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ASSOCIATION OF PERIPROCEDURAL HAEMOGLOBIN REDUCTION AND MYOCARDIAL INJURY IN PATIENTS WITH UNSTABLE ANGINA UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

Cardiology

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ABSTRACT

Background: Patients undergoing percutaneous coronary intervention are at risk of different complications such as periprocedural bleeding and acute haemoglobin reduction that can lead to myocardial injury. Blood loss through catheter during procedure and through puncture site haematoma causes periprocedural acute haemoglobin drop. **Objectives:** To find out the association of acute haemoglobin reduction and myocardial injury after PCI in patients with unstable angina. **Methods:** This prospective observational study was conducted at National Institute of Cardiovascular Diseases (NICVD) for one year of time. Total 130 patients were enrolled based on inclusion and exclusion criteria during the study period. Haemoglobin and troponin-I were measured before and after PCI within 24 to 48 hours of the procedure. On the basis of post procedural acute haemoglobin level the study population were categorized into two groups: Group I patients with normal haemoglobin level and Group II patients with significant acute haemoglobin reduction (≥1 gm/dl). **Results:** Total 24 patients developed periprocedural myocardial injury, among them 17 (70.8 %) were in reduced haemoglobin group and 7(29.2%) in normal haemoglobin group. Elevation of troponin I after PCI had higher in group II than group I patients with statistically significant difference. Multivariate logistic regression analysis showed that haemoglobin reduction was an independent predictor of PMI (OR 1.94; 95% CI, 1.241-8.684; p=0.01). **Conclusion:** Periprocedural haemoglobin reduction in patients of unstable angina was associated with myocardial injury after percutaneous coronary intervention (PCI).

KEYWORDS

Periprocedural Haemoglobin Reduction, Myocardial Injury, Unstable Angina, Percutaneous Coronary Intervention

INTRODUCTION:

About one-third of all elective PCI procedures are associated with significant myocardial injury (termed peri-procedural myocardial injury, PMI), which has been associated with increased subsequent mortality (Ioannidis, Karvouni and Katritsis, 2003). This underscores the importance of risk stratifying prior to the procedure to identify the patient group most likely to develop PMI. If PMI incidence can be reduced clinical outcomes would be expected to improve.

Troponin(Troponin-I and Troponin-T) are more sensitive and specific markers of cardiac injury than CK-MB (Katus, et al., 1991; Adams, et al., 1994). A meta-analysis of 15581 patients from 20 studies over a 19-year period reported the incidence of troponin release post-PCI in elective PCI to be 33% and increased mortality was significantly associated with troponin elevation after PCI(4.4 vs 3.3%, P= 0.001; OR 1.35) (Nienhuis, et al., 2008). Peri-procedural MI can be difficult to rule out as the symptoms, electrocardiographic changes, angiography and others imaging modalities can be uncertain due to older ischaemic injuries and discomfort associated with the procedure itself. A study showed that on angiography only approximately 60% of peri-procedural MI could be explained (Muschart, et al., 2012). Clinicians must therefore rely considerably on cardiac biomarkers.

Peri-procedural bleeding and haemoglobin drop have emerged as a common complication of percutaneous coronary intervention that negatively impacts a patients prognosis (Manoukian, et al., 2007). In patients undergoing percutaneous coronary intervention (PCI) for stable or unstable coronary syndromes, antiplatelet and anticoagulant agents are frequently utilized to minimize ischaemic complications. These agents are associated with significant risk of bleeding complications and haemoglobin drop (O'Neill, 2006). The adverse impact of anaemia concurrent with cardiovascular, medical, and surgical conditions are likely mediated by multiple mechanisms including diminished oxygen delivery to tissues, increased cardiac output resulting in increased myocardial oxygen demand, with resultant myocardial ischaemia. This phenomenon is exacerbated by balloon inflation during the procedure (Turner, et al., 2008).

Haemoglobin drop(›1gm/dl) during PCI is an important predicting factor for contrast-induced nephropathy(CIN) that is associated with an increased risk of death and late cardiovascular events after PCI (Lee, et al., 2010). Dual anti-platelet therapy(DAPT) can unmask or exacerbate underlying processes such as occult gastrointestinal bleeding and bleeding diathesis, leading to substantially increased bleeding frequency and severity (Bassand, et al., 2010) .

Post- Percutaneous Coronary Intervention (PCI) anemia was associated not only to higher mortality but also to increased rate of Major Adverse Cardiac Events (MACE) (Kruk, et al., 2010). A recent work analyzed prognostic implications not only of post-PCI anaemia but also of longitudinal Hb levels following the first Acute Myocardial Infarction(AMI), showing that Hb drop was associated to worse outcome independently from an anaemic state (Leshem-Rubinow, et al., 2013).

This study aim to evaluate the association between peri-procedural haemoglobin drop and myocardial injury.

METHODS:

This prospective observational study was conducted at National Institute of Cardiovascular Diseases (NICVD) for one year of time. All the patients with unstable angina undergoing PCI with stenting admitted in NICVD during specified period of time was the study population. Total 130 patients were enrolled based on inclusion and exclusion criteria during the study period. Demographic data & risk factors were enlisted. Haemoglobin and troponin-I were measured before and after PCI within 24 to 48 hours of the procedure. On the basis of post procedural haemoglobin level the study population were

categorized into two groups: Group-I: Patients without significant haemoglobin reduction (Hb drop 1gm/dl after PCI). Group-II: Patients with significant haemoglobin reduction (≥1gm/dl). The samples for Troponin i was analyzed using Immuno Fluorescent Assay by access2 machine (Bekman Coulter).

Ethical consideration was maintained as per Helsinki Ethical guideline, supervised by Hospital Ethical Committee.

RESULTS:

The results and observations are documented below.

The mean age of the study population was 53.2±8.7 years ranging from 35 to 65 years, 53.6±9.1 years in Group I and 52.8±8.3 years in Group II. The mean age difference was not statistically significant (p=0.63) between two groups.

The sex distribution of this study population in group I, 53 (81.5%) patients were male and 12(18.5%) patients were female. In group II, 46 (70.8%) patients were male and 19 (29.2%) were female. Male female ratio was 3.2:1. No significant (p=0.56) difference was observed between two groups

Total 24 patients developed periprocedural myocardial injury, among them 17 (70.8 %) were in reduced haemoglobin group and 7(29.2%) in normal haemoglobin group. Elevation of troponin I after PCI had higher in group II than group I patients with statistically significant difference (p=0.001). Multivariate logistic regression analysis showed that haemoglobin reduction was an independent predictor of PMI (OR 1.94; 95% CI, 1.241-8.684; p=0.01). The sensitivity and specificity of periprocedural haemoglobin reduction for myocardial injury were 70.8% and 54.7% respectively.

Table I : Age distribution of the study population (N=130)

Age group (years)	Group-I (n=65)		Group-II (n=65)		Total (N=130)		p-value
	Number	%	Number	%	Number	%	
≤40	5	7.7	6	9.2	11	8.5	
41 – 50	27	41.5	27	41.5	54	41.5	
51 – 60	19	29.2	23	35.4	42	32.3	
>60	14	21.5	9	13.8	23	17.7	
Mean±SD	53.6±.9.1		52.8±8.3		53.2±8.7		0.63ns

Table II: Gender distribution of the study population (N = 130).

Gender	Group-I (n=65)		Group-II (n=65)		Total (N=130)		p-value
	Number	%	Number	%	Number	%	
Male	53	81.5	46	70.8	99	76.2	0.15ns
Female	12	18.8	19	29.2	31	23.8	

Table III: Risk factors among the study population (N= 130)

Risk factors	Group-I (n=65)		Group-II (n=65)		Total (N=130)		p-value
	Number	%	Number	%	Number	%	
Smoking	45	69.2	40	61.5	85	65.4	0.35ns
Hypertension	31	47.7	32	49.2	63	48.5	0.86ns
Diabetes mellitus	24	36.9	26	40.0	50	38.5	0.72ns
Dyslipidemia	26	47.3%	41	63.1%	67	55.8%	0.08ns
F/H of CAD	30	46.2	38	58.5	68	52.3	0.16ns

Table IV: Biochemical status of the study population (N= 130)

Variables	Group I (n=65)	Group II (n=65)	Total (N=130)	P value
	mean±SD	mean±SD	mean±SD	
Haemoglobin before PCI	11.6±0.5	11.6±0.5	11.6±0.5	1.00ns
Haemoglobin after PCI	11.5±0.5	9.9±0.7	10.7±1.0	<0.001s
Troponin I ng/ml before PCI	0.36±0.16	0.39±0.0.20	0.43±0.29	0.30ns
Troponin I ng/ml after PCI	3.9±2.6	4.1±2.6	3.9±2.6	<0.001s

Table V: Association between periprocedural haemoglobin reduction and myocardial injury among the study population (N = 130)

Study patients in terms of haemoglobin reduction	Troponin I ng/ml				p-value
	Without significant raised (n=106)		With significant raised ≥ 5 times (n=24)		
	Number	%	Number	%	
Group I	58	54.7	7	29.2	0.02s
Group II	48	45.3	17	70.8	

Table VI: Procedural variables among the study population (N= 130)

Variables	Group-I (n=65)		Group-II (n=65)		Total (N=130)		p-value
	Number	%	Number	%	Number	%	
Size of vascular access sheath (7 Fr)	65	100.0	65	100.0	130	100.0	1.00ns
Use of Unfractionated Heparin	60	92.3	63	96.9	123	94.6	0.44ns
Use of Bivalirudin	5	7.7	2	3.1	7	5.4	0.22ns
Balloon inflation time (mean±SD Second)	14.4±2.2		15.6±2.8		14.9±2.5		0.51ns
Procedural duration (mean±SD Minute)	53±27		58±32		56.9±31		0.02s
Multivessel stenting (≥2 stents)	11	16.9	21	32.3	32	24.6	0.04s
Complex PCI (LM & bifurcation lesion)	4	6.2	12	18.5	16	12.3	0.03s

Table VII: Post Procedural variables among the study population (N = 130)

Variables	Group-I (n=65)		Total (N=65)		Total (N=130)		p-value
	Number	%	Number	%	Number	%	
Haematoma	0	0.0	11	16.9	11	8.5	0.001s
Major bleeding	0	0.0	1	1.5	1	0.8	1.00ns

Table VIII: Association between periprocedural haemoglobin reduction and myocardial injury among the study population (N = 130)

Study patients in terms of haemoglobin reduction	Troponin I ng/ml				p-value
	Without significant raised (n=106)		With significant raised ≥ 5 times of URL (n=24)		
	Number	%	Number	%	
Group I	58	54.7	7	29.2	0.02s
Group II	48	45.3	17	70.8	

DISCUSSION:

Among the risk factors of ischemic heart disease smoking habit was found 69.2% in group I and 65.4% patients in group II followed by hypertension 47% versus 48%, diabetes mellitus 36% versus 38.5%, dyslipidemia 47.3% versus 63% and family history of coronary artery disease 25% versus 28%. There was no statistically significant difference of incidence of these risk factors between the two group (p>0.05). One of study in Bangladesh (Jamaluddin, et al., 2015) found that smoking (61.6%) was the highest risk factor, followed by hypertension (47%), diabetes mellitus (38.3%), dyslipidemia (34%) and family history of CAD (27.3%). This is almost consistent with our study regarding the higher incidence of smoking, hypertension, diabetes mellitus and family history of CAD. Another study in Bangladesh (Akanda, et al., 2011) found patients who were suffering from ischemic heart diseases smoking is the most prevalent risk factor, it is about 60% which is consistent with our study.

Among the procedural variables multivessel stenting was used

significantly more in group II patients than that of group I patients (32.3% vs. 16.9%, p=0.04). Complex PCI was observed significantly higher in group II compared to group I (18.5% vs. 6.2%, p=0.03).The remaining variables had almost identical in group I compared to group II with no statistical significant association (p>0.05).

Haemoglobin before PCI between two groups had similar with statistically insignificant difference between (p=0.72). Haemoglobin after PCI between two groups had significantly lower in group II in compared to group I where mean haemoglobin was 11.5±0.5gm/dl in group I and 9.9±0.7 in group II with statistically significant difference between (p<0.001).Troponin I before PCI was found insignificantly higher in group II than group I (p=0.30). Troponin I after PCI had higher in group II (4.1±2.6) than group I (3.9±2.6) patients with statistically significant difference (p<0.001). Islam et al, in his study found that the mean CK-MB level was 44.3±11.2 U/L in low haemoglobin group and 40.7±8.6 U/L in group with normal haemoglobin. The mean increase in CK-MB above baseline after PCI was more in the former group of patients, which was statistically significant (p<0.05) (Islam, et al., 2009).

In our study, post procedural variables haematoma was significantly occurred in group II patients in compared to group I patients with p value 0.001. Major bleeding was occurred in 01 patient in group II and none in group I with statistically insignificant association (p=1.00). But the patient who developed major haematoma after PCI had significant reduction of haemoglobin (>3 gm/l) . Sattur et at , in their study found that 40% of patient with post-PCI anaemia had documented TIMI (major or minor) bleeding and 55% exhibited a haemoglobin drop of ≥ 3 gm/dl after PCI (Sattur, et al., 2009). Jaffery et al, in their study shown that 41% of PCI and 49% of PVI (peripheral vascular intervention) had a peri-procedural haemoglobin fall ≥ 1gm/dl in the absence of clinically evident bleeding.

By using the definition of peri-procedural myocardial injury (raise of troponin-I ≥ 5 times of upper reference limit) we identified that patients with significant haemoglobin reduction, 17 (70.8%) patients had significant raised of Troponin I and 48 (45.3%) patients without significant raised of Troponin I. Patients without significant reduction of haemoglobin,7(29.2%) had significant raise of troponin-I and 58(54.3%) patients without significant raise of troponin-I. It signify that haemoglobin reduction was associated with myocardial injury which had statistically significant association (p=0.02). Alizadeh et al shown that post procedure haemoglobin drop was associated with post PCI cardiac enzyme elevation, particularly troponin-I. This means that haemoglobin dropping can lead to worse clinical outcomes in patients undergoing catheterization procedure (Alizadeh, et al., 2013). McKechnie and colleagues have proposed that a lower haemoglobin level might be a marker of post PCI adverse outcome and that it could identify patient at higher risk of complication after intervention procedures.

To find out the association of haemoglobin reduction and myocardial injury the binary logistic regression analysis of Odds Ratio for characteristics of the subjects was done. The variables multi vessel stenting and low haemoglobin level were found to be significantly associated with myocardial injury with the ORs being 2.78 and 1.94 with 95% confidence interval of 1.888 – 12.277 and 1.241 – 8.684 respectively.

The present study demonstrated that peri-procedural haemoglobin reduction in patients of unstable angina was associated with more incidence of significant troponin-I elevation after percutaneous coronary intervention (PCI). Peri-procedural haemoglobin dropping may be considered as a predictor of cardiac adverse outcome in patients undergoing PCI.

Limitations:

Though the results are significant statistically even then this study have some limitations. We did not seek data on the specific cause of peri-procedural haemoglobin drop. The procedure, percutaneous coronary intervention, itself is a risk factor of periprocedural myocardial injury which could not be excluded. PCI were done by multiple operators

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