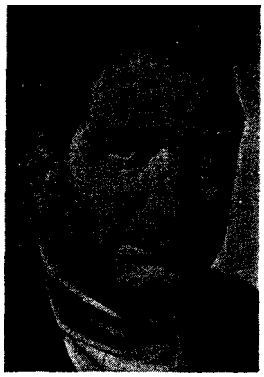
A Five-Year Field Trial of Massive Nicotinic Acid Therapy of Alcoholics in Michigan



RUSSELL F. SMITH, M.D. [1]

Several factors originally intrigued us concerning the possible benefits of massive doses of nicotinic acid in the alcoholic population. This study was undertaken in May of 1966 at a time when some very interesting insights into alcohol metabolism were in the research literature. In addition we were reacting to the substance-abuse epidemic in our young people with frantic literature searches, speculation, and accelerated research in Psychopharmacology. It was in this climate that this study was conceived and implemented. The specific background factors that convinced us such a trial of massive nicotinic acid treatment would be valuable were:

1. Nicotinic acid was proving a useful treatment tool with schizophrenics, and a portion of the alcoholic population was known to have the same disorder.

2. Alcoholics, during early withdrawal, are consistently diagnosed as schizoid by the unsophisticated, suggesting similar biochemical mechanisms, perhaps triggered by alcohol toxicity.

3. The suggested effectiveness of nicotinic acid in reducing serum cholesterol and enhancing circulation made the agent a justifiably valuable adjunct to alcoholism therapy on the basis of lipid changes and hypercholesterolemia seen with acute fatty liver changes.

4. Reports indicated that nicotinic acid was having a beneficial effect on hallucinations induced by various street drugs as well as the residual flashbacks induced by some.

5. The 5-OH-tryptamine - monamine oxidase axis of cerebral metabolism was beginning to be implicated in alcohol's CNS effects and the alcohol tolerance mechanism and nicotinic acid plays an important role in this neurohormonal mechanism.

6. Substantial numbers of alcoholics continued to fail in conventional self-help and mental health treatment methods, and an organic factor was being pragmatically implicated.

In 1966 we had at our disposal huge clinical and limited financial resources. This was a period that antedated any interest in either private or governmental funding sources in the field. Certainly since nicotinic acid at that time was cheap, a situation that has since dramatically changed, any thought of economic support for a sophisticated study from the pharmaceutical industry was unthinkable. We elected to use what we had to conduct a pilot field trial of nicotinic acid in a group of alcoholics to determine: If any beneficial effects could be

1 P.O. Box 518, Whitmore Lake, Michigan 48189

determined.

What these beneficial effects were.

Whether further studies were justified.

Which and what kind of alcoholics would benefit from nicotinic acid, if at all.

If possible, to establish criteria for the use of nicotinic acid in the alcoholic population and for dosage adjustment.

If there were side effects or serious deterrents to the use of nicotinic acid in various categories of alcoholics.

Method

We began with certain preliminary assumptions, some of which we refined during the study as more information became available and our skills improved. We assumed that nonrecidi-vists in our clinical sample were functioning well without chemical aids and any nicotinic acid effects would be difficult if not impossible to detect. We then confined our observations to multiple recidivists who had been exposed to, if not actively involved in, conventional treatment programs and methods. Three groups were selected. Two represented hard-core multiple recidivists while the third was selected as a cooperative, intact group of alcoholics with a high probability of positive treatment response with or without nicotinic acid.

The outpatient group represents a group involved in a county highway safety court program. All participants are known alcoholics with long histories of withdrawals, complications, and repeated treatment attempts that failed. Most participants were poorly motivated and at least initially had been forced into treatment with antabuse through legal coercion. They tended to be somewhat older than the average age for alcoholics in 1966. Most had serious health problems related to long alcohol use and poor nutrition. Similar populations are found in rescue missions and homeless men facilities.

The hospital group represents alcoholics who are primarily seeking treatment voluntarily. All except perhaps state-financed admissions enjoy more personal and economic resources than the first group. All were repeated treatment failures at this or other facilities. Physically the group had demonstrated repeated severe withdrawals and complications of alcoholism. Most were from a higher socioeconomic group and enjoyed better medical treatment and nutrition than the outpatient group. Both groups had significant numbers of members complaining of persistent insomnia, intermittent severe depression, or intermittent agitated states that nearly always prompted serious drinking.

The third group was selected randomly from a facility where every available treatment technique was employed. The facility treated patients who, although physically demonstrating moderately advanced alcoholism, had good educational resources and life style. All members of this group were highly motivated and had a high treatment success rate. All volunteered for nicotinic acid therapy.

The observers for the study were selected because they represented staff of these programs and had rapport and background knowledge of participants. As criteria became evident we developed a mail follow-up system backed up by telephone sampling and observations by local alcoholics known to the three programs. The sample population was evaluated in the fall of each year of the study. In November mail sampling was carried out. Telephone and on site personal follow-up were attempted until the end of the year when treatment success figures were compiled. We expected significant attrition of our original sample, and for the purposes of this study we have included all individuals dropped from the study as treatment failures. Certainly individuals receiving substantial benefit from nicotinic acid would be more interested in continuing in the study.

It took nearly three years to develop criteria by which we could measure degree of treatment response. For this reason the study was extended an

additional year to produce five years of consistent measurement.

This response criteria is as follows: **Poor Response**

1. No objective or subjective change.
2. Continued unaltered drinking pat tern.
3. No change in sleep pattern.
4. No change in mood or affect.
5. No change in supportive medication needs.
6. Psychological state compatible with Menninger scale classes one and two.

Fair Response

1. Reduced rate of recidivism.
2. Improved sleep pattern.
3. Decreased supportive medication needs.
4. Psychological state compatible with Menninger scale class three.

Good Response «

1. Marked reduction in recidivism.
2. Normal sleep pattern.
3. Marked reduction in supportive medication needs.
4. Absence of extreme depression or euphoria.
5. Psychological state compatible with Menninger scale class four.

Excellent Response

1. Total alcohol abstinence for two or more years.
2. Mood stability.
3. No need for supportive medication other than nicotinic acid.
4. Psychological state compatible with Menninger scale class five.

During the intervening years we have had occasion to initiate nicotinic acid

Statistical Observations

Year	Poor Result	Fair Result	Good Result	Excellent Result	Total Responses
		(Outpatient Treatment Group)			
1967	18	70	109	42	239
1968	3	45	123	62	233
1969	0	- 20	125	69	214
1970	0	21	102	71	194
1971	0	16	34	59	109
1972	0	10	34	56	100
		(Hospital Treatment Group)			
1967	40	19	111	46	216
1968	21	45	87	57	191
1969	0	20	91	63	174
1970	0	24	73	64	161
1971	0	25	64	62	156
1972	0	25	62	60	147
		(Sanatorium Group)			
1967	8	9	20	15	52
1968	3	8	23	19	50
1969	0	3	25	21	49
1970	0	6	27	14	47
1971	0	10	23	7	40
1972	0	13	21	6	40

Percentage Total Responses BY Year Baseline 651 individuals started.

1967	507-100%	1970	402-79.6%
1968	474-93.5%	1971	305-60.0%
1969	437-86.0%	1972	287-56.6%

therapy on several thousand additional alcoholics not included in this study. This additional clinical experience has been invaluable in evaluating the study group.

Observations

At the end of five years the involuntary, coerced, court-motivated group of 239 low-bottom alcoholics had 4 percent who demonstrated a fair response to nicotinic acid. These individuals through relapses and regression really represent fallout from the group originally classified as good results. Fourteen percent had what could still be classified as a good result. Twenty-four percent of this group still qualified as excellent result at the end of five years. Those persons lost from the study were from persistent symptoms primarily histamine in origin, persistent gastrointestinal distress, flushing, visual disturbances. Since this group was also initially on antabuse another fact was quickly discovered. With exhaustion of body stores of histamine the classical reaction to antabuse is lost. Apparently histamine is a necessary participant in the antabuse reaction.

In the hospital group of 216 individuals 11 percent could be categorized as fair responses. Again nearly all of these individuals retrogressed with time from the good response column. Twenty-eight percent of the original sample could be found in both the good and excellent categories at the end of five years. Less attrition could be expected since this group had better motivation, health, and resources. During the first two years many of these patients continued out of loyalty, placebo effect, or patient expectation. It was not until later in the study that these factors became less important.

In the very highly motivated sanatorium group there was far less attrition. This is an artifact since all are in a common profession and their location is listed annually in a national directory and it was possible to assess their status
from their immediate supervisors. Here the factor of loyalty and compulsive compliance with the study protocol are evident. In this group 27 percent were still taking nicotinic acid even though their response only met our criteria for fair. Forty-four percent were classified as good response at the end of five years. Eleven and a half percent were in the excellent category at the end of our five-year period of observation. Here many participants continued in the study instead of dropping out, as we suspect was the case in the previous two groups.

Profiles of the various response categories also reveal interesting and suggestive findings.

Of the 9.5 percent of the original sample remaining at the end of five years in the fair category the following profile is characteristic:

Younger.
No history of serious withdrawals.
Minimal persistent insomnia.
Minimal physical complications.
Fairly evident emotional and social problems.
Many magical thinkers, suggestible individuals.
A high tendency to rely on chemical solutions.
Insecure with few personal coping resources.

Of the 23 percent of the original sample still classified as a good response the following profile can be compiled:

Average age 55-65 years.
Long history of alcoholism.
Multiple severe DT's or near DT's withdrawals.
High incidence of hepatic complications.
Evidence of toxic brain syndrome when started on nicotinic acid.
Straightforward alcoholism at organic stage.

Of the 24 percent who still qualified as excellent results at the end of five years the following profile is true:

Average age 55-65 years.
Long history of alcoholism.
Documented DT's, seizures, severe withdrawals.

Evidence of advanced organic alcoholism.
Long episodes of toxic brain syndrome.
Severe, persistent insomnia.
Serious depressions and euphoria.

The above profiles suggest that in severe advanced alcoholism, where organicity, particularly toxic organic brain syndrome, is evident, nicotinic acid therapy is m6st valuable. This observation may gain enhanced credibility if the new neurohormonal studies in senile brain syndrome now underway at the Miami Heart Institute confirm involvement of the 5-OH-tryptamine axis. The small control group of more average alcoholics tends to confirm the fact that the more organic the alcoholism the better the nicotinic acid response. In the more organic group far less histamine response symptoms were noted. Of course this could also be a function of age as well.

If we visualize alcohol withdrawal a function of distorted 5-OH-tryptamine metabolism our observations are easily explained. Severe distortions may mimic senility as does the commonly encountered toxic brain syndrome. Distorted serotonin and dopamine metabolism would explain insomnia, and hallucinosis variations in this neurohormonal metabolic axis could explain mood extremes so often encountered in the treatment success group often unrelated to external events. Nicotinic acid in theory could have a dramatic effect on this chemical process, and this possibility is borne out by our observations. This theoretical approach also offers an explanation for the fact that nicotinamide has produced no results in our groups.

Summary

A five-year longitudinal field trial of nicotinic acid was conducted on 507 known alcoholics to determine what effects and benefits might result. Our experience strongly suggests that:

1. Nicotinic acid can benefit 50 to 60 percent of alcoholics in the organic stage.
2. Nicotinic acid can benefit about 30 percent of the total alcoholic population.
3. Benefit can be measured in terms of:
Reduction of insomnia.
Mood stabilization. Reduction of sedative tolerance. Restoration of nontoxic sensorium. Reduction of drinking recidivism. Enhanced ability to use other treatment resources.
Enhanced social and emotional function.
Reduction or absence of the need to use other forms of medication.
4. Potential drawbacks include:
Persistent uncomfortable histamine effect.
Blocking of antabuse reaction. Occasional visual disturbance. Occasional gastroenteritis. Distortion of diabetes mellitus status.
5. Nicotinic acid can be a potent pharmacologic agent.
6. Double-blind and controlled studies should be undertaken if the mechanical problem of histamine symptoms initially can be overcome.
7. Studies concerning the site of action of nicotinic acid could potentially reveal significant new insights into the toxic brain syndrome, senile brain syndrome, alcohol tolerance, and alcoholism itself.