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Evidence on Prevalence, Age and Sex Differences in Tardive Dyskinesia

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R N Sahu ,

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- *Department of Psychiatry, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*
Sanjeev Sarmukaddam, - *Society for Education, Action and Research in Community Health, P. O. District Gadchiroli, Maharashtra*

Abstract

In order to derive comprehensive conclusions, it is essential to combine the information provided by several indepedent studies. In case of independent tests of significance, sometimes it happens that few or none can be claimed individually as significant, yet the aggregate gives the impression that the probabilities are on the whole, lower than otherwise would have occurred by chance. To combine the evidences regrading Tardive Dyskinesia (TD) prevalence, sex and age differences, four methods reviewed in this paper have been used. We conclude that TD prevalence is more in females and old age ($p<0.001$), although any acceptable figure could not be arrived at.

Key words -
Combining results,
Tardive dyskinesia,
Prevalence
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Number of studies on prevalence of Tardive Dyskinesia (TD) and related variables are reported in the literature. It is difficult to draw any conclusion on the basis of available studies since these studies have applied different criteria for the diagnosis of TD and have reported vastly different prevalence retes, ranging from 0.5% to over 60% [1], [2]. Most of the articles reviewing these studies have not attempted to combine the results to reach any acceptable, most probable conclusion to resolve the controversies, at least to some extent.

It is often not feasible or even appropriate to consider reanalyzing the original raw data from several studies in a single overall analysis. But there are number of statistical methods to combine the results from several independent studies in order to reach one comprehensive conclusion. In this paper, four such methods are briefly reviewed and an attempt is made to combine the evidences on prevalence of TD, and sex and age differences from several studies. This might provide clearer understanding about the sex and age differences in prevalence of TD.

Material and Methods

Evidences of TD prevalence, sex differences and age differences have been combined from 39, 28 and 10 studies respectively. Results of thirty nine studies for prevalence rates and few others are taken from a review article [2]. Three hypotheses, for which the results are combined are -
(i) whether prevalence of TD is consistent across the studies with change in the time period;
(ii) whether TD prevalence is same for both the sexes and
(iii) whether TD prevalence is same in young and old age groups.

To test the first hypothesis, weighted prevalence rates for different time periods are calculated and hypothesis of equivalence with the rate is tested in all the studies independently with Z test. To test other two hypothesis against one sided alternatives, that TD prevalence is more in females and old age group, again Z test is used.

To combine these results provided by several independent studies in order to reach one comprehensive conclusion, the following four methods are used.

1.Adding Zi's

Since the sum of normal deviates is again a normal deviate with variance equal to the number of observations summed (K), we can use the test statistic as $Z=\Sigma Zi / (K)^{½}$

(Note: If the test statistic used in studies are other than Z, transform the corresponding p-values to standard normal deviates).

2.Adding weighted Zi's

We can weight each standard normal deviate by the size of the sample on which it is based or by any other desirable positive weighting. If we use sample sizes (ni) as weights, The test statistic will be

$Zwt=\Sigma niZi / (\Sigma ni^2)^{½}$.

3.Testing the mean Z

Mosteller and Bush [3] have suggested to compute a t-test on the mean value obtained, with the degrees-of-freedom for t equal to the number of studies to be combined, minus one.

$tk-1=[\Sigma Zi / K] / S.D.(Z)/(K)^{½}$

4.Chi-square test

Rosenthal and Rubin [4] have suggested the use of

$\chi^2 k-1=\Sigma (Zi -Z)^2$

to test the consistency of results across studies.

Several other methods for combining the results from independent studies were critically reviewed by one of the authors elsewhere [5].

Results and Discussion

Table 1 - Period specific weight prevalence rates of TD

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Table 2 - Pervalence of TD in various studies by sex

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N: Number of patients

$Z = 9.072$, $P < 0.001$

$Zwt = 9.133$, $P < 0.001$

$tk\text{-}1 = 5.646$, $P < 0.001$

Σ^2 k-l=74.890 $P < 0.001$

Negative Zi value indicates that pervalence of TD is more in Males. * Quoted in Jest & Wyatt [2]

Table 3 - Pervlence of TD in various studies by age (A)

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N: Numbers of patients

$Z = 11.914$, $P < 0.001$

$Zwt = 14.848$ $P < 0.001$

$tk\text{-}1 = 3.298$ $P < 0.05$

Σ^2 k-1=91.33 $P < 0.001$

Table 4 - Prevalence of TD various studies by age (B)

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N=Number of patients

$Z = 8.427$, $P < 0.001$

$Zwt = 11.942$ $P < 0.001$

$tk\text{-}1 = 2.449$, $P < 0.05$

Σ^2 k-1=101.692, $P < 0.001$

Weighted prevalence rates in different time periods and values of test statistics applied are given in table 1. Findings of different studies regarding sex and age differences and values of test statistics along with P-values are given in tables 2, 3 & 4.

All the period specific weighted prevalence rates are on the whole, significantly different from those of different studies in those periods (table 1). Since, for all the periods the corresponding P-values are significant, by almost all the methods, we cannot conclude that the prevalence rates are consistent across the studies in any period.

In our opinion, prevalence figures for TD are seldom very useful. Difference in diagnostic techinques, length of neuroleptic treatment and prevalence of spontaneous dyskinesias, which should be subtracted form the TD figures, constitute part of the problems. The fact that symptoms may be concealed by on-going neuroleptic treatment and that some withdrawal dyskinesias are reversible after some years of drug abstinence adds to the confusion.

Although, in four studies the TD prevalence is more in males and in thirteen studies it is not significantly more in females (table 2), on the whole we can conclude that the TD prevalence is

significantly more in females ($P < 0.001$).

In six studies the age groups are less than 50 years and 50 or more years of age (table 3). In seven studies the age groups are less than 60 years and 60 or more years of age (table 4). Three studies are included in both the categories. From tables 3 and 4 it can be seen that the TD prevalence is significantly more in old age ($p < 0.001$).

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