

CSF 5 - HIAA IN VIOLENT AND NON-VIOLENT SUICIDE ATTEMPTERS

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ABSTRACT

Many studies have reported involvement of monoamine neurotransmission in suicide through measurement of serotonin and its main metabolite, 5-HIAA, in brain of suicide victims and in CSF of suicide attempters. 23 non-depressed non-psychotic suicide attempters and equal number of controls were selected, and all the subjects were screened on Cornell Medical Index. Suicide attempters were assessed on Risk-Rescue Rating Scale and were divided into non-violent suicide attempters (N= 12) and violent suicide attempters (N=11). CSF of all subjects was collected by lumbar puncture and CSF 5-HIAA was measured by high performance liquid chromatography with electro-chemical detector. Risk-rescue rating score was significantly higher in violent suicide attempters as compared to non-violent suicide attempters. Mean CSF 5-HIAA was significantly lower in suicide attempters as compared to normal controls. Mean CSF 5-HIAA was significantly lower in violent suicide attempters as compared to non-violent suicide attempters.

Key-words: CSF 5-HIAA, suicide, non-violent suicide attempters, violent suicide attempters

Suicide attempt is defined as a deliberate, self inflicted injury, regardless of the lethality, provided that the subject was aware of the risk of dying.

The role of biological factors in the chain of events that terminates in a suicide is now a well established fact. Recent research has identified two clusters of biological factors that tend to correlate with suicide behaviour, namely variables associated with monoaminergic neurotransmission and variables with certain neuroendocrine function.

The most convincing evidence for an involvement of monoamine in suicide, stems from measurement of serotonin and its main metabolite, 5-HIAA in brain from suicide victims and in CSF from patients who have attempted suicide.

Van Praag et al. (1970) reported the occurrence of diminished post-probenecid accumulation of 5-HIAA in CSF in depression. Asberg et al. (1976) confirmed the findings of a low CSF 5-HIAA subgroup in depression and added the important observation that the low CSF 5-HIAA group contained significantly more suicide attempters than the group of depressives with normal CSF 5-HIAA.

Palaniappan et al. (1983) also found negative correlation between CSF 5- HIAA level and total score of Hamilton Rating Scale for Depression. He concluded that CSF 5-HIAA level would decrease when patient attempted suicide during depression.

Similarly, in our previous work (Trivedi et al. 1992) we found significant lowering of CSF 5-HIAA levels in suicide attempters. In these studies three groups were taken, non-depressed non-psychotic, depressed, and normal controls. Maximum lowering of CSF 5-HIAA was detected in depressed suicide attempters, although lowering of CSF 5-HIAA was also significant in non-depressed non-psychotic suicide attempters as compared to normal controls.

Many workers like, Asberg et al. (1976), Brown et al. (1979), Transkman et al. (1981), Banki et al. (1984), Pultick and Van Praag (1989) found low CSF 5-HIAA in violent suicide attempters than in non-violent suicide attempters.

Van Praag in 1991 (by using Risk Rescue Scale) concluded that low CSF 5-HIAA also relates strongly to suicide intent.

Linnoila et al. (1983), Virbbuncen et al. (1987)

showed lowering of CSF 5 - HIAA level in violent offenders (subjects with personality disorder or having impulsive behaviour), and male arsonists. Concluding that suicide attempt itself is in some way related to lowering of CSF 5-HIAA level. Further, literature is not very rich, especially in this part of the continent, regarding the relationship between serotonin and suicide attempt in non psychotic subjects.

The present study has been conducted in a sample of non-depressed non-psychotic subjects who have history of recent suicide attempt, with the aim "To compare the CSF 5-HIAA levels in non-violent and violent suicide attempters."

MATERIAL AND METHOD

Sample was drawn from hospitalized patients on specified beds in the departments of Medicine and Surgery of King George's Medical College, Lucknow.

The sample comprised of two groups :-

- (i) Non-depressed non-psychotic suicide attempters.
- (ii) Normal controls.
- (i) **Non-depressed non-psychotic suicide attempters:**

All consecutive patients admitted on specified beds in the department of Medicine and Surgery during the period of study (1.3.94 to 30.11.94) with history of suicide attempt were considered for this study. Only those patients who fulfilled the following selection criteria were included in the study.

The inclusion criteria were -

- (a) Age between 17 to 45 years.
- (b) Less than 10 YES responses on Cornell Medical Index (CMI) (Section M to R).
- (c) Written consent for the study including lumbar puncture was obtained from the patient/relative.

The exclusion criteria were -

- (a) Presence of any depressive or psychotic disorder according to ICD-10.
- (b) Any serious physical illness requiring medication which could affect CSF 5-HIAA value.

- (c) History of alcohol or drug abuse during the last 6 months.
- (d) Evidence of mental retardation, organic brain syndrome or epilepsy.
- (f) Pregnancy or lactation.

(ii) **Normal controls :**

This group comprised of subjects admitted in the department of surgery who were being operated under spinal anaesthesia and fulfilled the following criteria.

The inclusion criteria were -

Age from 17 to 45 years, less than 10 YES responses on CMI (Section M to R), and consent for the study including lumbar puncture.

The exclusion criteria were -

Presence of any psychiatric disorder, according to ICD-10, of any serious physical illness requiring medication which could affect CSF 5-HIAA levels. Presence of family history of psychosis, depression, alcoholism or suicide. Presence of pregnancy or lactation.

Subjects selected in non-depressed non-psychotic suicide attempters group were further divided into two groups :

- a) **Non-violent suicide attempters :** Patients with history of suicide attempt by non-violent means i.e. drug overdosage and superficial wrist cuts.
- b) **Violent suicide attempters :** Patients with history of suicide attempt by violent means e.g. jumping from height, burn, stab injury, shooting and deep wrist cuts.

Similar classification of non-violent and violent suicide attempt has also been done by Weisman and Worden (1972).

Following instruments were administered -

1. Screening schedule and Cornell Medical Index (CMI) M to R section.
2. Semistructured proforma prepared for the present study.
3. Risk-Rescue Rating Scale (Weisman and Worden, 1972).
4. ICD - 10.

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Patients admitted on specified beds in the departments of Medicine and Surgery with a history of suicide attempt were closely observed for the first week. After their settlement in the ward an attempt was made to establish rapport with them as well as with their close relatives (especially first degree relatives). Thus screening schedule including CMI (Section M to R) was administered to all these patients. Patients fulfilling the selection criteria were requested to give consent for the study following which detailed physical and psychiatric evaluation was done and only after preparing them well for lumbar puncture, CSF collection was done. In collecting all this information and CSF sample at least 3 to 5 visits were made for each patient.

In all subjects of drug overdose non-violent suicide attempter group the CSF was collected only after two weeks duration from the day of suicide attempt so as to minimise any possible effect of drug overdose on serotonin levels. Whereas for the patients with violent suicide attempt lumbar puncture was planned between 1 to 2 weeks from the day of their suicide attempt.

All the patients of non-violent, violent and control group were instructed not to take food items like tea, coffee, chocolate, bananas, plums, nuts and eggs till the period of their CSF collection as these items are known to effect serotonin metabolism (Moja et al., 1979; Furnstorm et al., 1971; Fuennayer, 1979).

Patients were kept fasting overnight and lumbar puncture was carried out between 8 A. M. to 10 A. M. to avoid diurnal variation in standard left lateral decubitus position between L₃ and L₄ ventricular lumbar gradient. From each subject 1/2 ml of CSF was collected in plastic tubes from an atraumatic lumbar puncture. These samples were stored immediately in ice box and were analysed on the same day or stored at -70° C and analysed within a week.

Each CSF sample was assayed by high performance liquid chromatography with electrochemical detector according to the method of Kim et al. (1977).

Student's 't' test was used for determining statistical significance between means of two groups taken at a time. This test was carried out for deter-

mining significance of mean values of CSF 5-HIAA between following groups :

- i) Suicide attempters vs. Control group.
- ii) Non-violent suicide attempters vs Control group.
- iii) Violent suicide attempters vs. Control group.
- iv) Violent suicide attempters vs. Non-violent suicide attempters.

Pearson's product moment correlation coefficient (r) was used for calculating correlation between:

- i) CSF 5-HIAA and method of suicide attempt.
- ii) CSF 5-HIAA and Risk Rescue Rating Score.

RESULTS

Suicide attempter group comprised of 23 subjects who fulfilled the selection criteria and equal number of age-group matched controls were selected for the study. Most of the subjects in both groups were below 30 years of age (78.3% in suicide attempter group and 82.6% in control group). Majority of the subjects were married, educated upto high school or more and coming from lower socio-economic class.

12 subjects attempted suicide by non-violent means (celphos = 41.65%, diazepam = 4% and organophosphorus compounds = 25.02%) while 11 subjects resorted to violent methods (burning = 45.45%, hanging = 36.36% and stabbing = 18.09%).

Mean risk-rescue rating score in suicide attempters was 53.0±12.08 and it was significantly higher ($p < .01$) in violent suicide attempters (60.98±10.69) as compared to non-violent ones (45.70±11.23), meaning that the intention to commit suicide is higher in violent suicide attempters.

Table - 1 shows the comparison of CSF 5-HIAA levels in suicide attempters and normal controls. There was a significant ($p < 0.001$) lowering of mean CSF 5-HIAA levels in suicide attempters (24.90±8.58 ngm/dl) as compared to the control group (63.13±5.42 ngm/dl.).

TABLE 1

COMPARISON OF CSF 5-HIAA LEVELS
IN SUICIDE ATTEMPTERS AND
NORMAL CONTROLS

Group	Mean (ngm/dl)	S.D. (ngm/dl)	Range (ngm/dl)
Suicide attempters (N=23)	24.90	8.58	14.0 to 40.2
Control (N=23)	63.13	5.42	51.5 to 72.5

$t = 18.07$; d.f. = 44; $p < 0.001$

Table - 2 shows the relationship between risk-rescue rating scores and mean CSF 5-HIAA level in suicide attempters. The correlation coefficient between risk-rescue rating score and CSF 5-HIAA level was found to be -0.95 which is highly significant ($p < 0.001$). The correlation coefficient was negative which means that as the risk rescue rating score increases, CSF 5-HIAA level decreases.

TABLE 2

RELATIONSHIP BETWEEN RISK RESCUE
RATING SCORES AND MEAN CSF 5-HIAA
LEVEL IN SUICIDE ATTEMPTERS

Group	Mean (ngm/dl)	S.D. (ngm/dl)	Range (ngm/dl)
Risk-rescue rating score (N=23)	53.00	12.08	30.0 to 80.0
CSF 5-HIAA levels (N=23)	24.90	8.58	40.0 to 40.2

$r = -0.95$; $p < 0.01$

Table - 3 shows a significant ($p < 0.001$) negative correlation between risk-rescue rating score and CSF 5-HIAA level in both non-violent and violent suicide attempters meaning that higher the risk rescue rating score, lower is the CSF 5-HIAA level i.e. stronger the intent of suicide, more lowering of the CSF 5-HIAA level.

TABLE 3

RELATIONSHIP BETWEEN RISK RESCUE
RATING SCORE AND CSF 5-HIAA LEVEL
IN NON-VIOLENT AND VIOLENT
SUICIDE ATTEMPTERS

Group	Mean (ngm/dl)	S.D. (ngm/dl)	Range (ngm/dl)
Non-violent (N=12) Risk-rescue rating score	45.70	11.23	30.0 to 66.0
CSF 5-HIAA level	29.82	7.76	17.5 to 40.2
$r = -0.90$; $p < 0.001$			
Violent (N=11) Risk-rescue rating score	60.98	10.69	50.0 to 80.0
CSF 5-HIAA level	19.51	5.71	14.0 to 27.2

$r = -0.95$; $p < 0.001$

Table - 4 shows a significant ($p < 0.001$) lowering of mean CSF 5-HIAA levels in non-violent suicide attempters (29.82 ngm/dl) as compared to control group (63.13 ngm/dl). There was also a significant ($p < 0.001$) lowering of mean CSF 5-HIAA level in violent suicide attempters (19.51 ngm/dl) as compared to control group (63.13 ngm/dl). Further, there was a significant ($p < 0.01$) lowering of mean CSF 5-HIAA level in violent suicide attempters (19.51 ngm/dl) as compared to non-violent suicide attempters (29.82 ngm/dl).

TABLE 4

COMPARISON OF MEAN CSF 5-HIAA
LEVELS BETWEEN NON-VIOLENT AND
VIOLENT ATTEMPTERS AND CONTROLS

Group	Mean (ngm/dl)	S.D. (ngm/dl)	Range (ngm/dl)
A. Non-violent suicide attempters (N=12)	29.82	7.76	17.5 to 40.2
B. Violent suicide attempters (N=11)	19.51	5.71	14.0 to 27.2
C. Control group (N=23)	63.13	5.42	51.5 to 72.5

A vs. C : $t = 14.85$; d.f. = 33; $p < 0.001$

B vs. C : $t = 21.59$; d.f. = 32; $p < 0.001$

A vs. B : $t = 3.60$; d.f. = 21; $p < 0.01$

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DISCUSSION

Although various markers of serotonergic activity in the brain are known and have been studied in relation to suicidal behaviour, the most commonly studied marker is CSF 5-HIAA. For prediction of suicide, studies have to be antemortem (Asberg et al., 1986) and with the help of CSF studies, brain is indirectly assessed. CSF is a far better representative of brain functioning than blood or urine (Traskman et al., 1981). 5-HIAA is by far the major metabolite of serotonin and its levels in the CSF have been shown to correlate with serotonergic function in the brain (Traskman et al., 1984).

Reason of choosing this non-psychotic non-depressed suicide attempters as a study sample is to test the hypothesis (Traskman et al., 1981) that suicide attempt itself is in some way related to alteration of CSF 5-HIAA level.

An attempt was made to exclude the factors which have known influence on CSF 5-HIAA level. Since age affects the level (Bowers and Gerebode, 1968; Gottfried et al., 1971), controls were group-matched for age with suicide attempters. Diurnal and circadian rhythm influences the CSF 5-HIAA level (Nicoletti et al., 1981; Carlsson et al., 1980) therefore, CSF was collected at a fixed time (between 8 a.m. to 10 a.m.) in all subjects. All subjects were instructed not to take food items like tea, coffee, chocolate, banana, nuts and plums which can affect the CSF 5-HIAA level (Moja et al., 1979; Fuennayer, 1979). Moreover, the sample was collected after overnight fasting. Pregnant/lactating females were excluded due to known alteration of serotonin metabolism in these conditions (Fotherby et al., 1963; Post et al., 1973). Other factors affecting CSF 5-HIAA level which were excluded were use of drugs like dexamethasone (Banki and Arato, 1981); isoniazid (Zeller et al., 1955) and beta blockers (Drayer, 1987), alcohol or drug abuse during last six months (Banki et al., 1984; Traskman et al., 1981) and presence of mental retardation, organic brain syndrome or epilepsy (Pare et al., 1960; Belendick et al., 1980). Psychiatric illness was ruled out in all control subjects as all other exclusion criteria of this group were same as those of suicide attempters.

At least 1 ml of CSF was collected in all subjects for correct estimation of CSF 5-HIAA level

(Curzon et al., 1980; Banki and Molnar, 1981). CSF was collected with the same bore of needle in left lateral decubitus position in all subjects so as to avoid alteration of CSF 5-HIAA because of ventricular lumbar gradient (Nordin et al., 1982).

Subjects, selected in non-depressed non-psychotic suicide attempter group were further divided into two groups (a) non-violent suicide attempters and (b) violent suicide attempters.

The findings of low CSF 5-HIAA level in suicide attempters as compared to normal controls and more significant lowering in violent suicide attempters as compared to non-violent suicide attempters could be explained as follows :

1. 5-HIAA is by far the major metabolite of serotonin, and its level in the CSF has been shown to correlate with serotonergic function in the brain.
2. Further, Mann et al. (1989) concluded that "some, but not all, studies reported low levels of 5-HIAA in brainstem of suicide victims. The reduction in brain levels of 5-HT or 5-HIAA was independent of the specific psychiatric diagnosis and therefore appeared to correlate with suicidal behaviour."
3. Stanley and Stanley (1989) found significant increase in 5-HT₂ binding in the frontal cortex of suicide victims.
4. Low levels of CSF 5-HIAA have been reported in subjects with impulsive and aggressive behaviour (Brown et al., 1979; Brown et al., 1982; Bioulac et al., 1980; Linnoil et al., 1983). Since suicide is also a type of impulsive behaviour, it can be inferred that lowering of CSF 5-HIAA is related with suicidal behaviour.

Thus, our study findings support this serotonin hypothesis of suicide.

In 1972, Weisman and Worden developed risk-rescue rating scale to evaluate the intent of suicide attempters, because any suicide attempt entails a calculated risk, but as any attempt must also take place in a psychosocial context or within a specific set of circumstances, survival of patient may depend upon the resources for rescue as well as upon the specific form of attempt.

Van Praag *et al.* (1986) used this rating scale in 44 patients admitted for suicide attempt. Twenty three had used violent and the others non-violent methods. The violent group had slightly but not significantly higher risk-rescue scores than the non-violent group. According to them violent method is not an adequate indicator of the seriousness of the attempt as measured with the risk-rescue rating scale. Later on Van Praag (1991) again used this risk-rescue rating scale and concluded that severity of method is not a parameter of the strength of the self destructive impulses. Low CSF 5-HIAA was found to correlate with severity of intent, not with the severity of the attempt. Whereas in our study there is a significant difference in risk-rescue scores between violent and non-violent suicide attempters (Table 4). So in our view risk-rescue rating scale could further substantiate that those attempting by violent methods of suicide are having more serious intentions to commit suicide as compared to non violent suicide attempters.

In our study the risk-rescue rating score of all those who attempted suicide (N=23) was 53.00 ± 12.08 and there is a significant increase ($p < 0.01$) of mean risk-rescue rating score in violent suicide attempters (60.98 ± 10.69) as compared to non-violent suicide attempters (45.70 ± 11.23) meaning thereby that in the violent suicide attempters the intention of the patients to commit suicide is likely to be higher.

An effort was made to establish relationship (if any) between risk-rescue rating score and CSF 5-HIAA levels. In suicide attempter group it was found to be significantly negative ($p < 0.001$; $r = -0.95$) meaning that higher the risk-rescue rating score, lower is the CSF 5-HIAA level. Several other workers such as Piltick *et al.* (1989), Van Praag *et al.* (1986) and Van Praag (1991) have observed similar results in their studies.

Further, when relationship between risk-rescue rating score and CSF 5-HIAA level was studied (Table 4), both with violent and non-violent separately, it was found that the level of significance was correlated negatively to highly significant levels. This observation substantiates our finding that violent and non-violent attempt per se demonstrate the lowering of CSF 5-HIAA value, and risk-rescue rating

score further confirms it.

Lastly, it can be concluded that markers of central serotonergic activity, especially CSF 5-HIAA, may be one of the strongest biological predictors of suicidal behaviour.

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