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STUDY OF SPIROMETRY AND AIRWAY REACTIVITY IN PATIENTS ON DISULFIRM FOR TREATMENT OF ALCOHOLISM

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ABSTRACT

The aim of our study was to examine the short term effect of disulfiram on pulmonary functions of alcohol dependent subjects, who were chronic smokers. We compared FEV1% values on spirometry and airway reactivity to histamine challenge in alcohol dependent subjects at baseline and after 2 weeks of treatment with disulfiram. Disulfiram did not significantly alter FEVI values and airway reactivity during the treatment period and can thus be used safely in alcohol dependent subjects who are current smokers.

Key words: Disulfiram, Alcohol Dependence, Spirometry, Airway Reactivity

Disulfiram is effective in the treatment of alcohol dependence syndrome, especially, when given under supervision (Azrain, et al.,1992; Chick et al.,1992; Fuller,1995). However the use of Disulfiram in the treatment of alcohol dependence syndrome is restricted by the presence of comorbid psychiatric and medical conditions like depression, psychosis, hepatitis and uncontrolled hypertension (Rossiter,1992; Mason,1989; Lake et al.,1977). It is also recommended that disulfiram should be used with caution in the presence of respiratory disorders (Thorley,1982) especially, in view of bronchospasm during a Disulfiram Ethanol reaction (Zapata & Orwin,1992). Alcohol was also found to be a significant independent predictor of decline in forced expiratory volume (FEV1) (Lange et al.,1980). In addition, disulfiram has several toxic metabolites of which carbon disulphide (CS_2) is mainly excreted through the lungs (Stromme,1965). Since there is a high prevalence of smoking and chronic obstructive pulmonary diseases among patients with alcohol dependence (Heinemann,1977; Burch & Depasquale, 1967., Srinivasan & Augustine,2000), we planned to study the effect of disulfiram on pulmonary function tests in alcohol dependent subjects.

The aim of the present study was to examine the effect of disulfiram on lung function spirometry and bronchial responsiveness to histamine in alcohol dependent subjects who were also chronic smokers.

MATERIAL AND METHODS

Subjects: The subjects were recruited from alcohol detoxification and inpatient treatment programme at the department of psychiatry, St. John's Medical College Hospital, Bangalore. This study was approved by the ethics committee of St.John's Medical College Hospital.

Male patients admitted and diagnosed to have alcohol dependence according to International Classification of Diseases (ICD)-version 10 (WHO,1992), with a history of chronic smoking and cough and willing to take disulfiram were included as subjects for the study after obtaining informed consent Those patients who had severe asthma and recent respiratory infection were excluded. Patients on antihistaminic drugs, steroids and bronchodilators were also not

included in the study.

Clinical assessment: The patients entered the study after the remission of alcohol withdrawal symptoms. The details regarding smoking, respiratory symptoms, intake of any concomitant medications, atopy and occupational dust exposure were noted. The alcohol history was obtained by a clinical interview and the severity of alcohol dependence syndrome was assessed using the Short Alcohol Dependence Data (SADD) (Davidson & Raistrick, 1986). Total score on SADD were interpreted as follows: 1-9 low dependence, 10-19 medium dependence and 20 or greater, high dependence.

Current smokers were defined as men who smoked 20 packs of cigarettes or more in a lifetime or at least 1 cigarette per day for 1 year and were smoking at the time of the study. Pack years (lifetime smoking) was calculated based on average daily consumption of cigarette packs multiplied by years of smoking.

Disulfiram was given under supervision. In our centre, after obtaining an informed consent, patients receive 250 mg of disulfiram twice a day for the first four days and later are maintained on 250 mg of disulfiram per day. Our previous experience suggests that 250 mg of disulfiram per day is an adequate dose for most of our patients (Srinivasan, et al., 1986).

Pulmonary Function Tests: Spirometry was done in a pulmonary function lab located within the hospital using Sensor Medics VMax 22 system according to standard guidelines of American Thoracic Society (1995). The tests were done after the remission of alcohol withdrawal symptoms. Each subject had to perform the test thrice i.e., before starting disulfiram , after 4 days of treatment with 500mg of disulfiram and at the end of 2 weeks of maintenance treatment on 250 mg of disulfiram. The best effort FVC and FEV1 values were noted from three stable values on each testing occasion. FEV1 was standardized for subject's height.

Histamine inhalation challenge test: Bronchial responsiveness was measured using histamine inhalation test by tidal breathing method described by Cockcroft et al.(1977). The histamine provocative test was done before starting treatment with disulfiram and repeated two weeks later while the patients were on a maintenance dose of 250mg of Disulfiram per day. Those patients who at baseline were positive to the histamine provocative test were excluded for the repeat challenge done after two weeks of treatment with disulfiram. The test was terminated if there was a fall of FEV1 greater than 20% from the post diluent FEV1 or when the maximum concentration of histamine reached 5mg/ml. The maximum dose of 5mg/ml was chosen because in our laboratory it defines patients with significant airway reactivity. Those who did not respond even to 5mg/ml of histamine were considered as non-reactors.

Data Analysis: Repeat measure ANOVA was used to analyse FEV1 values obtained at all 3 spirometric pulmonary function test occasions.

RESULTS

27 patients were screened for the study. Of these 27 subjects, eight patients dropped out during the follow-up period. 19 patients underwent spirometry tests on all 3 occasions namely, at baseline, and after 4 days of initiating disulfiram therapy and 15 days later while on maintenance treatment. 27 patients underwent histamine bronchoprovocation tests at baseline of which 12 patients were sensitive to histamine and hence did not undergo the second histamine provocation after 15 days of treatment with disulfiram. One patient could not undergo second histamine challenge because he had acute respiratory infection. In all 14 patients underwent histamine challenge test on both the test occasions.

The mean age of the patients included in study was 40.66 years (± 6.50). All the subjects had moderate to severe alcohol dependence syndrome (SADD score=20.81± 6.33) and were current smokers (pack years 24.23± 16.17).

There was no significant change in the FEV1 done at baseline (before initiating therapy with Disulfiram) and after 4 days and 15 days of treatment with disulfiram on repeat measure

analysis of variance (F=0.295, p= 0.816, df=2 & 36). Histamine bronchoprovocation tests done after 2 weeks of treatment with disulfiram were negative in all the 14 patients.

DISCUSSION

The literature on disulfiram treatment for alcohol dependent subjects suggests cautious use of this drug in presence of chronic obstructive pulmonary disease (Thorley, 1982). In addition, bronchospasm is known to occur during a disulfiram ethanol reaction (Zapata & Orwin,1992). In this study, we tried to assess the short term effect of Disulfiram on pulmonary function tests in alcohol dependent subjects who were current smokers.

During the study period no significant change in smoking pattern was observed among the subjects. Among our subjects with normal baseline spirometry (FEV1, over, 80%), we found no decline in FEV1 when assessed during the two weeks of therapy with disulfiram. In those with baseline normal airway response to histamine, we found no change in responsiveness pattern to histamine after 2 weeks of treatment with Disulfiram. The present study was based on a small unrandomised sample. There is a need for further placebo controlled studies to establish whether disulfiram is safe in alcohol dependent patients who have comorbid obstructive respiratory conditions.

In conclusion, we found that disulfiram did not significantly alter pulmonary functions during the initial two weeks of treatment in moderate to severe alcohol dependant subjects who were also current smokers.

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