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Effectiveness of Dose of Drug Applied for the Treatment of Depression

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Abstract- Depression as a disease is rampart to people regardless of sex, class, position in the community and it is common to old people and adult. In order to prevent and reduce the rate of depression, this research give work has born. It was born out of a mindset that is ready to the economy everything the community had given. This paper examined the effect of hormone related drug in relieving depression and 3 level of drug was administered, a placebo treatment, a moderate dose and a high dose. The data was collected from Ekiti-State Police Clinic, the data are in quarters for the year 2012 and it is a secondary data. The aim of the paper is to find out whether gender or level of dose of drug administered has anything to do with the relieving of depression. Based on the analysis it can be seen that either high level of dose, placebo treatment or moderate dose we obtain averagely the same of outcome but there other method used for treatment of depression that will not make the drug to work. And also gender does not have anything to do with the relive of depression.

Index Terms- Depression, Placebo, Drug, Treatment

I. INTRODUCTION

Depression is the common cold of metal disorder- most people be affected by depressed in their lives either directly or indirectly, through a friend or family member. Depression is not a disease of people in developed countries, but is a worldwide phenomenon.

Depression is a medical illness that causes a constant feeling of sadness and lack of interest. Depression affect how the person feels, behaves and thinks, World Health Organization (WHO 2012) estimated that about 350 million people worldwide suffer from depression. According to a study supported by WHO, in (2012) in any community, almost 5% of the resident have suffered from depression and many of the victims do not recognize their illness and not seek treatment. This disease occurs in both sexes and between the poor and the rich. It is theorized that men express their depressive feelings in more external ways that often don't get diagnosed as depression.

The causes of depression can point to cardiovascular disease, economic pressures, unemployment, disasters or conflicts. In the United States, depressions affect 2% of grade school kids and about one in 10 teenagers. It interferes with the ability to play, make friends, and complete school.

Depression is a severe disorder, and one that can often go undetected in some peoples' lives because it can creep up on you. Depression doesn't need to strike all at once, it can be gradual and nearly unnoticeable withdrawal from your active life and enjoyment of living or it can be caused by a clear event, such as break up of a long-term relationship, a divorce, family problems (Grohol, J. 2006).

Depressive disorders are common, chronic and costly lifetime prevalence levels from community-based surveys range from 4.9% to 17.1% (mike 2002).

Longitudinal studies suggest that about 80% of individuals experiencing a major depressive episode will have at least 1 more episode during their lifetime, with the rate of reoccurrence even higher if minor episodes are included. Approximately 12%of patients who experience will have a chronic, unremitting course (cynthia 2003).

The burden of suffering from depression is substantial suicide, the most severe of depressive sequelea, has a rate of approximately 3.5% among all cases with major depression, a risk that increase to approximately 15% in people who have required psychiatric hospitalization. The specific risk for suicide associated with depressive disorders is elevated 12 to20 fold compared to the general population(cynithia 2003)

The World Health Organization (WHO), identified major depression as the fourth leading causes of worldwide disease burden in 1990, causing more disability than either ischemic heart disease or cerebrovascular disease. Its associated morbidity is expected to increase, unipolar depressive illness is projected to be the second leading cause of disability worldwide in 2020.

Prevalence and Comorbidty of Depression in Dementia

Depressive symptom is very common in mild cognitive impairment and across the various types of dementia. The reported prevalence of depression in older patients with dementia ranges from 30 to 96% (Amore et.al 2007) and moderate to high rates of depression or its symptoms are consistently reported for persons with mild cognitive impairment.

Comorbidity of depression in older persons with mild cognitive impairment has been associated with greater impairments in activities of daily living (Teri et.al 2009). Likewise, increasing cognitive impairment appears to interact with the presence of depressive symptom to further impair functional performance. The presence of depression in cognitively impaired persons also appears to increase the level of other BPSD. Comorbid depression and dementia are associated with higher rates of institutionalization of older adults, likely due to negative impact on ceregivers (Black & Almeida, 2004: Potter & Steffens, 2007). Untreated depression has also related to higher treatment costs for persons with dementia (Hemels, Lanctot, Iskedjian & Einarson, 2011).

II. Placebo Response in Depression

Placebo controlled trials are appropriate when there is no existing treatment for a disorder, otherwise comparison trials are indicated. No new treatments should be introduced into medicine unless they have been shown, in randomized controlled trials to be superior to existing treatments or equivalent to existing treatments but cheaper or safer (Briks, 2006). In depression, new drugs are advertised as being superior to placebo even though, to gain regulatory approval, most are also tested against existing treatments. Doctors are not routinely provided with this information on comparative efficacy, effectiveness, safety and cost. The propriety of doing placebo controlled trials in depressions was the topic of a recent article (Khan et al, 2000) and one of the conclusions was that the size of response in the placebo group was sufficient to justify continuing with placebo controlled trials, even though the existence of proven treatments would normally render placebo trials unethical. Sometimes antidepressants drugs, and for that matter cognitive-behavioral therapies, fail to show superiority over placebo, simply because the treatments are not very powerful compared with change in the placebo group the placebo effect proper, which arises from the sensitivity of patients to the encouragement that comes from being treated, plus improvement due to the natural history of remission and fluctuating symptom levels in the disorder. Kirsch & Sapirtein (2005) identified 19 placebo controlled trials of antidepressants that reported data on the progress of the placebo group. The placebo groups averaged a 1.5 standard deviation (s.d) units of improvement, 75% of overall progress shown by the drug groups, whose superiority over groups was only 0.5 s.d. others had noted that the size of the progress attributed to the placebo group in depression trials was greater than the additional progress attributed to the drugs, so the findings is not new. What was new was that the correlation of 0.9 between the placebo effect and drug effect indicated that virtually all the variation between the improvement in the drug- treated groups in the different trials could be predicted by the response in the subjects randomized to the placebo groups. Discussants to the Kirsch & Sapirstein paper argued that it was a sampling phenomenon, and that the overall change depended on the sensitivity to non-specific factors of the whole pool of subjects, whether they were randomized to the placebo or drug group. Kirsch & sapirstein used data from additional studies to separate the change in the placebo groups into change due to the placebo effect and change due to natural history. Their final conclusion was that one-quarter of the improvement observed in the drug-treated group was due to the active medication, one-quarter to natural history and half to the placebo effect. They then raised the possibility that the improvement attributed to the drug could even be a non-specific response to the side-effects generated by the medication. Moncrierf et al (2008), in a small mata analysis of nine studies, addressed this and found that the superiority of drug over the active placebo atropine was reduced from an effect size of 0.50 in non-active placebos, consistent with the kirsch & sapirstein suggested people in trials respond more positively if they experience side effects.

III. Background to the Analysis

Complete Randomized Block Design with Interraction

Complete randomized block design utilizes experimental units that are matched sets, assigning one from each set treatment. The matched sets of experimental units are called blocks. The concept of the complete randomized block design is that the sampling variability of the experimental units in each block will be reduced

The word in interaction has a very specific meaning in the context of (CBRD) We say there is interaction if Y depends on factor A differently for different values of factor B, and vice versa. Similarly, there is no interaction if Y depends on factor A in the same way for all values of factor B, and vice versa.(Hinkle Mann and Kempthrone 2008).

This analysis is used when there are two or more fixed-effect factors. Usually the aim is to see whether these interaction.

This experiment takes consideration of the different in experiment materials in the course of experimentation. It is a two-way classification model with interaction, designed to control extraneous source of variation. Present here are two qualitative independent variables namely: Block and Treatment. This analysis is used when there are two or more fixed-effect factors. Usually the aim is to see whether these interaction.

Data Arrangement of Complete Randomized Block Design With Interaction

FACTOR A

Source of variation	**Degree of freedom**	**Sum of square**	**Mean of square**	**F ratio**
Treatment	t-1	SStr	SStr/t-1	MSTr/MSE
Blocks	b-1	SSb	SSb/b-1	MSB/MSE
Interaction	(t-1)(b-1)	SS(t×b)	$SSb\times t/(t-_1)(_{b-1})$	MSt×t/MSE
Error	By difference	SSE		
Total	nbt-1	SST		

FACTOR B

Treatment			B
1	2		B
y111 y121 …. y11	y121 y122 ….. y12n		y1b1 y1b2 …. y1b2
y211 y212 ….. y21n	y221 y222 ….. y22n		y2b y2b2 …. y2bn
ya12 ya12 ….. ya12	ya21 ya22 …. Ya2n		yab1 yab2 …. Yabn

Statistical Model

$Y_{ijk}= \mu+\tau_i+\beta_j+(\tau\beta)_{ij}+e_{ijk}$

For i= 1,2,..t, j=1,2,…b, k=1,2,..n., μ= represent overall mean, τ_i= represent the treatment effect of the row. β_j=represent the effect of the jth column, $(\tau\beta)ij$= represent the interaction effect, e_{ijk}= represent the error . Where y_{ijk} is the kth observation at the ith level of A and jth level of B and is the error term.

Anova Table for a Complete Randomized Block Design With Interaction

Hypothesis Testing

An appropriate null hypothesis against alternate hypothesis always set for each term in which represent an experimental effect.

The three(3) hypothesis to be tested are

Effect of Treatment

Ho: τi=0 for every i (effect of treatment is not significant)

Hi: τi≠0 for at least one i (effect of treatment is significant)

Effect of Block

Ho: β_j=0 for every j(effect of block is not significant)

Hi: β_j=0 for at least one j(effect of is significant)

Effect of interaction
Ho: $(\tau\beta)_{ij}=0$ for every ij (interaction effect is not significant)
Hi: $(\tau\beta)_{ij}=0$ for at least $_{ij}$(interaction effect is significant).

Critical Region and Decision Rule

Based on the table above the condition for accepting and rejecting the hypothesis are: Reject Ho: if the significant value is lesser than the α value (0.05) and hence otherwise.

IV. Result of Analysis

ANALYSIS FOR THE FIRST QUARTER

Levene's Test of Equality of Error Variances[a]

Dependent Variable:response to the drug

F	df1	df2	Sig.
.886	5	12	.519

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

Design: Intercept + dose * gender + dose + gender
Test of equality of variance
Since sig-value > p-value i.e 0.519 > 0.05 We have no sufficient reason to reject

Tests of Between-Subjects Effects

Dependent Variable:response to the drug

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	409.833[a]	5	81.967	19.413	.000
Intercept	15312.500	1	15312.500	3626.645	.000
dose * gender	27.444	2	13.722	3.250	.074
Dose	366.333	2	183.167	43.382	.000
Gender	16.056	1	16.056	3.803	.075
Error	50.667	12	4.222		
Total	15773.000	18			
Corrected Total	460.500	17			

Test of difference value to drug

Since sig- value < p- value i.e 0.000 < 0.05, we reject the null hypothesis. Conclusion: There is significant difference effect in the response on the level of dose of drug applied to the depressed patient.

Test of interaction

Since sig-value > p- value i.e 0.74 > 0.05, we have no sufficient reason to reject null hypothesis. Conclusion: There is no significant interaction between the drug and gender of the depressed patient.

Tests of Between-Subjects Effects

Dependent Variable:response to the drug

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	409.833[a]	5	81.967	19.413	.000
Intercept	15312.500	1	15312.500	3626.645	.000
dose * gender	27.444	2	13.722	3.250	.074
Dose	366.333	2	183.167	43.382	.000
Gender	16.056	1	16.056	3.803	.075
Error	50.667	12	4.222		
Total	15773.000	18			
Corrected Total	460.500	17			

Test of difference value to gender

Since sig-value > p-value i.e 0.75 > 0.05, we have no sufficient reason to reject null hypothesis

Conclusion: Gender has no effect no the cure of depression.ANALYSIS FOR THE SECOND QUARTER

Levene's Test of Equality of Error Variances[a]

Dependent Variable:response to the drug

F	df1	df2	Sig.
.707	5	12	.629

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + dose * gender + dose + gender

b.

Test of equality of variance

Since sig-value > p- value i.e 0.629 > 0.05, we have no sufficient reason to reject.

Conclusion: The variance are equal

Tests of Between-Subjects Effects

Dependent Variable:response to the drug

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	316.278[a]	5	63.256	9.988	.001
Intercept	14506.722	1	14506.722	2290.535	.000
doze * gender	21.000	2	10.500	1.658	.231
Dose	294.778	2	147.389	23.272	.000
Gender	.500	1	.500	.079	.784
Error	76.000	12	6.333		
Total	14899.000	18			
Corrected Total	392.278	17			

Tests of Between-Subjects Effects

Dependent Variable:response to the drug

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	316.278[a]	5	63.256	9.988	.001
Intercept	14506.722	1	14506.722	2290.535	.000
doze * gender	21.000	2	10.500	1.658	.231
Dose	294.778	2	147.389	23.272	.000
Gender	.500	1	.500	.079	.784
Error	76.000	12	6.333		
Total	14899.000	18			
Corrected Total	392.278	17			

a. R Squared = .806 (Adjusted R Squared = .726)

Test of difference value to drug

Since sig-value < p-value i.e 0.000 <0.05, we reject null hypothesis. Conclusion: There is significant difference effect in the response on the level of dose of drug applied to the depressed patient.

Test of interaction

Since sig-value > p-value i.e 0.231 > 0.05, we have no sufficient reason to reject null hypothesis
Conclusions: There is no significant difference interaction between the drug and gender of the depressed patient.

Test of difference value to gender

Since sig-value > p-value i.e 0.784 > 0.05, we have no sufficient reason to reject null hypothesis
Conclusions: Gender has no effect on the cure of depression.

Response to the drug

	level of doze	N	Subset 1	Subset 2
Tukey HSD[a,,b]	moderate dose	6	22.6667	
	high dose	6		31.1667
	Placebo	6		31.3333
	Sig.		1.000	.993
Duncan[a,,b]	moderate dose	6	22.6667	
	high dose	6		31.1667
	Placebo	6		31.3333
	Sig.		1.000	.911

Means for groups in homogeneous subsets are displayed.
Based on observed means.
The error term is Mean Square(Error) = 6.333.

a. Uses Harmonic Mean Sample Size = 6.000.

ANALYSIS FOR THE 3RD QUARTER

Levene's Test of Equality of Error Variances[a]

Dependent Variable:RESPONSE TO TREATMENT

F	df1	df2	Sig.
1.605	5	12	.232

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + GENDER * DOSE + GENDER + DOSE

Since sig-value > p-value i.e0.232 > 0.05, we have no sufficient reason to reject
Conclusion: The variance are equal.

Dependent Variable:RESPONSE TO TREATMENT

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	223.167[a]	5	44.633	4.206	.019
Intercept	13612.500	1	13612.500	1282.853	.000
GENDER * DOSE	8.333	2	4.167	.393	.684
GENDER	.500	1	.500	.047	.832
DOSE	214.333	2	107.167	10.099	.003
Error	127.333	12	10.611		
Total	13963.000	18			
Corrected Total	350.500	17			

a. R Squared = .637 (Adjusted R Squared = .485)

Test of difference value to drug

a. R Squared = .637 (Adjusted R Squared = .485)

Test of difference value to drug

Since sig-value < p-value i.e 0.03< 0.05, we reject null hypothesis

Conclusion: There is significant difference effect in the response on the level of dose of drug applied to the depressed patient.

Test of interaction

Since sig-value > p-value i.e 0.684 > 0.05, we have no sufficient reason to reject null hypothesis

Conclusions: There is no significant difference interaction between the drug and gender of the depressed patient.

Test of difference value to gender

Since sig-value > p-value i.e 0.832 > 0.05, we have no sufficient reason to reject null hypothesis

Conclusions: Gender has no effect on the cure of depression.

RESPONSE TO TREATMENT

			Subset	
	DOSE	N	1	2
Tukey HSD[a,,b]	MODERATE DOSE	6	22.6667	
	PLACEBO	6		29.3333
	HIGH DOSE	6		30.5000
	Sig.		1.000	.812

Means for groups in homogeneous subsets are displayed.
Based on observed means.
The error term is Mean Square(Error) = 10.611.

a. Uses Harmonic Mean Sample Size = 6.000.

b. Alpha = .05.

ANALYSIS FOR THE FOURTH QUARTER

Levene's Test of Equality of Error Variances[a]

Dependent Variable:RESPONSE TO TREATMENT

F	df1	df2	Sig.
1.304	5	12	.326

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + GENDER * DOSE + GENDER + DOSE

Tests of Between-Subjects Effects

Dependent Variable:RESPONSE TO TREATMENT

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	302.944[a]	5	60.589	15.147	.000
Intercept	13068.056	1	13068.056	3267.014	.000
GENDER * DOSE	5.444	2	2.722	.681	.525
GENDER	.056	1	.056	.014	.908
DOSE	297.444	2	148.722	37.181	.000
Error	48.000	12	4.000		
Total	13419.000	18			
Corrected Total	350.944	17			

a. Squared = .863 (Adjusted R Squared = .806)

Test of difference value to drug

Since sig-value < p-value i.e 0.00< 0.05, we reject null hypothesis

Conclusion: There is significant difference effect in the response on the level of dose of drug applied to the depressed patient.

Test of interaction

Since sig-value > p-value i.e 0.525 > 0.05, we have no sufficient reason to reject null hypothesis

Conclusions: There is no significant difference interaction between the drug and gender of the depressed patient.

RESPONSE TO TREATMENT

			Subset	
	DOSE	N	1	2
Tukey HSD[a,,b]	MODERATE DOSE	6	21.3333	
	HIGH DOSE	6		28.6667
	PLACEBO	6		30.8333
	Sig.		1.000	.188

Means for groups in homogeneous subsets are displayed.
Based on observed means. The error term is Mean Square(Error) = 4.000.

a. Uses Harmonic Mean Sample Size = 6.000.

b. Alpha = .05.

The levene's test uphold the assumption of equality of variance which enable us to proceed to the Analysis of Variance (ANOVA). For the first quarter it can be seen that there is significant difference in the response to the level of dose but there is no significant difference in the gender and the interaction between gender and dose of drug applied. Further test were carried out using multiple comparison test and in particular Tukey's test and it can be seen that there significant difference between the moderate level of dose and the other two levels but there is no significant difference in the placebo dose and the high dose. From the second quarter it can be seen from the second quarter that every observation of the first quarter is the same as the second quarter and hence there is no significant difference in the gender and interaction between gender and level of dose. Also it can be seen that there is significant difference in the level of dose. Thus further analysis was done using multiple comparisons and especially the Tukey's test and it can also be seen that there is no significant difference between the placebo treatment and high level of dose but there is significant difference between the two level of dose and the moderate level of dose. From the third quarter it can be seen that every observation of the first quarter is the same as the second quarter and the third quarter and hence there is no significant difference in the gender and interaction between gender and level of dose. Also it can be seen that there is significant difference in the level of dose. Thus further analysis was done using multiple comparisons and especially the Tukey's test and it can also be seen that there is no significant difference between the placebo treatment and high level of dose but there is significant difference between the two level of dose and the moderate level of dose.

Finally, from the fourth quarter it can be seen that every observation of the first quarter is the same as the second quarter, third quarter and the fourth quarter and hence there is no significant difference in the gender and interaction between gender and level of dose. Also it can be seen that there is significant difference in the level of dose. Thus further analysis was done using multiple comparisons and especially the Tukey's test and it can also be seen that there is no significant difference between the placebo treatment and high level of dose but there is significant difference between the two level of dose and the moderate level of dose. We can therefore conclude that either high level of dose or placebo treatment we will obtain averagely the same level of outcome because if the patient given moderate dose , high dose of drug does or placebo treatment does not change is mindset or mood the drug may not work . Depression rate doesn't depends in series hence either male or female depression is real enough concentration should be given more to eradicate depression. Depression requires higher dose of therapy so as to relieve people of depressed mind.

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