

Relative Efficacy of Alcohol and Propranolol in Action Tremor

A. H. RAJPUT, H. JAMIESON, S. HIRSH AND A. QURASHI

SUMMARY: *Thirty-nine patients with a variety of diseases, including essential tremor, Parkinson's Disease, olivopontocerebellar degeneration, ataxia telangiectasia, and cervical cord injury with action tremor, were evaluated for the effect of one ounce of absolute alcohol ingestion. Tremor significantly subsided in 61.9% of E.T.; 46.6% of P.D.; one patient with A.T.; and one patient with C6 lesion. The tremor became worse in one patient with O.P.C.D. Twenty of these patients were treated with propranolol, an average dose of 92 mgm. per day, and re-evaluated three to six*

months later. All those who improved on alcohol improved on propranolol and the one whose tremor accentuated with alcohol had a similar response to propranolol. It is concluded that the tremorolytic effect of alcohol is neither specific for, nor limited to, essential tremor and is of no value in differentiating various neurological disorders which manifest as action tremor. It is recommended that one ounce of absolute alcohol by mouth be used as an office procedure to predict the response of patients' tremor to propranolol.

Benign essential tremor is perhaps the commonest action tremor encountered in clinical practice. Alcohol ingestion relieves this tremor for short periods of time in most patients. Though most neurologists consider the response to alcohol an important observation, major textbooks of pharmacology, (Goodman and Gilman, 1965) and neurology, (Handbook of Clinical Neurology, 1968) do not mention the use of alcohol in the diagnosis or treatment of essential tremor. Prolonged use of alcohol for symptomatic control of tremor may result in other serious problems.

RÉSUMÉ: *Trente-neuf patients atteints de tremblement essentiel, maladie de Parkinson, dégénérescence olivopontocérébelleuse, ataxie-télangiectasie ou lésion cervicale, avec tremblement d'action, furent évalués pour mesurer l'effet de l'absorption d'une once d'alcool absolu. Le tremblement fut diminué significativement chez 61.9% des cas de tremblement essentiel; 46.6% des cas de maladie de Parkinson; un cas d'ataxie-télangiectasie et une cas de lésion en C6. Le tremblement a empiré chez un patient avec dégénérescence olivopontocérébelleuse. Vingt de ces patients furent traités au propranolol, à une dose moyenne de*

92mg. par jour, et réévalués 3 à 6 mois plus tard. Tous ceux qui étaient améliorés par l'alcool, furent également améliorés par le propranolol. Il est conclu que l'effet tremorolytique de l'alcool n'est ni spécifique ni limité au tremblement essentiel et, par conséquent, n'est pas valable dans la différenciation des désordres neurologiques variés qui se manifestent par un tremblement d'action. Il est recommandé d'utiliser une once d'alcool absolu, ingurgit oralement, comme procédure rapide, pour prédire au bureau la réponse du tremblement au propranolol.

Search for a drug to control this tremor resulted in clinical trials of different tranquilizers, sedatives, and anti-Parkinsonian medications. None of these however, were effective, (Dupont Hansen and Dalby, 1973). In 1971 Winkler and Young first reported effective control of essential tremor with propranolol — a beta adrenergic blocking agent. Other workers have confirmed this observation. In view of the known side-effects on short term therapy, safety of the drug on prolonged use remains to be established. Action tremor may be a feature in some Parkinsonian patients and is well recognized in cerebellar disorders. There is no known relationship between the pathophysiology of benign essential tremor and other neurological disease manifesting as action tremor. Marshall (1968) believes that essential tremor is an accentuated form of physiological tremor, due to impairment of dampening mechanisms.

While the effectiveness of alcohol in essential tremor has been recognized, its effect on action tremor due to other diseases is not known.

From the University Hospital, Saskatoon, Saskatchewan.

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Reprint requests to Dr. A. H. Rajput, University Hospital, Saskatoon, Canada S7N 0W8.

Propranolol, on the other hand, has been found useful in Parkinsonian tremor (Owen and Marsden, 1965; Abramsky Cameron and Lavy, 1971; and Gilligan, 1972); in lithium-induced tremor, (Kirk and Bastrup, 1972); as well as in benign essential tremor.

We chose to determine: (1) if the effect of alcohol was specific to benign essential tremor and (2) the relative usefulness of the two drugs — ethyl alcohol and propranolol, in action tremor seen in different neurological disorders.

MATERIALS AND METHODS

All patients were seen at the University Hospital and were evaluated by the same neurologist (A.H.R.). Those who had an action tremor, regardless of their neurologic disease, were selected for the study. After general physical and neurological examination, the occupational therapist administered three special tests to the patient to evaluate the hand tremor during action. These included handwriting samples, threading four beads on a string, and drawing a line in a maze with each hand separately. After completion, the patients were asked to drink one ounce of absolute alcohol mixed with water over two to three minutes. Thirty minutes later a blood sample to determine blood alcohol level was obtained and hand function tests were readministered by the occupational therapist.

Thirty-nine patients suffering from different neurological diseases — benign essential tremor (E.T.), Parkinson's Disease (P.D.), olivopontocerebellar degeneration (O.P.C.D.), ataxia telangiectasia (A.T.) and spinal cord lesion at sixth cervical segment level (C6 lesion) were evaluated. Following evaluation, each patient was informed about possible use of propranolol to control his tremor. Those who chose to undergo a trial on propranolol were further investigated with complete blood count, serum electrolytes, and an electrocardiogram. If no contraindications to the use of a beta adrenergic blocking agent were

discovered, the patient was started on propranolol. Initial dose was ten mgm. three times daily and further adjustments were made on the basis of the patient's own evaluation of treatment, objective evaluation of tremor, and the presence or absence of side-effects. Each patient was evaluated by the neurologist and the occupational therapist one month after initiation of treatment and again three to six months later. Complete blood count, serum electrolytes, and electrocardiogram were obtained at the time of each evaluation. Twenty patients received an uninterrupted trial on propranolol, with an average dose of 92 mgm. per day for more than three months. Of the five P.D. patients, three had been on a steady dose of levodopa for more than one year before starting propranolol. The dose of levodopa was not altered while they were taking propranolol. Two new Parkinsonian patients were given only propranolol. Because of day-to-day or hour-to-hour fluctuation in the tremor, we evaluated the patients at different times on successive testing. Only the patients who manifested improvement on every evaluation were considered improved.

The patient with both a spinal cord lesion and an action tremor warrants a more detailed description. This 31 year old male had fractured the seventh cervical vertebra and dislocated cervical six and seven in an automobile accident at age 22 years. He was left with a neurological deficit characterized by sensory impairment below the C5 segment on the right and C8 on the left. There was weakness and wasting of the small muscles in the right hand, hypoactive right triceps jerk and a spastic paraplegia. Eight years after the injury he noted the insidious onset of tremor in the right hand when attempting to eat. Examination one year later revealed an intermittent, flexion-extension type, resting tremor in the right hand fingers. The tremor became more sustained when the arm was stretched out in front and was further accentuated on attempting to use the right hand.

RESULTS

Neurological diagnosis in the 39 patients was as follows: E.T. — 21 patients; P.D. — 15; O.P.C.D. — 1; A.T. — 1; and C6 lesion — 1 patient (Table 1). Improvement in action tremor was observed in 13 of 21 patients (61.9%) with E.T. and in 7 of 15 patients (46.6%) with P.D. In the lone patient suffering from O.P.C.D. the tremor became worse. One A.T. patient and the one with a C6 lesion experienced improvement with oral alcohol (Table 1). The average blood alcohol level in those E.T. patients who improved was 0.031%; while in the non-improved group it was 0.025%. Blood alcohol level in individual patients in the improved group varied from a trace to 0.06% and in the unimproved group from a trace to 0.05%. Average blood alcohol level in P.D. patients whose action tremor improved was 0.029% and in those who did not improve it was 0.015% (Table 1). The range of alcohol level in P.D. patients varied from a trace to 0.06%.

Twenty patients with the following neurological disorders: E.T. — 12 patients; P.D. — 5; O.P.C.D. — 1; A.T. — 1; and C6 lesion — 1 patient had three months or longer of uninterrupted trial on propranolol. The dose of propranolol ranged from 30 mgm. to 240 mgm. per day, an average of 92 mgm. per day. The last tremor evaluation after three to six months of propranolol therapy was used for comparison with the effect of alcohol and baseline performance on no drugs. On propranolol improvement in tremor was noted in 11 of 12 (91.7%) E.T., and all 5 P.D. patients. Improvement was also noted in one patient with A.T. and the one with a C6 lesion. The patient suffering from O.P.C.D. was worse on propranolol, a response similar to that while on alcohol (Table 2). Effects of the two drugs, ethyl alcohol and propranolol, in the 20 patients, are compared in Table 2. The results indicate a larger number of patients with action tremor improved on propranolol than on a single, one ounce, dose of alcohol. All patients who improved on alcohol showed improvement on propranolol and the

one who became worse on alcohol had a similar response to propranolol. All those who initially benefitted from propranolol maintained the improvement up to the time of final evaluation.

DISCUSSION

Benign essential tremor is a monosymptomatic disorder characterized by postural and action tremor (Ashenhurst, 1973). The diagnosis is easy and accurate in most cases on the basis of history and clinical examination. Errors in the diagnosis, however, are not unknown (Marshall, 1968; Critchley, 1972; and Pakkenberg, 1972). Typical Parkinsonian tremor is present during rest and subsides during action; occasional patients with Parkinsonism may have prominent postural or action tremor. At an early stage of the disease, when other features of Parkinsonism are not obvious and postural or action tremor is a dominant manifestation, a patient could be thought to have E.T. (Marshall, 1968; and Pakkenbert, 1972).

Action and postural tremor is a well-recognized manifestation of cerebellar dysfunction; usually these patients have other manifestations of cerebellar dysfunction, thus making the diagnosis easy. When tremor is the most prominent feature, differentiation from E.T. may be difficult (Marshall, 1968). When the diagnosis of E.T. is not possible on the basis of clinical evaluation, no laboratory test can assist in arriving at the correct solution. The prognosis and treatment in E.T., P.D., and cerebellar disorders are different; therefore an accurate diagnosis is necessary for counseling and management.

Because temporary improvement in E.T. is frequently obtained with oral alcohol, it has been assumed that any action tremor which improves on alcohol is benign, essential, tremor. Our data shows that tremorolytic effect of alcohol is not universal in patients with E.T.; only 61.9% of these patients improved with one ounce of alcohol. The average blood alcohol level in this group was 0.031%; while in the un-

improved group it was slightly lower at 0.025%. There were wide variations in individual blood alcohol levels in each group. Although improvement was not universal, none had worsening of the tremor. It could be argued that a higher dose of alcohol might relieve tremor in all patients with E.T. While our study does not answer this, it clearly shows that tremorolytic effect is neither specific for, or limited to, E.T. patients. A large percentage (46.6%) of P.D. patients, as well as a variety of other neurological conditions in whom action tremor was a prominent feature, also experienced relief on alcohol. Use of alcohol to differentiate one kind of action tremor from another is unreliable.

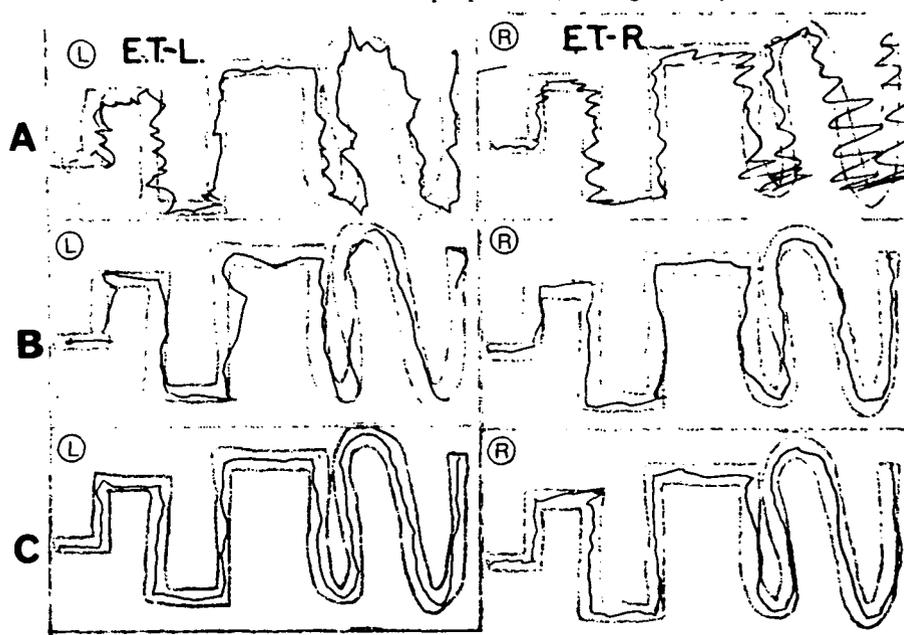
Although it has been recognized that alcohol provides temporary relief in E.T. (Winkler and Young, 1971; and Dupont, Hansen and Dalby, 1973) there was no controlled study on this observation until the report by Rajput, Jamieson, and Hirsh (1973). The mechanism of alcohol action is not fully established. A recent report by Growdon, Shahani, and Young (1974) suggests that alcohol relieves tremor by its

central action. The relief is short-lived (in most cases no more than two hours), followed by an increase in the tremor. In order to keep the tremor under reasonable control, the patient needs alcohol at frequent intervals. Furthermore, the amount gradually increases as time goes by. The use of alcohol is therefore not desirable in these patients on a regular basis. Though most patients with E.T. are only socially embarrassed, the tremor may cause functional handicap in some depending on the amplitude of the tremor. The patient may seek relief of tremor for either of these reasons. Tranquilizers and sedatives have been used without encouraging results and anti-Parkinsonian drugs, — anticholinergic drugs, and levodopa have no beneficial effect (Dupont, Hansen and Dalby, 1973).

In 1971 Winkler and Young demonstrated improvement in benign essential tremor with propranolol. Other workers (Murray, 1972; Pakkenberg, 1972; Gilligan, 1972; and Morgan Hewer and Cooper, 1973) later substantiated this observation. There is now some optimism that propranolol may control benign es-

Figure 1 — Maze test by 64-year-old female (E.T.) suffering from E.T. performed with Left (L) and Right (R) hands.

- A Maze on no drugs
- B Thirty minutes after intake of one ounce alcohol
- C Patient for four months on propranolol, 80 mgm. daily



sential tremor over long periods of time. We compared the effectiveness of one ounce of absolute alcohol assessed thirty minutes after ingestion to that of a maintenance dose of propranolol (average dose of 92 mgm. per day in three to four divided doses) on action tremor due to E.T. and other neurological diseases in 20 patients — Table 2. Although the number that improved on propranolol is considerably higher than those with one ounce of alcohol there was no consistent difference in the degree of tremor relief in most cases. Where the difference was evident, improvement on propranolol was more marked. No patient in our series had complete relief of tremor on either drug.

There is no clinical or laboratory test that can predict the response of action tremor to propranolol in any given patient and a clinical trial for several days is required to establish its effectiveness. Our observations that the response to alcohol and propranolol is similar in most cases permits an office procedure to predict the response to propranolol. The test would be most valuable where the response to alcohol is

definite, i.e. improvement or worsening of tremor. In these cases similar response to propranolol may be expected. Where no change is seen with alcohol the tremor may or may not respond to propranolol.

Figure 1 is a maze test performed by a 64-year-old female who suffered from E.T. for 15 years. Her mother had a similar problem. Figure 1A shows her tremor while she attempts to draw a line without touching the maze with left t and right hand separately, when off medication. Figure 1B shows her attempt thirty minutes after ingesting one ounce of absolute alcohol. Figure 1C shows the test carried out four months later when on propranolol, 20 mg. four times a day. The improvement on each drug is obvious. At the time of her last test she maintained that her tremor was not different on the medication, although the family had noted significant improvement. Once the patient gets used to a lower level of disability without complete relief of symptoms, the severity of the previous handicap may be forgotten and the patient may interpret the new status as "no change". Total relief

from tremor was not observed in any of our patients.

Impairment of co-ordination on excess alcohol is a well-recognized phenomenon. It was assumed that alcohol intake would accentuate action tremor in cerebellar disorders. D.S., a 52 year-old male who suffered from ataxia telangiectasia, had severe postural and action tremor. Figure 2A shows an attempt by this patient to complete the maze with his left and right hand when on no medication. Figure 2B shows the same attempted thirty minutes after one ounce of absolute alcohol intake. Figure 2C shows the test attempted after three months of continued use of propranolol, 20 mg. three times a day.

Improvement of tremor on propranolol was fairly well sustained through the day in our patients. The drug produces no impairment of higher cortical functions comparable to alcohol. Propranolol is therefore an advancement over previously known drug regimes. Propranolol is a potent biochemical agent with the following well-recognized side-effects: fatigue, lethargy, depression, hallucinations, insomnia, vivid dreams, acute organic brain syndrome, bronchospasm, suppression of rebound to hypoglycemia, congestive cardiac failure, peripheral neuropathy, thrombocytopenia, and agranulocytosis (Kosman, 1973).

In our series bradycardia of some degree was noted in all patients on propranolol. The other side-effects of significance were excessive sweating — one patient, reduced sexual potency — one patient, and increased frequency of urination — one patient. Unlike alcohol, which is believed to have a central tremor-relieving effect (Growdon Shahani and Young, 1974), propranolol is believed to have both central and peripheral actions (Morgan Hewer and Cooper, 1973).

Though most studies including our own indicate some control of tremor with propranolol over the short term, long term efficacy of the drug remains to be established. In patients with essential tremor where the drug is used for symptomatic

Figure 2 — Maze test by 52-year-old male (D.S.) suffering from A.T. performed with Left (L) and Right (R) hands.

- A Maze on no drugs
- B Thirty minutes after intake of one ounce alcohol
- C Patient for three months on propranolol, 60 mgm. daily

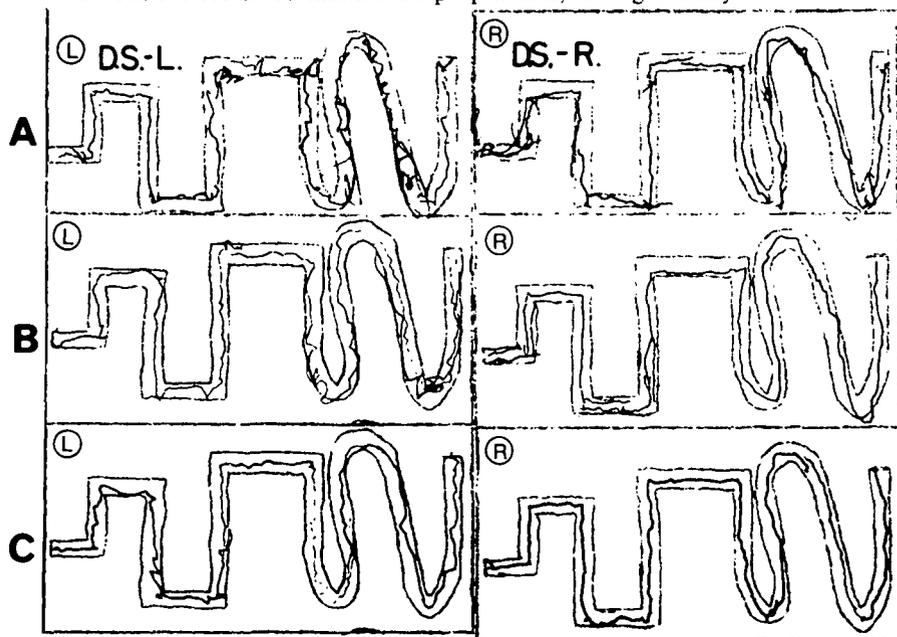


TABLE 1

Effect of alcohol (one ounce) on action tremor, 30 minutes after ingestion.

Diagnosis	Number Tested	Number Improved	Average Blood Alcohol in Improved	Average Blood Alcohol in Non-Improved
E.T.	21	13 (61.9%)	0.031%	0.025%
P.D.	15	7 (46.6%)	0.029%	0.015%
O.P.C.D.	1	0 (0%)	Trace	
A.T.	1	1 (100%)	0.02%	
C ₆ Lesion	1	1 (100%)	0.02%	

E.T. = Benign Essential Tremor; P.D. = Parkinson's Disease; O.P.C.D. = Olivopontocerebellar degeneration; A.T. = Ataxia Telangiectasia; C₆ Lesion = Injury to spinal cord at C₆ level.

TABLE 2

Comparison of one ounce of absolute alcohol effect after 30 minutes to the effect of maintenance dose (average 92 mg. day) of Propranolol on action tremor in 20 patients.

Diagnosis	Number Tested	Number Improved With Alcohol	Number Improved With Propranolol
E.T.	12	7 (58.3%)	11 (91.7%)
P.D.	5	3 (60%)	5 (100%)
O.P.C.D.	1	0 (0%)	0 (0%)
A.T.	1	1 (100%)	1 (100%)
C ₆ Lesion	1	1 (100%)	1 (100%)

E.T. = Benign Essential Tremor; P.D. = Parkinson's Disease; O.P.C.D. = Olivopontocerebellar degeneration; A.T. = Ataxia Telangiectasia; C₆ Lesion = Traumatic lesion of spinal cord at C₆ level.

control rather than a cure, the patient would require the drug for the rest of his life. In view of the known side-effects and not yet proven long-term efficacy of the drug, propranolol should only be used when the disability is significant.

CONCLUSION

Oral alcohol can temporarily alleviate action tremor in different neurological diseases. This action is neither specific for, nor limited to, benign essential tremor. Effect of alcohol cannot be used to differentiate E.T. from other neurological disorders which have an action tremor. All patients suffering from action tremor who had relief of tremor with alcohol had improvement with propranolol; while in the case where

the tremor was aggravated on alcohol, accentuation of tremor occurred on propranolol. In those cases where no discernible change in tremor severity was noted with alcohol, improvement on propranolol was seen in some patients. Alcohol, one ounce, may be used to predict the response of action tremor to propranolol. Propranolol is effective in controlling action tremor in a variety of neurological disorders. Because of its known side-effects and unknown efficacy over the long-term, the drug should be used only in those cases where the psychological or physical disability produced by the tremor is significant. It is recommended that the patients who wish to take the drug over a long period should be monitored carefully.

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