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A Review of LSD Treatment in Alcoholism[1]

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Abstract. A total of 31 investigations involving 1,105 patients, on the effect of LSD in the treatment of alcoholics are reviewed. There were 13 single large-dose studies without controls, 5 such studies with controls, 4 studies of multiple low-dose LSD without controls, 3 multiple low-dose studies with controls, and 6 miscellaneous investigations that did not fit any of these categories. Single doses ranged between 50 and 800 μg, while multiple doses ranged (per single dose) from 25 to 800 μg, with a total maximum dose of 100–6,400 μg (maximum of 6 doses). Follow-up ranged from none to 65 months. The overall effectiveness of this controversial treatment of alcoholics remains disappointing. It was difficult to reach meaningful generalizations from the variety of published investigations with different designs and variant criteria for improvement.

The administration of lysergic acid diethylamide (LSD) in alcoholism stems from a pragmatic clinical observation that delirium tremens sometimes scare the alcoholic patient to such a degree that he looks at his problems and decreases his alcoholic intake. Analogously, electroconvulsive therapy is used in psychiatry because some psychotic patients seem to be clinically improved after a seizure. Such reasoning led to the introduction of lysergic acid in the treatment of alcoholics, in 1953, by *Hoffer, Osmond* and *Hubbard.* Since that year, several conflicting studies have been published, and 3 books on this controversial treatment have appeared (2, 22, 40). It is difficult to draw safe generalizations from the published studies because most investigators used different methods, varied doses, and divergent criteria for improvement.

Our own disappointing experience with LSD treatment in 9 alcoholics with 3–5 years follow-up (1) prompted us to review published studies cited in the

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Cumulative Index Medicus through June, 1970. Although previous reviews have appeared (3, 7, 14, 37, 39), the last one, in 1969 (7), covered studies done through 1966 only. (Numerous communications reflecting the general interest in this area have also appeared [11, 13, 24, 27, 34, 35, 41, 43].)

For the purposes of this review, studies on LSD and alcoholism are divided into (a) single large-dose administration, sometimes called psychedelic (2), (b) multiple low-dose administration, also referred to as psycholytic (2), and finally (c) miscellaneous studies.

a) Single Large-Dose Studies

Single-dose studies of LSD in alcoholism can be subdivided into 2 groups: those with control or comparison groups, and those with none. Single-dose studies without control are summarized in table I. These 13 studies plus one later follow-up (6, 9, 12, 14, 20, 21, 25, 26, 28, 29, 32, 36, 42, 44) have utilized a total of 408 patients (a range of 2–69 patients per study). The patients included in 7 of these studies (6, 12, 25, 28, 29, 32, 42) had been drinking for from 8–20 years, with a mean of 12.15 years; the 6 remaining authors did not specify length of alcoholic intake. The single dose of LSD, administered orally in all investigations, ranged from 50 to 450 μg, with a mean dose of 233.9 μg. The degree of improvement varied from 100 % in the 2 studies with 2–3 patients each (14, 36), to 25 % in another study (21), but length of follow-up was not reported in any of these 3 studies. Ten studies reported follow-up, which varied from prior to discharge from the hospital, to 55 months after LSD treatment.[2] The study of *Ditman et al.* (9) showed that the longer the follow-up, the lower the percentage of improvement: They reported improvement in 67 % of his patients at 6–18 months after treatment, but this had dropped to 50 % after 2 years. *Fox* (12) reported an interesting variable, the difference in self-assessment of improvement *versus* physician-assessment. She rated 80 % of her patients as improved, while the patient's own estimate was only 42 %. This is unusual since most alcoholics try to present a rosy picture. Of course the longer the follow-up, the greater patient attrition is likely to be, which would affect the percentages. The average length of follow-up for all investigations combined was 19.4 months.

The 5 single-dose studies with controls (17–19, 23, 38) are summarized in table II. These studies included 384 patients with a mean of 76.8 patients per study, and 170 controls, a mean of 34 per study. Unfortunately, none of these studies reported length of alcoholic illness prior to LSD treatment, an important lack of information, especially in comparing control patients with those who

2 In 1965 *MacLean et al.* (26) published a further follow-up to his 1961 study (25). The figures for that follow-up were not used in computing averages, since no number was specified. See table I.

Table I. Summary of uncontrolled single large-dose studies of LSD in alcoholism

Author	Year	Number of patients	LSD, μg	Years of drinking	Follow-up months	Improvement			Total improved	
						none	some	much	number	%
Chwelos et al. (6)	1959	16	200–400	11.6	6	1	5	10	15/16	95
Ditman et al. (9)	1962	27	100	–	6–18	9	0	18	18/27	67
					24	8	0	8	8/16	50
Fox (12)	1965	20	200	15	36	4	5	11	16/20	80
						11	4	4	8/19	41 (Pat. estimate)
Hoffer (14)	1965	2	200	–	not stated	0	0	2	2/2	100
Kurland et al. (20)	1965	60	50–450	–	–	45	0	15	15/60	25
Kurland et al. (21)	1967	69	450	–	6	46	0	23	23/69	33⅓
MacLean et al. (25)	1961	61	400	14.3	9	15	16	30	46/61	75
(MacLean) et al. (26)[1]	(1965)	not stated			55	(52 %)	(23 %)	(25 %)		(48 %)
O'Reilly (28)	1965	68	200	> 10	2–34	42	0	26	26/68	38
O'Reilly et al. (29)	1962	33	200	8.05	< 2–22	10	10	7	17/27	63
Rolo et al. (32)	1960	12	100–200	8–20	at disch.	2	2	8	10/12	83
Sherwood et al. (36)	1962	3	100–200	–		0	0	3	3/3	100
Smith et al. (42)	1958	24	200–400	12.1	2–36	10	4	3	7/17	41
Taus et al. (44)	1967	13	120–160	–	24	1	3	9	12/13	92
Total/Range		408	50–450	8–20	7–238 wks.	193	45	173	218/411	
Average			12.15 (n = 7)	19.4 (n = 12)	–	–	–	–		53

1 This further follow-up by *MacLean et al.* was not included in tabulating averages since no 'n' was given.

Table II. Summary of controlled single large-dose studies of LSD in alcoholism

Author	Year	Number of subjects	LSD, μg	Follow-up months	Improvement			Total improved	
					none	some	much	number	%
Jensen (17)	1962	58	200	6–18	13	7	34	41/54	76
control		35		6–18	9	4	4	8/17	47
control		45		6–18	12	3	7	10/22	45
Jensen et al. (18)	1963	70	200	6–18	16	7	39	46/62	74
control		55		6–18	17	4	8	12/29	41
Johnson (19)	1969	70	300 (i.v.)	12	significant improvement in both groups				
control		25		12	with no difference between groups				
Ludwig et al. (23)	1969	176 total	3 μg/kg	3, 6, 9, 12	significant improvement in both groups				
control			(210)[1]	3, 6, 9, 12	with no difference between groups				
Smart et al. (38)	1966	10	800	6	34 % > gain in abstinence time				
control		10		6	20 % > gain in abstinence time				
Totals/Range		384	200–800	3–18	29	14	73		
Average		76.8	342	9.9					75
Control total		170							
Average		34		10.2	38	11	19		44.1

1 Based on the assumption that the average patient weighs 70 kg (154 lb).

received LSD. The dose of LSD ranged from 200 to 800 μg with a mean of 342 μg. (In one study [24], the dose was more accurately calculated as 3 μg/kg of body weight; for purposes of calculating means, we assumed the average patient to weigh 70 kg, hence the total dose was figured as 210 μg.) Follow-up varied between 3 and 18 months for LSD patients and controls, but LSD treatment groups were followed an average of 9.9 months, whereas controls were followed an average of 10.2 months. *Jensen et al.* (18) used 2 control groups; one had psychotherapy identical to that of the LSD group but received no drug, the other group received no drug and individual psychotherapy only: Data on both of these groups was used in reaching the mean.

The results from these 5 studies are more difficult to tabulate than the uncontrolled studies reported earlier because the authors used different measures of improvement. In 3 studies (19, 23, 38) there was significant improvement in both LSD and control groups, with no difference between groups (19, 23) or only slight differences (38). In the remaining 2 studies by *Jensen* (17) and *Jensen et al.* (18), 76 and 74 % of the LSD-treated groups improved *versus* 47, 45 and 41 % of the controls. In summary, of these 5 studies by 4 groups of investigators, 3 failed to substantiate LSD effects, and only 1 investigator in 2 separate studies demonstrated the efficacy of LSD treatment in alcoholics.

b) Multiple Low-Dose Studies

Seven such studies have been reported, 4 without controls and 3, with controls (table III). The 4 uncontrolled studies (1, 10, 15, 33) used a total of 39 patients, with an average of 7.8 patients per study. In none of these investigations was length of alcoholic illness stated. The total dose of LSD varied between 100 and 6,400 μg (mean, 1,278 μg) given in a range of 1.5–8 doses (mean, 4) with the individual dose varying between 25 and 800 μg (mean, 274 μg). Follow-up ranged between 3 and 65 months (mean, 29.8 months). Improvement varied between 0 and 100 % with an overall total of 24 patients of 39, or 61.5 % showing improvement with LSD.

The 3 controlled studies published (26, 30, 45) treated a total of 274 patients with LSD, an average of 91.3 patients per study. Controls totalled 167, or 55.7 patients per study. (Only 1 investigator, *Van Dusen et al.* [45] reported length of alcoholic illness prior to the study and matched his control by age and Mindlin Index to the experimental group [45]; the average length of illness for both groups was 7.82 years.) Total LSD dosage ranged from 300 to 1,200 μg (mean, 562 μg) given in 1–3 doses. *MacLean et al.* (26) reported using from 1 to more than 2 doses with no difference in response. *Van Dusen et al.* (45) similarly noted no difference in response per number of doses (he gave from 1 to 3 doses) and so reported improvement as a group. Follow-up for both controls and LSD groups was 3–38 months, a mean of 20.7 months in the experimental group and 19.7 months in the control group.

Table III. Summary of multiple low-dose studies of LSD in alcoholism, with and without controls

Author	Year	Number of subjects	Total LSD, μg	Number of doses	Single dose, μg	Follow-up months	Improvement			Total improved	
							none	some	much	Number	%
Uncontrolled studies											
Hoffer (14)	1965	6[1]	300	1.5	200	38.2	6	0	0	0/6	0
Hoffer (15)		7[2]	400	2	200	49	0	7	0	7/7	100
Rydzynski et al. (33)	1968	14	600–6,400	6–8	100–800 (i.m.)	3–18	2	10	2	12/14	86
Eisner et al. (10)	1958	3	100–3,000	4–6	25–500	6–17	1	2	0	2/3	66
Abuzzahab (1)	–	9	215–1,065	2–6	65–300	26–65	6	1	2	3/9	33
Total/Range, Uncontrolled studies		39	100–6,400	1.5–8	25–800	3–65	15	20	4	24/39	61.5
Mean, Uncontrolled studies		7.8	1,278	4	274	29.8					
Controlled studies											
MacLean et al. (26)	1965	217	400–?	1–> 2	400	38	102	48	67	115/217	53
Comparison[3]		121				38	21	45	55	100/121	83
Osmond et al. (30)	1965	28	300–400	2	150–200	3	10	1	17	18/28	64.3
						6	7	10	8	18/25	72
						12	7	10	8	18/25	72
Control		34				3	15	1	15	16/31	51.3
						6	15	6	9	15/30	50
						12	12	11	7	18/30	60
Van Dusen et al. (45)	1967	29	400–1,200	1–3	400	6	3.71				
						12	3.97				
						18	3.97				
Control						18	4.03				

Average Score on Scale 3 = NC, 4 = 1

LSD total	274	300–1,200	150–450						
Average	91		325	19.7	126	69	100		57.5
Control total	167								
Average	55			20.7	42	18	31		53.8[4]

1 Malvarian alcoholics not treated with nicotinic acid.
2 Malvarian alcoholics pretreated with nicotinic acid.
3 Non-alcoholic psychiatric patients.
4 Computed by exclusion of *MacLeans* non-alcoholic comparison group.

Table IV. Summary of the 4 basic types of study on LSD in alcoholism

Type of study	Number of studies	Number of patients (mean/ study)	Number of controls (mean/ study)	Dosage Range μg (mean dose)		Follow-up range, months (mean)		Improved, %	
				single-dose	Multiple-dose total	patients	controls	patients	controls
1. Single-dose									
a) without controls	13	408 (31.4)	–	50–450 (233,9)	–	0–55 (19.4)	–	53	–
b) with controls	5	384 (76.8)	170 (34)	200–800 (342)	–	3–18 (9.9)	3–18 (10.2)	75	43.7
2. Multiple-dose									
a) without controls	4	39 (7.8)	–	100–800 (274)	100–6,400 (1,278)	3–65 (29.8)	–	61.5	–
b) with controls	3	274 (91)	167 (55)	150–400 (325)	400–ca. 1,200[1] (?)	3–38 (19.7)	3–38 (20.7)	57.5	70.5

1 *MacLean et al.* (26) did not report his maximal total dose.

MacLean et al. (26) showed a higher percentage of improvement in his comparison group than his LSD-treated group (table III). However, the comparison group consisted of non-alcoholic psychiatric patients. *Van Dusen et al.* (45) had a higher improvement in his control than in the LSD group. The overall improvement rate for the LSD group was 57.5 *versus* 53.8 % for the control group, omitting the non-alcoholic comparison group of *MacLean et al.* (26).

c) Miscellaneous Studies

Eight studies (5, 8, 16, 23, 31, 39, 46, 47) of LSD in alcoholic patients do not fit the categories discussed above. These findings are of great heuristic value, however, and therefore will be individually discussed without an attempt at tabulation since they are heterogeneous in methodology and results. Two groups of investigators, *Smart et al.* (39) and *Hollister et al.* (16), gave an active drug to their control groups, *Smart et al.* (39) using 60 mg of ephedrine, and *Hollister et al.* (16) 60 mg of amphetamine. *Smart et al.* (39) gave an 800 µg single dose of LSD, while *Hollister et al.* (16) used 600 µg of LSD. Neither group found a significant difference in improvement between LSD and control groups which took psychoactive drugs other than LSD.

Bryce (5) gave an unspecified dose of LSD to 113 patients, but did not evaluate these patients himself on follow-up. 19 of 75 patients (25 %) claimed improvement from LSD therapy when they were sent a questionnaire. *Ludwig et al.* (23) gave 3 µg of LSD/kg body weight to a group of alcoholics without any concomitant psychotherapy. The overall improvement in this group did not differ from controls without LSD or patients who received LSD and psychotherapy. *Ditman et al.* (8) gave 100 µg of LSD to 70 patients in a group setting with 20 patients who had experienced delirium tremens serving as control. Card sort showed that the LSD experience had characteristics similar to delirium tremens.

Ramsay et al. (31) reported an increase in religious attitudes and beliefs after giving an unspecified amount of LSD to 47 patients. *Vojtechovsky et al.* (46), in 1966, compared the effects of 200 µg of LSD, 40 mg of benactyzine, or placebo in 13 patients. The LSD pattern of delirium showed depersonalization, derealization, and limb paresthesias, while the benactyzine group had trivial delirium and amnestic syndrome. In 1969, the same investigators (47) gave 200 µg of LSD and 40 mg of benactyzine to 16 alcoholics. Eleven of the 16 subjects developed non-alcoholic psychoses.

General Comments

Final tabulation of all studies reviewed here shows that 75 % of the patients receiving a single dose of LSD in controlled experiments showed improvement after 9.9 months follow-up, whereas 44.1 % of their control groups were improved at 10.2 months follow-up. The results in uncontrolled single-dose LSD

studies showed 53 % improved at 19.4 months follow-up. Of the multiple-dose LSD patients, 57.5 % were improved at 19.7 months follow-up, whereas 53.8 % of their control groups were improved at 20.7 months follow-up. Discrepancies in improvement might be related to longer follow-up; the longer the follow-up, the less the improvement. However, this hypothesis is not borne out in multiple-dose LSD patients. In the uncontrolled studies, 61.5 % were improved at 27.8 months follow-up, whereas 57.5 % of the multiple-dose LSD patients in the controlled studies were improved at 19.7 months.

There was no obvious correlation between length of alcoholism and improvement. This is a very weak generalization since only 8 groups of authors (6, 12, 27, 29, 32, 43, 45) reported length of alcoholic illness prior to LSD treatment. The mean length of alcoholic illness was 11.6 years (specifically, 7.8, 8.05, 10.0, 11.6, 12.1, 14, 14.3, and 15 years). This treatment was, therefore, tried on a chronic population that might be refractory to treatment. It is interesting to note that none of the authors included any patients who had been drinking for less than 7 years. It probably takes an average of 11.6 years in the natural history of alcoholism to bring these patients to formal psychiatric treatment.

There was a correlation between total dose and number of patients showing improvement only in the patients from the uncontrolled, multiple LSD-dose studies (1, 10, 45). 86 % improved when the total dose ranged between 600 and 6,400 μg, 66 % when the dose was 100–300 μg, and 33 % when the dose was 215–1,450 μg. No formal studies have adequately explored the dose-response relationships between administered LSD and therapy outcome. It is probable that in order to be meaningful, such investigations will either have to be carried out by the same group of investigators with a consistent methodology, or await the development of a standard set of criteria for evaluation.

In the uncontrolled single-dose LSD studies without control, a dosage range of 100–200 μg tended to be reported as most effective. Seven of 8 groups of investigators using this dosage range reported improvement in more than 60 % of their patients.

Discussion

Few if any meaningful generalizations can be made out of the published studies of LSD therapy in alcoholism. Three main factors may contribute to the existing confusion about the efficacy of this treatment: (a) the investigators, (b) the patients, (c) experimental design.

a) The Investigators

The only accepted method to control for the bias of investigators is the double-blind method. Of course, this is difficult if not impossible to apply with a drug such as LSD, since the obvious clinical signs of LSD ingestion will give it

away immediately. Investigators could have used independent blind judges to interview patients on follow-up without revealing treatment modality to the judges. This can be achieved, for example, by having the panel of judges go over a censored videotape of patient interviews.

Some investigators (6, 15) point out that patients should not be exposed to LSD if the investigators themselves have not taken the drug and thus gained first-hand experience with its effects. To our minds, this renders LSD therapy a cult rather than a scientific treatment. Unwittingly, this attitude could have also contributed to the lay abuse of LSD. More objective data can be collected if the investigators themselves do not lose track of their roles by taking LSD themselves.

b) The Patients

Alcoholics are a heterogeneous group with a variety of personality conflicts, divergent social backgrounds, and sometimes complex medical complications secondary to alcoholism. No investigators have tried to control these factors.

The severity of the alcoholic illness sometimes is measured in length of years of alcoholism or in amount of ethanol imbibed per day, and – more accurately – in the degree of disruption of the psychosocial adjustment of the patient. Only the length of alcoholism was taken into account, and by only 8 groups of investigators. As mentioned previously, they tended to take the chronic recalcitrant alcoholic who failed other treatments.

The motivation of the alcoholic is a very crucial factor in determining the outcome of treatment. If an alcoholic seeks help on his own, he will be more willing to invest his time and emotional energy in the therapy. Alcoholics who are not self-referred but come to treatment under duress from their family, employers, or friends may have a totally different response to treatment. In none of the studies reviewed was the motivation of the alcoholic taken into account in designing the study and in arriving at the outcome.

Since informed, signed consent is necessary for such studies, volunteer alcoholics had to be recruited. The motivation of seekers of such therapy might have contaminated the results. (For example, it might appeal to some in a drug-oriented subculture.)

c) Experimental Design

Aside from single or multiple doses and variable dosage levels, numerous other factors enter into adequate study design. Only *Ludwig* (22) based dose level on body weight of his patients and assigned subjects randomly to LSD or control groups.

The treatment setting itself is controversial. Some authors (6, 18, 21, 25, 29) emphasized the need for an environment free from distraction and conducive to introspection, with music and art objects available.

An additional question is who should be present with the alcoholic patient during LSD treatment? A nurse, an alcoholic counselor, a psychiatrist, a social worker, and psychologists have been present in different investigations. In a given investigation, no attempt was made to control this factor by having the same person conduct LSD sessions for all patients.

Most important are the criteria for improvement. Some investigators have used the rigid Alcoholics Anonymous model of complete abstinence as the *sine qua non* of improvement, while others have used moderation in drinking, improvement in family relationships, vocational attainment, and even increased intrapsychic insight as measures of successful outcome. These less rigid criteria of improvement may reflect the growing acceptance in our society of addictive states (e.g., the methadone treatment of heroine addicts, the clamor for legalization of marijuana). Alcoholism itself may have become more acceptable, at least in terms of there being more units for alcoholic treatment in general hospitals, medical insurance coverage available, and lifting of the legal definition of public drunkenness. Successful treatment of alcoholism should render the alcoholic a social drinker, since alcohol is an established intoxicant in our society. An analogy to obesity is in order: The obese are not asked to abstain from food but to moderate their intake. The intent of LSD administration varies from producing a person who can function socially, while still consuming moderate amounts of alcohol, to demanding complete abstinence as fulfilling the criterion of 'much improved'. Perhaps entirely too much emphasis has been placed on producing 'much improved' rather than 'improved' patients, and that further work in the area of LSD and alcoholism should be aimed toward evaluating whether the drug aids in the rehabilitation of a socially afunctional alcoholic to a person who, though still alcoholic and consuming alcohol, does so to a lesser, manageable degree, and can function as a socially productive being.

Finally, the interaction of LSD therapy with the accepted medico-psychosociological treatment of alcoholism would have been a fascinating area to explore; albeit a difficult one. LSD could play a therapeutic role in addition to the established treatments, thus giving an added therapeutic advantage.

Note

In computing overall totals for each improvement category, and the overall improvement percentage, we regarded each evaluation (e.g. 6, 12, 18 months) to be independent. Thus the totals were arrived at by adding all patients in each improvement category at all lengths of follow-up; computing an average for each category; and the computing an average follow-up length.

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