the serum during treatment with psychotropic drugs." J Nerv Ment Dis (1996) 143: 369- 376.

9. Tsung SH ".Several conditions causing elevation of serum CK –MB and CK –BB", Am J Clin Pathol 1981;75:711-5