The effect of Risperidone and Haloperidol on clinical picture and some biochemical parameters of schizophrenia Libyan patient.

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ملخص البحث:

الانفصام (Schizophrenia) هو اضطراب عقلي شديد، يتميز بالاضطرابات الأساسية في التفكير والإدراك والعواطف. أكثر من 100 سنة من الأبحاث لم تكن قادرة تماما على حل اللغز الذي يمثل الانفصام. الانفصام يشار إلى أنه اضطراب وليس مرض ، لأنه لا يوجد هناك أي عامل مسبب للمرض واضح وموثوق به ومحدد. وعلي الرغم من أن الانفصام ليس مرضا متكرراً ، فهو من أكثر الأمراض المرهقة والمكلفة في جميع أنحاء العالم . الوقاية من الانتكاس (prevention of) relapse هو الهدف الرئيسي من العلاج في المرضى الذين يعانون من اضطرابات نفسية . الدليل الطبي قسم أعراض المرض إلى فئتين كبيرتين : الأعراض الإيجابية (positive symptoms) والأعراض السلبية (negative symptoms). الأعراض الإيجابية هي الانحرافات السلوكية التي تشمل الهلوسة والأوهام ، وضعف الإدراك وضعف التفكير الاستدلالي ، والتفكير الغير منطقي ، والسلوك الغريب .أما الأعراض السلبية فهي العجز السلوكي التي قد يشمل نقص الطاقة والمبادرة، بالإضافة إلى ضعف التركيز و الانتباه، والانسحاب الاجتماعي ، ونقص التجاوب العاطفي ، ونقص المهارات الاجتماعية و ضعف المعيشة اليومية (الجمعية الأمريكية للطب النفسي ، 1994). هدا البحث سوف يتضمن اجراء مقارنة بين أحدث الأدوية المهدئة ريسبيريدون (Risperidone) مع أحد الأدوية التقليدية المهدئة هالوبيريدول (Haloperidol)، والمقارنة بينهما من حيث التأثير على وظائف الكلى ووظائف الكبد ومن حيث وجود الأعراض السلبية والأعراض الإيجابية في المرضى الذين يعانون من الانفصام و الاضطراب الانفصامي العاطفي بعد ثلاثة أسابيع وخمسة أسابيع من العلاج.

Keywords : Schizophrenia, Haloperidol, Risperidone, positive and negative symptoms.

Introduction

Schizophrenia is a severe mental disorder, it is characterized by fundamental disturbances in thinking, perception and emotions. More than 100 years of research have not been able to fully resolve the puzzle that schizophrenia represents (Bentall, 2004, Rsssler et al., 2005). The Diagnostic and Statistical Manual (DSM-IV) is considered the most authoritative resource for the characterization of mental health disorders (American Psychiatric Association, 1994,2000). The Manual divides the symptomology of the disease into two broad categories: positive symptoms and negative symptoms. Positive symptoms are behavioral abnormalities that include "hallucinations, delusions, impaired perception, impaired inferential thinking, illogical thought progression, bizarre behavior **(**Stahl, 2002)**.** The "negative symptoms" are behavioral deficits that may include a lack of energy, drive, initiative, and interest, in addition to poor concentration and attention, social withdrawal, emotional unresponsiveness, and impaired social and daily living skills **(**Winograd-Gurvich et al., 2006). The disease is further complicated by the unwillingness of those affected by the disease to report the symptoms of their illness. In addition to the costs of treatment and lack of productivity, the devastating consequences on an individual's family life, social relations, and productive cognitive capacities affect his or her future employment prospects **(**Andreasen and Schultz**,** 1996).

Material and methods

Site of the study:

All participants included in the study were Libyans from the whole country. Patients were chosen from private mental hospital (AL- Razi) in Tripoli.

Materials:

1- New 50 cases of schizophrenia Libyan patients

2- Needle and Syringe (sterilized).

3- Disinfectant (alcohol) to clean up the place drawing blood, cotton and medical bandages.

4- Tourniquet.

5 - Diaper to save the blood samples of temperatures.

6 - Centrifuges to separate blood samples.

7- ARCHITECT c4000. 8- Spinreact spinlab -180.

9- Test tube carrier. 10- Biochemistry tube.

11- Questionnaire format. 12- S.P.S.S V.20.

13- Drugs (haloperidol and risperidone).

Method:

50 new cases of patients with positive disorder of schizophrenia were diagnosed by a specialist of Psychiatry Hospital, AL- Razi Psychiatric and Neurological unit Tripoli, Libya and taken for therapy. Patients were divided on the basis of the presence of positive and negative symptoms of schizophrenia. The positive symptoms were dominant in the hospital. And includes 46 cases and cases of negative symptoms were four. All cases were divided into two groups, i.e. 25 cases treated with Haldol and another 25 cases treated by risperidone. Samples blood was taken after 3 weeks of treatment is for the first time under the supervision of a Psychiatrist, hailed all the cases that are diagnosed were conducted for analysis of liver and renal functions as part of routine before taking it therapy medical laboratory of private hospital AL-Razi psychiatric and neurological unit. Blood samples were withdrawn again after 5 weeks of treatment taken.

Blood samples (5 ml each) were collected in separate test tubes from each patient by qualified Nurse in Medical Laboratory of AL-Razi Hospital for Psychiatric and Neurological disease. Each test tube and patient questionnaire

were marked with special number for each patient sample. All samples were centrifuged for 6 minutes at 4000 rpm . The upper layer (serum) from each sample was separated and kept in a test tube and each test tube was labeled with a special number as marked on patient questionnaire. The samples were kept in snow Portfolio in order to maintain the normal effectiveness of enzymes such as (GOT, GPT, ALK. Phosphatase) and kidney functions. Samples were taken out from snow portfolio and kept for 15 -30 minutes at room temperature (30 ºC) for conducting further enzymes and kidney function tests as follows:

1-GOT, GPT, bilirubin, creatinine, urea, Na, K and Cl by ARCHITECT c4000.

2- ALK. Phosphatase conducted by spinreact spinlab -180.

Statistical methods:

Statistical results were done by the Statistical Package for Social Sciences (SPSS), version 20, Echo soft Corp USA, 2011.

Analytical statistics (Student's-t-test):

Differences between the mean of groups were assessed by Student's t-test adopted for either equal or unequal variances.

$$t = \frac{M_1 - M_2}{\sqrt{\frac{(SD_1)^2 - (SD_2)^2}{N_1 + N_2}}}$$

M_1 = mean of first group. M_2 = mean of second group.
SD_1 = SD of first group. SD_2 = SD of second group.
N_1 = number of cases of first group. N_2 = number of cases of second group.
N.B.: P. Value (probability) means level of significance
- P> 0.05 not significant. - P< 0.05 significant.

Results

Table (1) *comparative Data Analysis by means of liver enzyme and kidney function test by dosage of Risperidone & Haloperidol treatment.*

Dosage	Type of test	Haloperidol		Risperidone	
		Means		Means	
		3 week	5 week	3 week	5 week
2 mg	GOT	16.50	18.50	15.22	13.89
	GPT	19.00	25.88	16.44	15.89
	Alk. Phosphatase	186.00	195.00	163.33	158.67
	Bilirubin	0.49	0.58	0.50	0.57
	Blood urea	25.05	20.70	20.11	18.20
	Creatinine	0.49	0.58	0.52	0.57
	Na	135.50	139.00	137.33	137.67
	K	4.14	4.00	3.83	3.84
	Cl	102.13	101.63	101.67	101.89
4 mg	GOT	31.08	29.77	32.87	34.87
	GPT	39.69	42.46	41.53	49.33
	Alk. Phosphatase	225.92	221.31	252.40	240.80
	Bilirubin	0.70	0.75	0.76	0.81
	Blood urea	21.73	22.91	21.65	20.23
	Creatinine	0.49	0.55	0.64	0.65
	Na	137.85	138.54	135.47	138.13
	K	3.88	4.06	4.07	3.76
	Cl	101.38	101.92	102.27	101.27
5 mg	GOT	124.50	75.00	89.00	76.00
	GPT	145.50	106.50	126.0	84.0
	Alk. Phosphatase	456.0	338.0	364.0	324.0
	Bilirubin	2.57	1.71	1.65	1.00
	Blood urea	35.50	33.60	15.30	17.40

	Creatinine	0.89	0.86	0.36	0.72
	Na	131.00	136.50	137.00	134.00
	K	4.65	4.20	3.80	4.60
	Cl	102.00	101.00	106.00	103.00
10 mg	GOT	78.00	50.00	------	-------
	GPT	99.50	63.50	------	-------
	Alk. Phosphatase	334.00	185.00	------	-------
	Bilirubin	1.57	0.78	------	-------
	Blood urea	30.35	26.55	------	-------
	Creatinine	0.73	0.58	------	-------
	Na	137.00	140.00	------	-------
	K	4.15	3.60	------	-------
	Cl	103.50	101.50	------	-------

It appears from the table 1 above comparative data of haloperidol and risperidone treatments (dosage 2 mg and 4 mg) that means test values of GOT enzyme, GPT enzyme, ALK. Phosphatase enzyme & bilirubin levels at 3 weeks of haloperidol treatments are slightly higher (GOT, GPT & alk. phosphatase) or almost equal (bilirubin) to risperidone treatments at a dosage of 2mg but lower at a dosage of 4mg, however, blood urea, creatinine, Na, K and Cl levels are insignificantly alter between haloperidol and risperidone drugs treatments after 3 weeks. GOT, GPT, alk. phosphatase enzyme levels are higher or equal (bilirubin) to dosage 2mg after 5 weeks in case of haloperidol treated patients than risperidone treated patients, but blood urea, creatinine, Na, K and Cl levels insignificantly alter between haloperidol and risperidone treated patients after 5 weeks. However, at dosage 4 mg treated patients with haloperidol GOT enzyme, GPT enzyme, alk. phosphatase enzyme & bilirubin levels after 5 weeks of haloperidol treatments are slightly lower than risperidone treated patients, but blood urea, creatinine, Na, K and Cl levels are insignificantly alter between haloperidol and risperidone drugs treatments after 5 weeks. At dosage 5mg treated patients, the means test levels of GOT enzyme ,GPT enzyme , alk.phosphatase enzyme , bilirubin , blood urea, creatinine, K and Cl levels are significantly higher

in haloperidol treated patients than risperidone treated patients after 3 weeks, however, the levels of the said liver and kidney functions variables are comparatively decreased in both drugs treated groups after 5 weeks of treatments but the levels of both liver and kidney functions variables are higher in haloperidol treated patients than risperidone treated patients. Comparative data of means test values of GOT enzyme ,GPT enzyme ,alk.phosphatase enzyme & bilirubin shows the significantly decreased levels after 5 weeks in haloperidol (dosage10mg) treated patients than 3weeks treated patients.

Table (2) *illustrates cases negative symptoms of schizophrenia Profile, which improved with medication after 3 weeks.*

Dosage (after 3 weeks)			Negative symptoms of schizophrenia		Total
			Improved	unimproved	
4mg	type of drugs	Risperidal	1	----	1
	Total		1	----	1
2mg	type of drugs	Haldol	----	2	2
		Risperidal	----	1	1
	Total		----	3	3
Total	type of drugs	Haldol	0	2	2
		Risperidal	1	1	2
	Total		1	3	4

Chi-square (x^2) table

Df	Chi-Square (X^2)	P. Value
1	1.333	0.248

From the data analysis in table 2 it appears that the P. Value = 0.248 (24.8%) exhibits largest level of significance of 5%, and therefore we accept that there is

independence of effect between drugs, risperidal treatment has improved negative symptoms better than haloperidol treatment.

Table (3) *illustrates cases negative symptoms of schizophrenia*

Profile, which improved with medication after 5 weeks.

Dosage (after 5 weeks)			Negative symptoms of schizophrenia		Total
			improved	unimproved	
4mg	type of drugs	Risperidal	1	----	1
	Total		1	----	1
2mg	type of drugs	Haldol	1	1	2
		Risperidal	1	0	1
	Total		2	1	3
Total	type of drugs	Haldol	1	1	2
		Risperidal	2	0	2
	Total		3	1	4

Chi-square (x^2) table

Df	Chi-Square (X^2)	P. Value
1	**1.333**	**0.248**

From the data analysis in table 3 it appears that the P. Value = 0.248 (24.8%) exhibits largest level of significance of 5%, and therefore we accept that there is independence of effect between drugs, risperidal treatment has improved negative symptoms better than haloperidol treatment.

Table (4) *illustrates cases positive symptoms of schizophrenia Profile, which improved with medication after 3.*

Dosage			Positive symptoms of schizophrenia		Total
			improved	Unimproved	
4mg	type of drugs	Haldol	4	9	13
		Risperidal	4	10	14
	Total		8	19	27
5mg	type of drugs	Haldol	----	2	2
		Risperidal	----	1	1
	Total		----	3	3
2mg	type of drugs	Haldol	1	5	6
		Risperidal	2	6	8
	Total		3	11	14
10mg	type of drugs	Haldol	----	2	2
	Total		----	2	2
Total	type of drugs	Haldol	5	18	23
		Risperidal	6	17	23
	Total		11	35	46

Chi-square (x^2) table

Df	Chi-Square (X^2)	P. value
1	**0.119**	**0.730**

From the data analysis in table 4 it appears that the P. value = 0.730 (73.0%) exhibits largest level of significance of 5%, and therefore we accept that there is independence of effect between drugs , and both drugs have improved positive symptoms .

Table (5) *illustrates cases positive symptoms of schizophrenia Profile, which improved with medication after 5 weeks.*

Dosage			positive symptoms of schizophrenia		Total
			improved	unimproved	
4mg	type of drugs	Haldol	4	9	13
		Risperidal	5	9	14
	Total		9	18	27
5mg	type of drugs	Haldol	----	2	2
		Risperidal	----	1	1
	Total		----	3	3
2mg	type of drugs	Haldol	2	4	6
		Risperidal	4	4	8
	Total		6	8	14
10mg	type of drugs	Haldol	----	2	2
	Total		----	2	2
Total	type of drugs	Haldol	6	17	23
		Risperidal	9	14	23
	Total		15	31	46

Chi-square (x^2) table

Df	Chi-Square (X^2)	P. value
1	**0.890**	**0.345**

From the table 5 data analysis it appears that the P. value = 0.345 (34.5%) exhibits largest level of significance of 5%, and therefore we accept that there is independence of effect between drugs , and both drugs have improved positive symptoms.

Discussion:

The causes of schizophrenia are still unknown and treatments mainly focus on eliminating the symptoms of the disease. Treatments include antipsychotic medications and various psychosocial treatments. Antipsychotic medications have been available since the mid-1950's. The older types are called conventional, or "typical" antipsychotics. Some of the more commonly used typical medications include: Chlorpromazine (Thorazine), Haloperidol (Haldol) ,Perphenazine (Etrafon, Trilafon) ,Fluphenazine (Prolixin) etc. In the 1990's, new antipsychotic medications were developed. These new medications are called second generation, or "atypical" antipsychotics. One of these medications, clozapine (Clozaril) is an effective medication that treats psychotic symptoms, hallucinations, and breaks with reality, but clozapine can sometimes cause a serious problem called agranulocytosis, which is a loss of the white blood cells that help a person fight infection. This problem and the cost of blood tests make treatment expensive with clozapine difficult for many people. Other atypical antipsychotics were also developed that not cause agranulocytosis include: Risperidone (Risperdal), Olanzapine (Zyprexa), Quetiapine (Seroquel), Ziprasidone (Geodon), Aripiprazole (Abilify), Paliperidone (Invega) etc. Some people have side effects when they start taking these medications. Most side effects go away after a few days and often can be managed successfully. People who are taking antipsychotics should not drive until they adjust to their new medication. Side effects of many antipsychotics include: drowsiness, dizziness when changing positions, blurred vision, rapid heart beat ,sensitivity to the sun ,skin rashes, menstrual problems for women. Atypical antipsychotic medications can cause major weight gain and changes in a person's metabolism. This may increase a person's risk of getting diabetes and high cholesterol (Lieberman et al, 2005). A person's weight, glucose levels, and lipid levels should be monitored regularly by a doctor while taking an atypical antipsychotic medication. Typical antipsychotic medications can cause side effects related to physical movement, such as: rigidity, persistent muscle spasms, tremors, restlessness. In the present investigation, the comparison of the effects of

treatments of currently used atypical antipsychotic drug, risperidone with a conventional antipsychotic typical drug haloperidol on the liver enzymes and kidney function tests revealed that mean test values of enzymes and bilirubin at three weeks have higher than 5 week treatment in case of Haldol treated patients than Risperidal treated patients. It is also apparent from the mean test values of Na, K, Cl, blood urea and creatinine in Haldol and Risperidal drugs treated patients that there occurs no significant alteration on these kidney function test values after three and five weeks of treatments. Previous authors concluded that haloperidol induces a cholestatic form of injury8, 9 or primary liver damage and injury, to liver cells caused by cholostasis (Thomas, 1995; Dolle and Martini, 1984).

The comparative data of haloperidol and risperidone treatments (2mg, 4mg, 5mg and 10 mg per day) in schizophrenic patients revealed that compared to haloperidol, resperidone is most effective and efficacious for the treatment of " negative" and "positive" schizophrenic symptoms in patients taking dose of 4mg/ day after five weeks of treatment than three weeks and had no significant harmful effect on liver and kidney functions. We therefore hypothesized that treatment with risperidone would be superior to haloperidol in reducing the risk of relapse among outpatients with schizophrenia or schizoaffective disorder. These findings are consistent with earlier findings (Glick et al, 2001).

Conclusion

Schizophrenia is a chronic illness with a lifetime prevalence of significant numbers in Libya and with a serious physical, social and economic consequences. The economic burden of schizophrenia in society was estimated significantly much of cost due to the consequences of psychotic relapse. The course of schizophrenia varies, but most potent have a chronic cause with frequent relapse, typically characterized by exacerbation of psychosis and rehabilitation. Successive relapses can reduce the degree and next recession. To prevent relapse maintenance

treatment with an antipsychotic drug is obligatory for most patients who have schizophrenia or schizoaffective disorders. Nevertheless, long term outcomes have generally been disappointing. The currently available antipsychotic agents are not useful in all psychotic patients and many a times they cause serious neurological side effects. Some patients responding to them are left with serious neurological side effects. Some patients responding to them are left with serious disabilities. Such limitations have made psychiatrists to look for agents with better or at least or similar efficacy and with lesser side effects causing potential.

Comparative results of the effects on negative schizophrenic symptoms after giving the treatments of Haldol and Risperidal (doses- 2mg &4mg) to schizophrenic patients for three weeks and five weeks revealed that one patient treated with risperidol (dose -4mg) showed significantly absence of negative symptoms after three weeks of treatment , however, total three patients including one with Haldol(dose-2mg) and two with Risperidol (dose-2mg , 4mg) treatments showed significant improved negative symptoms in patients after five weeks .

Comparative results of the effects on positive schizophrenic symptoms after giving the treatments of Haldol and Risperidal (doses- 2 mg ,4mg,5 mg,10 mg) to schizophrenic patients for three weeks and five weeks revealed that total eleven patients including- six patients (4 cases with 4 mg dose & 2 cases with 2 mg dose) treated with Risperidol and five patients (4 cases with 4 mg dose & 1 case with 2 mg dose) showed significantly absence of positive symptoms after three weeks of treatments , however, total fifteen patients including six with Haldol (4 cases with 4 mg dose & 2 cases with 2 mg dose) and nine with Risperidol (5 cases with 4 mg dose & 4 cases with 2 mg dose) treatments showed significant improved positive symptoms in patients after five weeks.

Comparative data on the effects of Haldol and Risperidone treatments on the liver enzymes and kidney function tests revealed that in most of the findings mean test values of GOT enzyme, GPT enzyme, alkaline phosphatase enzyme and bilirubin at three weeks are higher than 5 week treatment in case of Haldol treated patients than Risperidone treated patients. It is also revealed from the mean test values of

Na, K, Cl, blood urea and creatinine in Haldol and Risperidone (2 mg, 4mg ,10 mg & 5mg of Risperidone) drugs treated patients that there is no significant alteration of these kidney function test values after three and five weeks of treatments. But, Haldol (5 mg) have changed in the mean test values (blood urea and creatinine) in three weeks and five weeks, but this change in the normal limit. It is apparent from the comparative data of haloperidol and risperidone treatments in schizophrenic patients that compared to haloperidol, risperidone had superior improvement of negative and positive symptoms of patients, no harmful effect on liver and kidney functions and greater efficacy and faster recovery from schizophrenic symptoms in patients. On the basis of our findings of the present study, we concluded that treatment with risperidone is superior to haloperidol in reducing the risk of relapse among outpatients with schizophrenic disorders.

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