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Meta-Analysis of Quality of Life Constructs in Antihypertensive Drug Therapies

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Abstract: Objectives : It is usually accepted that some of the treatments affect not only the survival times but as well the quality of life of patients. The aim of study is to reach more reliable conclusions by using the meta-analysis method on published studies which deal with the effects of antihypertensive therapies on the quality of life of patients.

Material and Methods : Meta-analysis is used to combine the results of different experiments or studies examining the same question. Meta-analysis is a systematic reviewing strategy for addressing research question that is especially useful when results from several studies disagree with regard to magnitude or direction of the effect, when sample sizes are small to detect an effect and label it statistically significant, or when a large trial is too costly and time consuming to perform. The effect size, *d*, is the difference between the means in standard score form ,i.e., the ratio of the difference between the means to the standard deviation.

Results : When quality of life is considered meta-analysis results showed, except sexual function, positive effect sizes for sleep, general well-being and psychomotor scores (ave(*d*)=-0.03; ave (*d*)=0.11; ave (*d*)=0.135; ave (*d*)=0.40 Standard Deviations, respectively). When the effect of drug groups on the

recovery of patients are studied ave (*d*) is found to be 0.17 for ACEI ($p>0.05$) and 0.20 SD ($p>0.05$) for BETA. When the effect of ACEI drug group on psychomotor scores of patients is considered, Meta-analysis results yielded a mean effect size of 0.50 SD ($p<0.01$). The mean effect size was 0.40 SD for BETA drug group ($p<0.01$). The effect of BETA drug group on sexual function scores was the smallest effect (ave (*d*)=-0.103 ; $p>0.05$).

Conclusions : Among all of the applied meta-analysis, none of the drug groups showed negative effects. Meta-analysis results when quality of life is considered showed, except sexual function positive effect sizes for sleep, general well-being and psychomotor scores (ave (*d*)=-0.03; ave (*d*)=0.11; ave (*d*)=0.135; ave (*d*)=0.40 Standard Deviation, respectively). Different drug groups have different effect sizes on the dimensions of quality of life of patients. Therefore, as well as this study, all other studies in this field meta-analysis which use , will help researchers to choose the best strategy on deciding the type of the drug.

Key Words: Meta-analysis, Antihypertensive Drug Therapy , Hypertension , Quality of life, Clinical Trials

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Introduction

It is usually accepted that some of the treatments effect not only the survival times, but as well, the quality of life of patients. For this reason , in the selection of the treatment, its effects on the quality of life of patients should also be taken into account (1). As an example hypertension, is a kind of disease which is sometimes asymptomatic or shows mild symptoms which does not have adverse effects on the life of patients. By means of antihypertensive treatments, the aim is not only to remove the symptoms but to avoid some possible complications that may occur in future as well. Since such treatments last too long, it is noted that nearly 50% of the patients drop out the treatment and only 30% of the patients obey the rules of the treatment with recom-

mended dosage and duration, which leads to failure to achieve success by means of the treatments. Some of the researchers indicate that, this is majorly due to the adverse effects of the treatment on the quality of life of patients. Therefore in the assessment of the success of many kinds of treatments, their role on the quality of life of patients started to gain importance in recent years (1).

The studies which deal with this topic are neither too much nor use adequate number of subjects, thus yielding results which are not very reliable and may produce incorrect results. This may primarily due to the subjects included in the studies have different characteristics . Meta-analysis brings these small or medium sized researchs together to produce more exact results and tries to explore the effects of different characteristics of subject

used in different studies on the quality of life of patients (2).

The aim of this study is to reach more reliable conclusions by using the meta-analysis method on published studies, which deal with the effects of antihypertensive drug therapies on the quality of life of patients.

Materials and Methods

Meta – Analysis : Meta-analysis is used to combine the results of different experiments or studies examining the same question (2,3,4,5,6,7). Meta-analysis is a systematic reviewing strategy for addressing research questions, that is especially useful when results from several studies disagree with regard to magnitude or direction of effect, when sample sizes are small to detect an effect and label it statistically significant, or when a large trial is too costly and time consuming to perform (4,8,9,10).

It's important to state the objectives of the meta-analysis at the beginning. First the goals of the meta-analysis should be formulated. The second step is the literature search in which the relevant published studies are gathered. Literature search can be made either by using computers or manually. However some researchers are in favor of manual research which will be conducted by a professional librarian. Studies are chosen for meta-analysis on the basis of inclusion and exclusion criteria. In order to reduce bias, the inclusion of studies should be based on predetermined criteria. The inclusion criteria may deal with study design, sample size, type of experimental and control therapies and the outcome of interest. The forth step is the data collection phase. It is probable that the results of the same study may be published in different articles with slight changes. The user, therefore, should be very careful and should not handle these articles as different studies (2,3,8).

There are different types of meta-analysis . For significance levels (p-values), correlation coefficients, ODDS ratios or relative risks and effect sizes (d-indices) different meta-analysis methods are used (2).

d-Index : The effect size, d , is the difference between the means in standard score, i.e., the ratio of the difference between the means to the standard deviation which is the pooled standard deviation used in analysis of variance. Generally, d-index is used when independent or dependent groups would be compared (2,5,11).

Cohen's classification for d-index is as following (11) ;

- d = 0.20 SD Small Effect Size
- d = 0.50 SD Medium Effect Size

d = 0.80 SD Large Effect Size

In different study designs, different formulations of d-index are used.

The d-index, in case of two independent groups is computed by (2) ;

$$d = (Y_E - Y_C) / S_w$$

Where ;

- Y_E = The mean of experimental group
- Y_C = The mean of control group
- S_w = The pooled standard deviation

In case of repeated measures design, the d-index (2) ;

$$d = [Ave(Y_2) - Ave(Y_1)] / SD$$

Where ;

- Ave(Y₂) : The mean of posttest values
- Ave(Y₁) : The mean of pretest values
- SD : The standard deviation and If SD(Y₂)=SD(Y₁)=SD

If SD(Y₂)≠SD(Y₁) then the mean of the two standard deviation is taken as SD.

The significance of d-index is tested with $t = [d / (N)^{1/2}] / 2$. The calculated t value is compared with the tabulated t value with (N-1) degrees of freedom and with α error probability (N is the total sample size) (2).

Bare-Bones Meta-Analysis : In this study Bare-bones meta-analysis, developed by J.E.Hunter and F.L.Schmidt, for the analysis of the effect sizes of group means (d-index) is used (2). This analysis allows a correction for sampling errors.

The average d-index in this type of meta-analysis is ;

$$Ave(d) = \sum W_i d_i / \sum W_i$$

Where ;

- W_i = The sample size of the i th study
- d_i = The d-index of the i th study

The correspondingly weighted variance of d-index is;

$$Var(d) = \sum W_i [d_i - Ave(d)]^2 / \sum W_i$$

The average sampling error variance is ;

$$Var(e) = \{ (N-1) / (N-3) \} \{ (4 / N) (1+Ave(d)^2 / 8) \}$$

Where ;

$$N = \sum W_i / K$$

W_i = The sample size of the i th study

K = The number of studies included in meta-analysis

Quality of Life Dimension :

I. Physical construct (sleep , sexual function)

II. Intellectual construct (Psychomotor)

III. Emotional (General well-being)

Inclusion of Studies to Meta – Analysis

Source of Data : Data for inclusion in the meta-analysis were identified through a medline search of literature from 1985 to 1992 by using “ quality of life, clinical trials, hypertension, antihypertensive therapy “ as keywords. No Turkish study could be found in this search.

Inclusion and Exclusion Criteria : Randomized single or double blind clinical trials which present the required quality of life parameters and type of antihypertensive drugs are included to the study (Table 1 and Table 2).

Table 1: The Studies Included In Meta-Analysis

Study	Reference No	Drug Group *
Blumenthal et.al. 1988	12	BETA
Blumenthal et al.1990	13	BETA,ACEI
Croog et al. 1986	14	ACEI, BETA
Croog et al. 1990	15	ACEI,BETA
Fletcher et al. 1990	16	ACEI,BETA
Goldstein et al.1990	17	BETA
Kales et al. 1988	18	BETA

* BETA ; β -blocker

ACEI ; angiotensin converting enzyme inhibitor

Results

Table 2 displays the patient characteristics and study design of 7 published articles in which 9 drugs among 2 pharmacological drug groups were used.

In this study physical (sexual function, sleep), intellectual (psychomotor) and emotional (general well-being) dimension of quality of life are evaluated. Other dimension such as social construct (life satisfaction, social participation and working performance) is not included due to the lack of sufficient data. For each study, effect size in repeated measures (d-index) is calculated by using Hunter and Schmidt bare-bones meta-analysis which is

defined by dividing the average change between the pre and post treatment values by the average of the standart deviation.

As a result, psychomotor construct is found to be the factor which has the greatest effect, according to Cohen's

Table 2: The Distiributon of Studies by quality of life construct and drug group *

Grouping Factor	Study (K)	Total Sample Size
All Studies	7	1407
By Construct		
General-Well Being	4	822
Sleep	5	828
Psychomotor	6	1368
Sexual Function	4	822
By Drug Group		
ACEI	5	357
BETA	5	325

* Studies which include the above constructs

effect size classification (Ave(d)=0.40 SD) (11). It was also concluded that sexual function had no positive effect and the baseline scores were better.

Therapy Effect by Quality of life Construct :

When the d-values related to “ General-well being “ from different studies are tested for significance, it was observed that none of them were statistically significant ($p>0.05$). After meta-analysis, however, the average effect size was found as 0.135 SD and this value is statistically significant ($p<0.05$). When sleep construct is considered , neither the effect size of individual studies, nor the average effect size (Ave(d)=0.11 SD) calculated by meta-analysis, were found to be significant. In case of psychomotor construct, one of the studies reported a highly significant result ($p<0.01$), three studies reported significant results ($p<0.05$), and the rest failed to find a significant difference. When meta-analysis is applied to all of these studies, the average effect size was 0.40 SD, which is a very significant result ($p<0.01$).

When sex scores are examined, none of the individual studies reported significant differences ($p>0.05$). These results also agree with that of the meta-analysis result, from which the average effect size was - 0.03 SD, which is a very small negative value, indicating a nonsignificant effect ($p>0.05$).

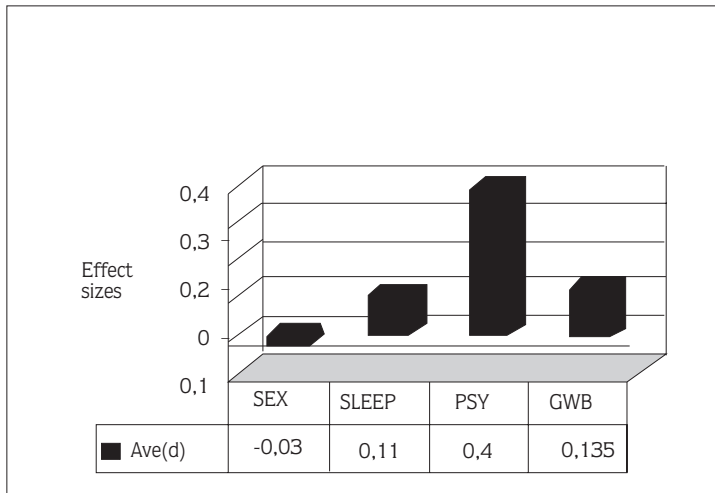


Figure 1. Treatment Effect Sizes by Quality of Life Constructs

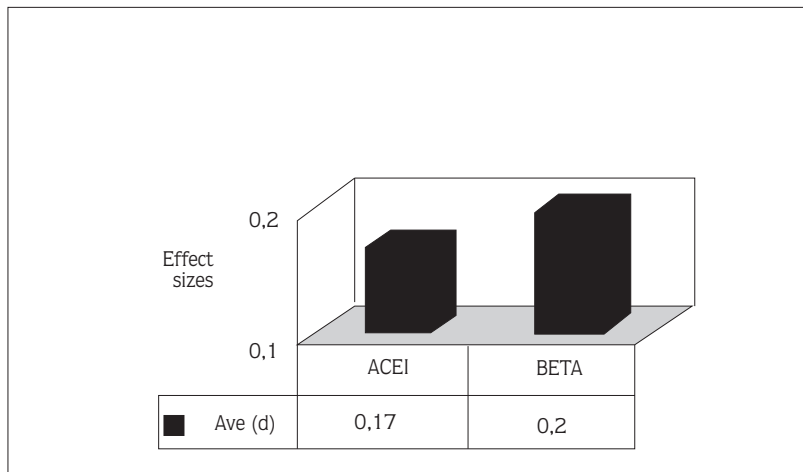


Figure 2. Treatment Effect Sizes By Drug Groups

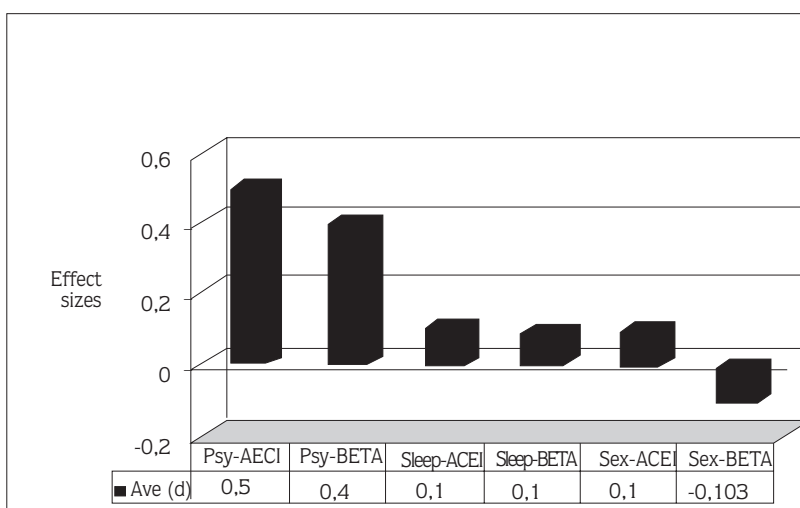


Figure 3. Treatment Effect Sizes by Drug Groups and Quality of Life

Therapy Effect by Drug Groups :

When the quality of life scores of patients before and after the therapy were studied for ACEI and BETA groups, average effect sizes were 0.17 SD ($p>0.05$), and 0.20 SD ($p>0.05$) respectively. These are classified as having small effect sizes (11).

Therapy Effect by Quality of Life Construct and Drug Groups :

When the effect of ACEI group drugs on the psychomotor scores of patients were evaluated in different studies, it was observed that two studies yielded highly significant results ($p<0.01$) and two studies nonsignificant results ($p>0.05$). However, when meta-analysis was conducted on these studies, the results was also significant with an effect size of 0.50 SD and an average effect according to Cohen's classification. For the BETA group , only one study reported significant, other studies reported nonsignificant results. Meta-analysis on this drug groups showed significant effect (Ave(d)=0.40 SD).

Both the individual studies and meta-analysis revealed that the BETA type drugs produced the smallest effect on sexual function scores (Ave(d)= - 0.103 ; $p>0.05$), and this led us to conclude that the sexual function scores of patients were higher (better) before the treatment.

Discussion

Although the side effects of antihypertensive drugs were clearly defined by many researchers , their effects in quality of life was not so explicit (19). For this reason , the need for meta-analysis is obvious.

Beto and Bansal (19) used the meta-analysis techniques derived by Hedges and Olkin .

In this study , Hunter and Schmidt's meta-analytic methods were used and the results were compared with the above mentioned method .

Our results agreed with Beto and Bansal's, in the sense that, both concluded psychomotor construct had the highest effect . However , the effect size found in this study was slightly higher (0.43 SD v.s. 0.283 SD). Non significant effect sizes for two drug groups also agree with Beto and Bansal's findings .

In both studies , when both drug groups evaluated together only sexual function construct had a negative effect size . The same was also observed in BETA drug group.

We expect , these meta-analysis results will be helpful to the researchers in their future antihypertensive clinical studies.

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