Original Article

A Study of Patterns of Platelet Counts in Alcohol Withdrawal

Devavrat G. Harshe, Harshal Thadasare[1], Sagar B. Karia[1], Avinash De Sousa[1], Rashmin M. Cholera[2], Sanjiv S. Kale[2], Omkar S. Mate[2], Nilesh Shah[1]

ABSTRACT

Aims: This study aimed to evaluate the patterns of platelet counts during the course of alcohol withdrawal and its relationship if any with liver enzymes. **Methodology:** Forty consecutive patients, with alcohol dependence according to the Diagnostic and Statistical Manual of Mental Disorders-fourth edition, Text Revision criteria, willing for a 10-day inpatient detoxification program and presenting within 12 h of the last consumption of alcohol were recruited in the study. Details about the diagnosis and alcohol consumption patterns were assessed with a detailed psychiatric interview. After admission, routine investigations (complete blood counts [CBCs] and liver function tests) were sent and records were kept. CBC was sent for platelet counts on the 2nd, 4th, 6th, 8th, and the 10th day of alcohol withdrawal. **Results:** Nearly 40% of the patients developed delirium tremens (DT group) and rest had an uncomplicated alcohol withdrawal (ND group). Platelet counts at baseline and all the 4 days of collection were significantly lower in DT group than the ND group. Platelet counts increased gradually from baseline till 10th day of alcohol withdrawal, mean increase in platelet counts being 88.61 ± 11.60% (median: 61.11%, range [23.41–391.23%]). Platelet counts in 63% of the patients showed a drop on the 4th day of withdrawal before rising till the 10th day of alcohol withdrawal. Platelet counts were not affected by liver enzymes or other alcohol consumption patterns. **Conclusions:** Transient thrombocytopenia and reverse thrombocytosis during alcohol withdrawal are associated with an initial drop in platelet counts. The synchrony between the drop and the onset of DT needs to be evaluated.

Key words: *Delirium, reverse, thrombocytopenia, transient*

INTRODUCTION

Alcohol withdrawal syndrome (AWS) is a clinical entity which ensues after a sudden cessation of or reduction in quantity of absolute alcohol consumed daily in those who are dependent on alcohol. AWS has a self-limiting course in most cases, 5%–20% of patients however develop a complicated AWS[1] with alcohol withdrawal seizures or delirium tremens (DT).

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Department of Psychiatry, Dr. D. Y. Patil Medical College, Kolhapur, [1]Department of Psychiatry, Lokmanya Tilak Municipal Medical College, [2]Department of Psychiatry, Dr. D. Y. Patil Medical College, Navi Mumbai, Maharashtra, India

Address for correspondence: Dr. Devavrat G. Harshe
Department of Psychiatry, Dr. D. Y. Patil Medical College, Kolhapur - 416 008, Maharashtra, India. E-mail: devavrat.harshe@gmail.com

Evidence suggests that low platelet count has a good predictive power in predicting the development of DT[2-6] in cases of AWS. Kim *et al*., 2015,[3] Berggren *et al*., 2009,[4] Eyer *et al*., 2011,[5] and Monte *et al*., 2009,[6] demonstrated that platelet count in patients with DT was in thrombocytopenia range ($<150 \times 10^9$/L) whereas Huang *et al*., 2011,[2] showed a nonsignificantly lower platelet count in DT group as compared to ND group. A recent systematic review and meta-analysis[7] substantiated this observation. Most of the authors hypothesized that chronic alcohol consumption, heavy alcohol intake, recent binging, and comorbid liver cirrhosis may be the causative factors for thrombocytopenia during alcohol withdrawal.

Interestingly, with the exception of Berggren *et al*., 2009,[4] who showed a significantly higher aspartate transaminase (AST) levels in patients with DT compared to those without DT, neither any study nor the meta-analysis showed any significant difference between DT and non-DT groups for AST and alanine transaminase (ALT)! Thus, we planned this study to evaluate the stability of platelet count during the course of alcohol withdrawal and its relationship if any with serum liver enzymes.

METHODOLOGY

Sample

The study was cleared by the Institutional Ethics Committee. Eighty consecutive patients diagnosed with alcohol dependence and presented within 12 h of their last drink were screened. Patients with (1) dependence on any other substance except nicotine, (2) a history of traumatic brain injury, peripheral vascular disease, past myocardial infarction and cerebrovascular accidents, comorbid psychosis and mood disorder, and alcohol withdrawal seizure during the past alcohol withdrawal, and (3) patients taking anti-platelet/anti-coagulation medications were excluded from the study. Patients willing for a 10-day inpatient detoxification program were recruited in the study after a written and informed consent ($n = 44$). Patients who developed alcohol withdrawal seizure during the course of alcohol withdrawal ($n = 4$) were excluded from the study.

Method

Patients ($n = 40$) were admitted after discussing the diagnosis and treatment strategy with a consultant (assistant professor and above). Routine investigations (complete blood count [CBC]; liver function tests; and renal function tests) were sent early morning on the 2nd day of alcohol withdrawal. Patients were started on tablet lorazepam (8–12 mg/day) in divided doses and injection thiamine 100 mg 12 hourly. Provision was made for (1) injectable lorazepam in cases of a seizure and DT, (2) tablet zolpidem (10 mg) for insomnia, and (3) tablet escitalopram for depressive symptoms during the course of AWS although they were not administered on any patient enrolled in the study. Patients were observed round the clock by on-duty residents, and an orientation chart was maintained. Dose of lorazepam was adjusted according to the clinical status, orientation, and higher functions and vital signs. CBC for platelet counts was sent on alternate days (day 2, day 4, day 6, day 8, and day 10) of alcohol withdrawal. Patients were shifted on oral multi-vitamin supplementation from day 5 of alcohol withdrawal. Lorazepam was tapered gradually from 6th day onward based on the clinical improvement and stopped completely by the time of discharge. Patients were prescribed appropriate medications for relapse prevention based on clinical status, affordability, and tolerability profile.

Data analysis

Data were pooled in a spreadsheet program and analyzed. Dichotomous variables were assessed with Chi-square test and 2×2 cross-tabs analysis. Quantitative variables (platelet counts on 5 days of blood collection) were compared with independent samples *t*-test. Pearson's correlation was used to study relationship between platelet counts, serum liver enzymes, and alcohol consumption details. Statistical significance was assumed at $P < 0.05$.

Demographic details

Sample of 40 was an all-male sample with a mean age of 38.47 ± 9.86 years (range: 21–56 years). Mean age at the onset of alcohol consumption was 21.27 ± 4.70 years. Nearly 63% of the patients (25/40) were consuming country liquor (CL) at the time of this study and the rest were consuming whiskey. Almost 40% of the patients developed DT during the course of AWS.

Platelet counts in AWS

Nearly 30% of the patients showed thrombocytopenia. Platelet counts were significantly lower in DT group than ND group, on all five occasions. Mean platelet count on day 4 was lower than that of baseline in both DT and ND groups. Mean platelet counts showed a gradual rise on days 6, 8, and 10 of alcohol withdrawal. Nearly 63% (25/40) of the patients showed a drop in platelet counts on the 4th day of withdrawal followed by a rise whereas the rest (15/40) showed a continuous rise from 2nd day in platelet counts till 10th day of alcohol withdrawal. Mean increase in the platelet counts on day 10 from baseline was 88.61 ± 11.60% (median: 61.11%; range [23.41–391.23%]). DT group showed a significantly higher increase in platelet counts as compared to ND group on the 8th (82.24 ± 56.54 [DT] vs. 38.29 ± 16.84 [ND]%, $Z = -2.457$, $P = 0.013$)

and the 10th day (151.77 ± 101.77 [DT] vs. 61.54 ± 32.08 [ND]%, $Z = -2.678$, $P = 0.007$) of AWS. Incidence of the initial drop in platelet counts did not differ between DT and ND groups (68 [DT] vs. 59 [ND]%, $\chi^2 = 0.444$, $P = 0.372$).

Factors affecting platelet counts

Platelet counts [Table 1] did not differ significantly in groups (1) with and without elevated liver enzymes, (2) consuming CL and Indian-made foreign liquor (IMFL), and (3) with duration of alcohol dependence (DAD) <10 and >10 years. The incidence of the initial drop in platelet counts was not affected by (1) the alcoholic beverage (74 [CL] vs. 56% [IMFL], $\chi^2 = 1.202$, $P = 0.241$), (2) course of alcohol withdrawal (69 [DT] vs. 60 [ND]%, $\chi^2 = 0.444$, $P = 0.372$), (3) serum AST (64 [elevated] vs. 60 [normal], $\chi^2 = 0.012$, $P = 0.597$), and (4) serum ALT levels (60 [elevated] vs. 66 [normal], $\chi^2 = 0.181$, $P = 0.465$). Platelet counts did not show a significant correlation with liver enzymes, age, and DAD [Table 2].

DISCUSSION

This study observed that platelet counts are not stable during the course of alcohol withdrawal. Platelet counts show a gradual rise from baseline till the end of alcohol withdrawal, a phenomenon which has been described as reverse thrombocytosis (RT) in literature. We also found that, in a large proportion of patients, platelet counts show a drop below the baseline in the first half of alcohol withdrawal (day 4), followed by a gradual rise till the 10th day of withdrawal. Fink and Hutton, 1983 ($n = 18$),[8] and Mikhailidis *et al*., 1986 ($n = 27$),[9] demonstrated RT in patients with alcohol withdrawal. Both studies, however, estimated platelet counts on day 1, day 8, and then on day 15 of alcohol withdrawal and did not report a decline in platelet counts on the 4th day. The 3rd and 4th days in the course of alcohol withdrawal have significant clinical attributes. It is the time when usually AWs and DT set in during AWS. Only further research can report whether this synchrony is of any clinical significance or is mere an accidental finding.

This study also supports the existing literature in showing that low platelet count in alcohol withdrawal is not associated with elevated liver enzymes. Thus, other possible causative factors need to be explored for the transient low platelet counts in alcohol withdrawal. Not only the count, but also platelets show structural as well as functional changes during the course of alcohol withdrawal. Platelets show a (1) decrease in platelet aggregation and thromboxane A2 secretion which returns to normal within 2 weeks of abstinence from alcohol,[8,9] (2) normalization of bleeding time during 2 weeks of abstinence,[9] and (3) a rise in platelet serotonin concentration[10] during the course of AWS among many other alterations. Thus, it can be hypothesized that alcohol withdrawal is associated with an array of changes in platelet structure and function. One of these changes is a transient thrombocytopenia (TT), which reverses eventually and in some cases, reverses after an initial drop in counts below the baseline count! The TT and the RT may be attributed to an initially increased platelet agreeability as shown by Fink and Hutton, 1983.[8] Berggren *et al*., 2009,[4] have hinted that thrombocytopenia at the onset of alcohol withdrawal is due to the cumulative hepatotoxic effects of alcohol. We, however, could

Table 1: Platelet counts (×10⁹/L) across various clinical and biochemical factors

	PLT2	PLT4	PLT6	PLT8	PLT10
Course of alcohol withdrawal					
DT	131.87 (58.81)[b]	129.06 (68.14)[b]	163.93 (67.33)[b]	214.62 (90.98)[b]	269.93 (87.91)[a]
ND	233.37 (68.49)	221.91 (71.13)	273.45 (71.91)	314.58 (73.12)	362.04 (76.85)
Alcoholic beverage					
IMFL	182.44 (93.45)[a]	181.96 (93.78)[a]	222.52 (101.110)[a]	262.68 (102.85)[a]	315.92 (99.20)[a]
CL	210.00 (54.74)	189.46 (63.92)	241.53 (61.74)	294.46 (75.34)	340.66 (80.75)
DAD					
0-10	215.33 (95.24)[a]	199.50 (104.31)[a]	253.91 (113.66)[a]	287.83 (126.29)[a]	333.00 (128.64)[a]
10-20	186.76 (83.99)	190.69 (76.92)	225.23 (79.65)	273.46 (79.76)	329.61 (86.51)
Elevated AST					
Yes	181.58 (88.27)[a]	174.37 (92.27)[a]	219.29 (103.30)[a]	258.70 (107.95)[a]	314.79 (106.94)[a]
No	197.14 (52.93)	186.92 (55.23)	234.07 (43.18)	289.28 (55.29)	330.78 (56.06)
Elevated ALT					
Yes	175.90 (88.79)[a]	167.95 (92.89)[a]	205.65 (102.90)[a]	256.55 (109.11)[a]	316.80 (108.29)[a]
No	200.00 (60.64)	191.27 (63.14)	245.94 (56.90)	284.88 (69.53)	325.00 (69.76)

[a]$P>0.05$; [b]$P<0.001$. Independent samples *t*-test, platelet counts on 5 days of collection across alcohol consumption details. PLT2 – Platelet count on day 2; PLT4 – Platelet count on day 4; PLT6 – Platelet count on day 6; PLT8 – Platelet count on day 8; PLT10 – Platelet count on day 10; DT – Patients who developed delirium tremens; ND – Patients who did not develop delirium tremens; IMFL – Indian-made foreign liquor; CL – Country liquor; DAD – Duration of alcohol dependence; AST – Aspartate transaminase; ALT – Alanine transaminase

Table 2: Platelet counts and various clinical variables

	PLT2	PLT4	PLT6	PLT8	PLT10
DAD	0.023^{NS}	0.029^{NS}	0.005^{NS}	0.000^{NS}	−0.018^{NS}
AAO	0.007^{NS}	−0.069^{NS}	−0.025^{NS}	−0.067^{NS}	−0.125^{NS}
AST	−0.091^{NS}	−0.133^{NS}	−0.123^{NS}	−0.041^{NS}	0.080^{NS}
ALT	−0.058^{NS}	−0.073^{NS}	−0.062^{NS}	−0.034^{NS}	0.066^{NS}

^{NS}Statistically nonsignificant ($P>0.05$). Pearson's correlation between platelet counts and various clinical and biochemical variables. DAD – Duration of alcohol dependence; AAO – Age at the onset of alcohol consumption; AST – Aspartate transaminase; ALT – Alanine transaminase

not find any correlation between liver enzymes and platelet counts at the initial and final phases of alcohol withdrawal.

Small sample size is a key limitation in this study. A significant number of patients had to be excluded from the study due to the stringent inclusion criteria such as presentation within 12 h of the last drink and willingness to stay for a 10-day inpatient detoxification program. Inpatient management was vital to ensure strict abstinence from alcohol. This study estimated platelet counts on days 2, 4, 6, 8, and 10. It is possible that there may be more changes in platelet counts on the days when platelet counts were not estimated (days 1, 3, 5, 7, and 9).

CONCLUSIONS

Thrombocytopenia associated with alcohol withdrawal and DT is transient and is associated with RT. RT is either continuous or is associated with an initial drop, which is followed by a continuous rise in platelet counts till withdrawal subsides. Platelet counts in alcohol withdrawal are not affected by serum AST and ALT levels, type of alcoholic beverage consumed, DAD, and quantity of daily intake of absolute alcohol.

Future directions

These findings need to be validated in a larger sample size. It would also be interested to know the patterns of platelet counts in the remaining days (day 1,3,5,7,9) of alcohol withdrawal.

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Conflicts of interest

There are no conflicts of interest.

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