



Original Article

Hepatic artery thrombosis versus neurological complications – Role of antiplatelet medications in adult living donor liver transplantation



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ABSTRACT

Aspirin used in the post-operative period as prophylaxis for hepatic artery thrombosis (HAT) increases the risk of neurological complications (NC) in adult living donor liver transplantation (LDLT) recipients was the hypothesis. Case control study was done on 1400 cases operated in our institute. Pediatric transplants, combined liver kidney, cadaver transplants, dual lobe transplants, preexisting organic neurological dysfunction and patients whose records were missing were excluded from the study. There were effectively 880 cases in non-aspirin group (NAG) and 440 cases in aspirin group (AG). The groups were matched for various factors. There were more alcoholics in AG and more ALFs in NAG. On subgroup analysis these two etiological factors were found to be statistically insignificant $P > 0.05$. So the prophylactic protocol was aspirin 75 mg once daily in all adults (age > 12 years) once the platelet counts have reached 50,000 and there is no evidence of bleeding elsewhere. In pediatric population our protocol is use of aspirin 75 mg and clopidogrel 75 mg once daily once the platelet counts have reached 50,000 and there is no evidence of bleeding anywhere else.

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1. Objectives

Neurological complications are reported in 13–47% of patients after orthotopic liver transplantation (LT).^{1,2} Our hypothesis was adult chronic liver disease (CLD) patients unlike the pediatric group have preexisting sub clinical neurologic damages which were aggravated by antiplatelet medications. Whether aspirin was effective in preventing hepatic artery thrombosis (HAT)? Whether neurological complications were attributable to aspirin? Was aspirin effective in preventing HATs? Were the aims of our study. We have analyzed the neurological complications (NC) post-living donor liver transplantation (LDLT) and the association of aspirin use in over 1400 cases over a period of eight years. Antiplatelet agents (aspirin and or clopidogrel) are routinely used in the post-operative period as prophylaxis against hepatic artery thrombosis in various liver transplantation centers across the world. Previously the incidence of HAT was 5–15% across centers all over the world. Risk was relatively high in pediatric group of population. Hence the use of antiplatelet agents routinely in post-operative period. Still many centers across the world continue to do so. We

observed that there was increase in the incidence of neurological complications in the aspirin group (AG). Hence we stopped using aspirin routinely in adults as HAT prophylaxis in the post-operative period. We found that there was no increase in the incidence of HAT and also there was decrease in the neurological complications in the non-aspirin group (NAG).

2. Materials and methods

It was a case control study. Total number of cases studied were 1400. AG group included all adult LDLTs done from 17/9/2006 to 31/3/2011. NAG group included all adult LDLTs done from 1/4/2011 to 15/9/2014. There were 82 pediatric cases. Pediatric transplants, combined liver kidney, cadaver transplants, dual lobe transplants, preexisting organic neurological dysfunction and patients whose records were missing were excluded from the study. There were effectively 880 cases in NAG and 448 cases in AG. The groups were matched for age, sex, CTP, MELD, hospital stay, WIT, CIT, platelets, HAT, NCs and etiological factors. Statistical analysis was done with Instat 3 software.

3. Results

There were more alcoholics in AG and more ALFs in NAG. On subgroup analysis these two etiological factors were found

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Table 1
Comparison of non-aspirin group versus aspirin group.

No.	Parameter	NAG	AG	P value
1	Number of cases	880	448	
2	Neurological complications	68 (7.7%)	66 (14.7%)	0.000336
3	HAT	4 (0.5%)	6 (1.4%)	0.08
4	Age	47.59 yrs	47.36 yrs	>0.05
5	Sex	82.8%:17.2%	83.4%:16.6%	>0.05
6	CTP	11	11	0.00
7	MELD	19.43	17.95	>0.05
8	Platelet	76,907	86,707	>0.05
9	CIT	116.68	113.46	>0.05
10	WIT	40.48	50.25	<0.001
11	ALF	4 (1.5%)	13 (0.9%)	0.000225
12	Hospital stay	25 days	30 days	<0.001
13	Mortality	105 (12%)	72 (16.5%)	0.068
14	Alcoholics	87 (9.9%)	81 (9.2%)	0.000217
15	HBV	126 (14.2%)	56 (6.4%)	0.42
16	HCV	424 (48.3%)	167 (37.9%)	0.17
17	Wilson	3 (0.3%)	2 (0.2%)	>0.05
18	Others	215 (24.5%)	96 (10.9%)	>0.05

to be statistically insignificant. There was significant difference in NC, WIT and hospital stay between the two groups. We further analyzed the neurological complication population of both groups separately. On subgroup analysis of AGNC and NAGNC we again found that WIT and hospital stay (HS) were prolonged. Hence we concluded that these were surrogate markers of our improvements in surgical technique and post-operative protocols over a period of time (learning curve). CIT and HS could well be the associated effect or cause of NCs. These parameters could not be analyzed further in this study. However on further subgroup analysis of NCs there was statistically significant increase in the neuropsychiatric manifestations and seizures in AG compared to the NAG. Conversely aspirin neither did increase the incidence of HAT nor did decrease the intracranial vascular complications. The statistical analysis between AG and NAG are given in [Table 1](#). Subgroup analysis between the two groups based on the neurological complications AGNC and NAGNC is summarized in [Table 2](#).

Table 2
Comparison of aspirin group neurological complications versus non-aspirin group neurological complications.

No.	Parameter	AGNC	NAGNC	P value
1	Number of neurological complications	66	68	NS
2	HAT	1 (1.5%)	0 (0%)	NS
3	Age	46.67 yrs	48.64 yrs	NS
4	Sex	86.4%:13.6%	85.3%:14.7%	NS
5	CTP	10.67	11.19	NS
6	MELD	24.17	20.52	NS
7	Platelet	99,601	66,696	NS
8	CIT	116 min	118.3 min	NS
9	WIT	48 min	39.5 min	<0.001
10	ALF	1 (1.5%)	1 (1.5%)	NS
11	Hospital stay	37.94 days	28.68 days	<0.001
12	Mortality	5 (7.6%)	7 (10.3%)	0.61
13	Alcoholics	15	10	0.323
14	HBV	13	5	0.067
15	HCV	21	34	0.16
16	Wilson	1	0	0.496
17	Others	15	19	NS

4. Discussion

Both the groups were matched for various parameters as listed in [Table 1](#). There was statistically significant difference of NCs, HS, WIT, alcoholic CLDs and acute liver failure (ALF) between two groups. More ALFs in NAG. ALF and alcoholism were further matched intergroup and intragroup and found to be statistically insignificant in causing NCs. HS and WIT were found to be high in all patients in the AG compared to the NAG. This gradual improvement in the WIT in the NAG may be secondary to refinements in surgical technique secondary to learning curve. Decrease in HS in the population in the later period of the study implies standardized post-operative protocols. Over the years we have avoided using wide bore drains which was one of the main culprits for prolonged hospital stay. Patients are fed early and ambulated early. Drains are removed by 10th post-operative day. Hence we were able to cut down on the hospital day by almost 10 days. We were not able to negate the cause effect of these two parameters on the NCs scientifically by this study. The neurological complications between the two subgroups were discussed under nine subheadings and are also summarized in [Table 2](#).

4.1. Hemorrhage and infarcts

Acute cerebrovascular disorders occur in 2–6.5% of LT recipients, mostly with cerebral hemorrhage, usually within 2 months after surgery.^{3–5} There was 12% in AG and 16% in NAG. There was no statistical difference in the significance. They definitely add to the morbidity. Few of them required neurosurgical intervention for evacuation for clots to reduce the intracranial tension. Altered higher functions lead to increased need for nursing care and nutritional support. These group of patients require prolonged ventilation and tracheostomy along with associated lung complications. Adjustment of cerebrovascular risk factors before, during, and after LT is the main preventive measure. Diagnosis and treatment are similar to those adopted in the general population. Attention is paid to the search for infection as a cause of acute cerebrovascular disorders, in order to institute prompt systemic antibiotic/antifungal therapy once infection occurs, especially in elderly patients.^{4,5}

4.2. Mononeuropathies

Neuromuscular disorders present with focal or generalized weakness.³ Focal weakness includes Mononeuropathies, with an incidence of 2–13%, and brachial plexopathy (1–5.8%). Axonal involvement is common. Invasive procedures, perioperative positioning and rarely medications are found to be causative factors. Various mononeuropathies noted in our study were isolated limb palsies, vocal cord palsy, optic neuritis and hearing impairment. There was no significant difference in the incidence between two groups. Isolated limb palsies included upper limb and lower limb monoplegia. The incidence was slightly higher in the NAG.

4.3. Seizures

Seizures occur in 0–40% of LT recipients,^{3,6,7} with a tendency to lower numbers in the more recent reports. Most are generalized tonic-clonic seizures. Convulsive or non-convulsive status epilepticus is rare. Seizures occur most often early after surgery, due to drugs, acute metabolic derangement, hypoxic-ischemic injury, cerebral lesions, sudden withdrawal of narcotic agents, or inadvertent discontinuation or changes in anticonvulsant drugs in patients with epilepsy. Immunosuppressant toxicity is the main etiology.³

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