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A PROSPECTIVE STUDY ON THE EVALUATION OF HEPARIN AND ITS ANALOGUES UTILIZATION IN A TERITIARY CARE HOSPITAL

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ABSTRACT

The objective of the study was to evaluate the utilization of heparin and its analogues in a teritiary care hospital. The prospective study was carried out in a total of 81 patients treated with heparin and its analogues. Details of inpatients who were treated with heparin and analogues were collected from patient files. Evaluation of demographic data revealed that 58% (n=47) were males while 42% (n=34) were females. A high percentage of patients aged between 59-68 years were found in the study population. Laboratory monitoring analysis shows that APTT test and INR test was done for 58%(n=47) of the total populations. The most prominent indication for which it was prescribed as Stroke 34.5%(n=28). The most commonly prescribed heparin analogue was Unfractionated Heparin(UFH). The commonly preferred route for administration was subcutaneous route 62.9%(n=51). In prescription analysis, it was found that maximum number of patients was receiving 5000 U (61.7%, n=50) of unfractionated heparin via subcutaneous route. During study period, the adverse drug reactions associated with heparin use were identified and monitored using Naranjo Causality Assessment Scale, 42 patients(51.8%) shown Adverse Drug reactions in the total population. The most common Adverse Drug Reactions were pain at injection site(19%) and Thrombophlebitis(19%).

KEYWORDS: UFH, LMWH, APTT, INR, subcutaneous route.

INTRODUCTION

Drug Utilization Evaluation (DUE) is a perfomance improvement method that focuses on evaluating and improving medication use process with the goal of optimal patient outcomes.[4] Unfractionated heparin (UFH) has been a widely used anticoagulant in the management and prophylaxisof thromboembolism and acute coronary syndromes for the last 20 years.[4] Low Molecular Weight Heparin (LMWH) are currently being devoloped for several newer indications, including management of ischemic and thrombotic stroke, treatment of unstable Angina and related coronary syndromes, prophylaxis of thrombosis during interventional cardiovascular procedures such as stenting, atherectomy and thrombolysis, management of transplant associated venocclusive disorders and management of cancer associated thrombosis.[1] At present, Low Molecular Weight Heparins are replacing Unfractionated Heparin because of greater bioavailability from subcutaneous site, longer duration of plasma half life, predictable anticoagulant effect and lower incidence of Osteoporosis, hyperkalemia and Heparin Induced Thrombocytopenia cases; However, UFH remains the parentral anticoagulants of choices in cases which immediate reversal of anticoagulation is needed or in subjects with significant renal impairment.[4] Despite its effectiveness, UFH has a narrow therapeutic window and may cause complications such as hemorrhage and HIT. Therefore close monitoring of Unfractionated Heparin therapy is highly recommended.[4] Like Unfractionated Heparin therapy, Low Molecular Heparin therapy have major risks of bleeding, Osteoporosis in long term use, heparin induced thrombocytopenia, hyperkalemia and altered hepatic function. Therefore it is necessary to evaluate the usage in the hospital settings.[1] The optimal utilization of heparin and its analogues is important to minimizing the adverse effects associated with use of heparin and its analogues in various clinical indications.[3] The anticoagulant response to heparin varies greatly over time between patients as well as in individual patients, this variability necessitate the appropriate monitoring in each patient receiving heparin therapy.[2] The significance of the study to improve the quality of use by analyzing various aspects of prescribing patterns and monitoring practices of heparin.

METHODOLOGY

The study was designed to be a prospective observational study, conducted in Karuna Medical College Hospital (KMCH) for a duration of 6months (October 2019 to March 2020) and was carried out in inpatient department from general medicine, intensive care unit and gynaecology departments. A total of 81 patients undergoing heparin therapy were enrolled in the study.

Inclusion Criteria: Inpatients of both sex of age 18 years and above. Patients undergoing heparin therapy (cerebrovascular diseases, cardiovascular diseases, hematological diseases and gynaecological disorders).

Exclusion Criteria: Patients who are not willing to participate in study. Patients suffering any kind of malignancy and hemorrhagic stroke.

The study protocol was approved by Institutional Ethics Committee of Karuna Medical College Hospital. Specially designed data entry form was used for collecting data for this study. Data collection included patient details, laboratory investigation, LMWH and UFH prescribed and adverse drug reactions.

RESULTS AND DISCUSSION

The study was conducted inorder to evaluate the utilization pattern of unfractionated heparin and low molecular weight heparin in a hospital settings. Gender distribution showed that male patients (58%) far exceeded than female patients (42%) in the study[table 1]. These findings are similar to the study carried out by Binu Mathew *etal*.,[1] where the male population predominate the female population. Age group analysis[table 2, fig 1] of the patients showed that in the study, the most prominent age groups were '59-68'years which constitutes 40%(n=32) followed by '49-58' years, which constitutes21%(n=17).

Table 1: Distribution based on gender of patients.

Gender	Number of Patients (n=81)	Percentage (%)
MALE	47	58%
FEMALE	34	42%

Table 2: Age distribution of patients.

Age (Years)	Number of patients(n=81)	Percentage (%)
18-27	4	5%
28-38	2	2.4%
39-48	9	11%
49-58	17	21%
59-68	32	40%
69-78	13	16%
79-88	4	5%

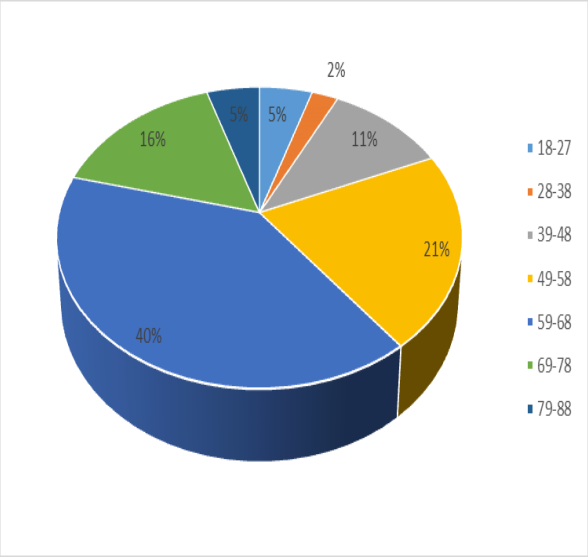

Fig. 1: Age wise distribution of patients.

In analysis of diagnosis where heparin analogues were prescribed includes, most prominent indication was Stroke 28(34.5%), of the total prescriptions. This was followed by Acute coronary syndrome 10(12.3%), Coronary artery disease 8(9.8%), Deep vein thrombosis 8(9.8%), Myocardial infarction 7(8.6%) and others 21.4% (Table 3,fig2,fig 3). In prescription analysis, the most prescribed type of heparin analogue was Unfractionated heparin 97.5%(n=79) followed by Low molecular weight heparin 2.4% (n=2) in total population (tab4,fig4). The commonly preferred route for administration was subcutaneous route 62.9%(n=51) (table 5,fig 5). In prescription analysis, it was found that maximum number of patients was receiving 5000 U (61.7%,n=50) of unfractionated heparin via subcutaneous route(table 6).

Table 3: Diagnosis wise distribution from the total population.

Clinical conditions	Nummber of patients
Stroke	28(34.5%)
Acute coronary syndrome	10(12.3%)
Coronary artery disease	8(9.8%)
Deep vein thrombosis	7(8.6%)
Myocardial infarction	7(8.6%)
Ischemic heart disease	4(4.9%)
Unstable angina	4(4.9%)
Left ventricular failure	2(2.4%)
Placental abruption	2(2.4%)
Prenatal bleeding	2(2.4%)
Atrial fibrillation	1(1.2%)
Tachycardia	1(1.2%)
Valvular heart disease	1(1.2%)
Thrombosis	1(1.2%)
Recurrent pregnancy loss	1(1.2%)
Post menopausal bleeding	1(1.2%)

Table 4: Commonly Prescribed Type Of Heparin Analogues.

Type of heparin prescribed	Number of patients
Unfractionated heparin	79(97.5%)
Low molecular weight heparin	2(2.4%)

Table 5: Distribution based on route of administration.

Route of administration	Number of patients
Intravenous route	20(24.6%)
Subcutaneous route	51(62.9%)
Intravenous and subcutaneous	10(12.3%)

Table 6 – Distribution based on dose of heparin analogues in total population.

Dose of unfractionated heparin	Number of patients
5000 IU	50(61.7%)
25000 IU	16(19.7%)
5000 IU + 25000 IU	13(16%)

Dose of low molecular weight heparin	Number of patients
60mg/0.6 mL	1(1.2%)
20mg/0.2 mL	1(1.2%)

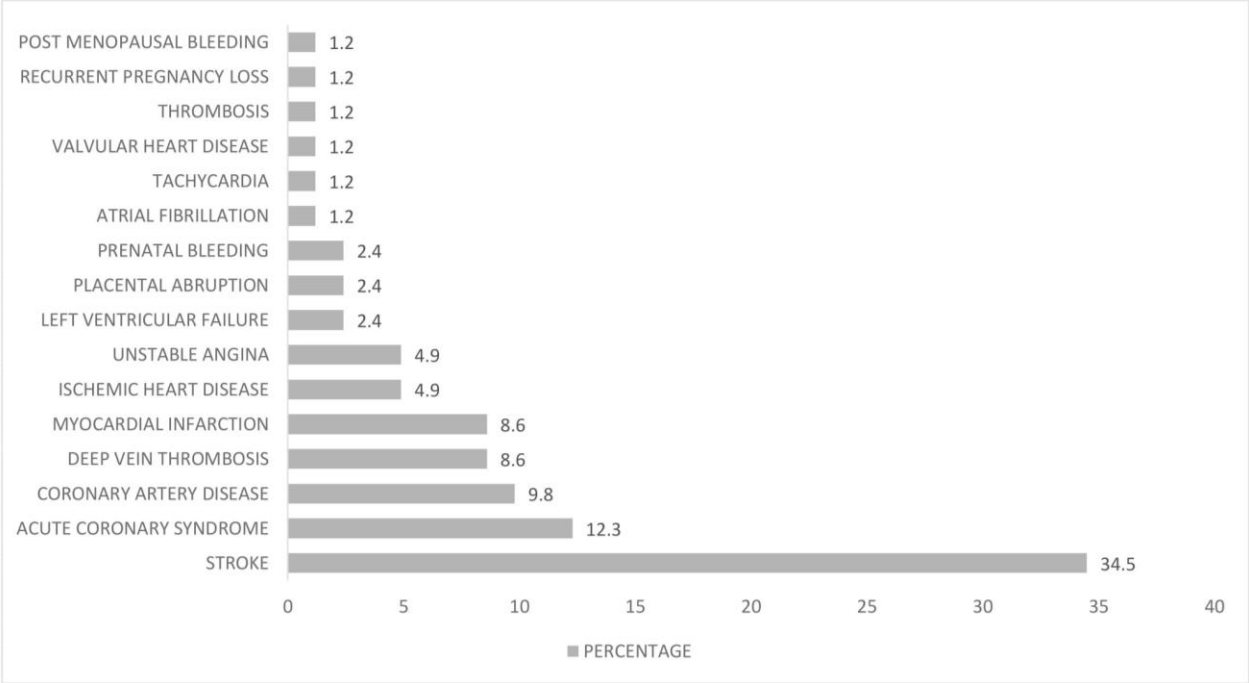

Figure 2: Diagnosis wise distribution from the total population.

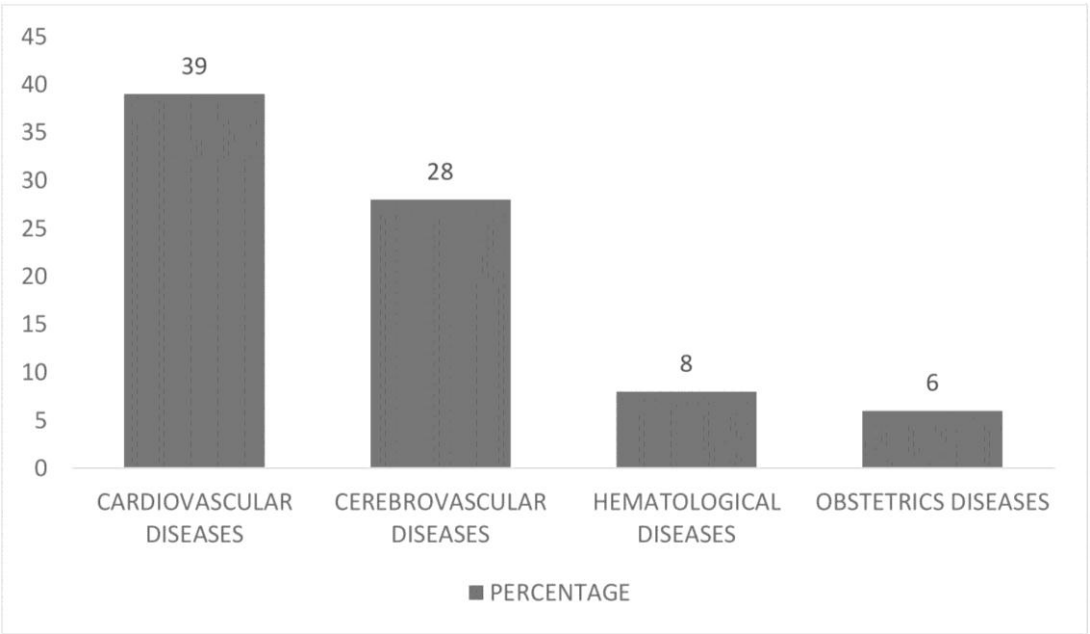

Figure 3: Disease category wise distribution from the total population.

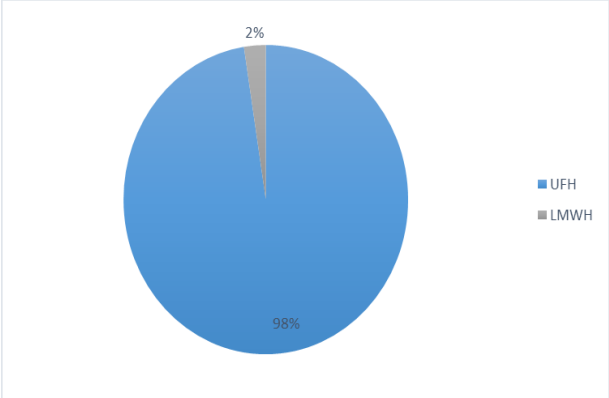

Figure 4 – Distribution based on type of heparin prescribed.

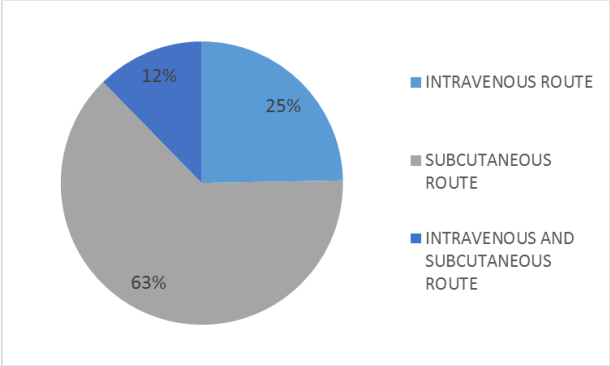

Figure 5: Distribution based on route of administration.

Laboratory monitoring analysis shows, APTT test(table 7) and INR test(table 8) was done for 58%(n=47) of the total populations, followed by bleeding time (74%) and clotting time(74%) of the total populations. The need for frequent laboratory tests, i.e, activated partial thromboplastin time(APTT), the time spent on these tests, as well as the staff involved from from patient's bedside to laboratory, could result in extra costs and potential complications in patients. APTT monitoring was recommended for the UFH therapy. In the case of LMWH therapy daily monitoring of APTT is not recommended. In the study it was found that 58% of APTT monitoring. So these will further increase the laboratory morning, this is brought to the notice of prescribing physicians in the hospital.

Adverse drug reaction analysis shows that, 42 patients(51.8%) shown Adverse Drug reactions in the total population(fig 6). The common ADRs identified are rashes(11.9%), pain at injection site(19%0, thrombophlebitis(19%), hyperkalemia(7.1%), bleeding(9.5%), thrombocytopenia(11.9%), elevated serum transaminase levels(9.5%) and rashes+thrombophlebitis+pain at injection site(11.9%)(table 9,fig 7). These findings are not similar to the study carried out by Iman Karimzadeh *etal*., where that study only focuses the details of bleeding episodes attributed to Unfractionated heparin in the study population. The identified ADRs are monitored and categorised into Definite, Probable, Possible and Doubtful by Naranjo Causality assessment scale. The probability of ADRs shown according to Naranjo Causality Assessment Scale was found to be Definite(61.9%), Probable (21.4%), Possible(16.6%)(table 10,fig 8).

Table 7: APPT wise distribution from the total population (n=81).

Appt monitoring	Number of patients
YES	47(58%)
NO	34(41.9%)

Table 8 – INR test wise distribution from the total population (n=81).

Inr monitoring	Number of patients
YES	47(58%)
NO	34(41.9%)

Table 9 – Distribution based on types of ADR among study population(n=42).

Adverse drug reactions	Number of patients (n=42)
Rashes	5(11.95%)
Pain at injection site	8(19%)
Thrombophlebitis	8(19%)
Rashes+pain at injection site+thrombophlebitis	5(11.9%)
Hyperkalemia	3(7.1%)
Bleeding	4(9.5%)
Thrombocytopenia	5(11.9%)
Elevated serum transaminases	4(9.5%)

Table 10: Distribution of ADRs based on Naranjo Causality Assessment Scale.

Probability of adr	Number of patients (n=42)
Definite	26(61.9%)
Probable	9(21.4%)
Possible	7(16.6%)

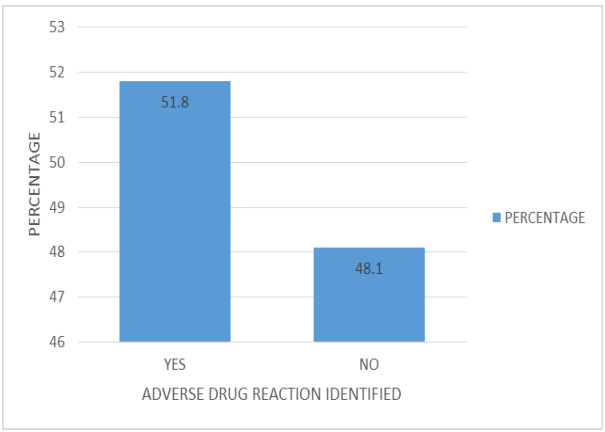

Figure 6: Adverse Drug Reaction Identified.

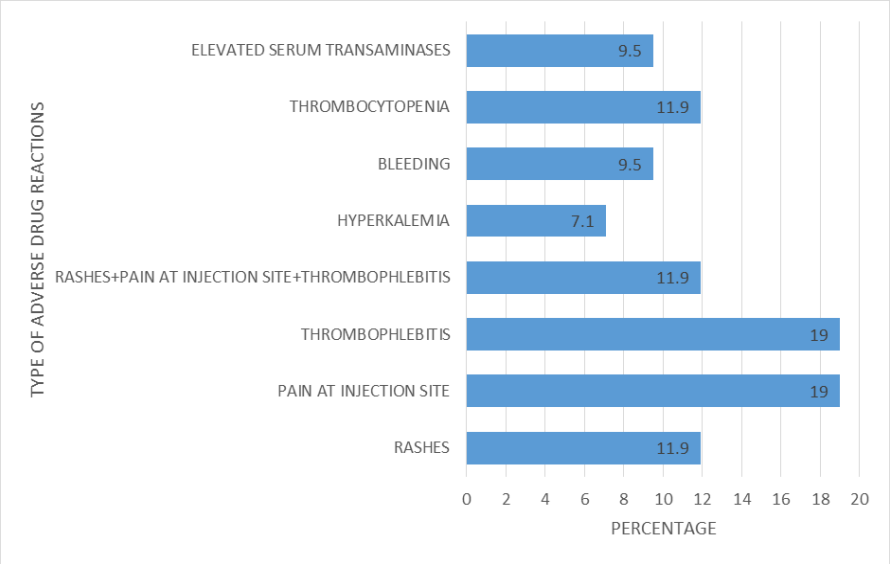

Figure 7: Distribution based on type of Adverse Drug Reactions.

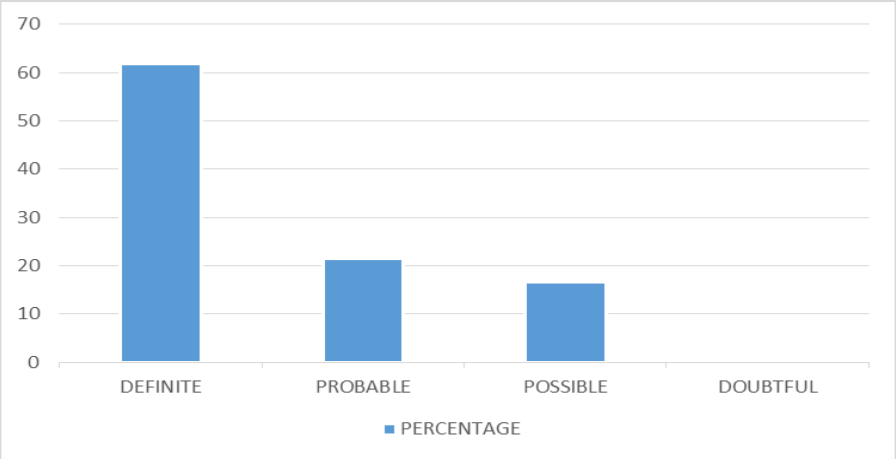

Figure 8: Distribution of ADR based on Naranjo Causality Assessment scale.

Finally the study suggests that the importance of education about heparin and its analogues to improve the quality of use of these agents. Also implementation of guidelines for the use of heparin analogues in hospital setting would promote the rational use of heparin and its analogues like UFH and LMWH.

CONCLUSION

During the study period it was observed that the UFH prescriptions are more when compared to the LMWH. This study shows that UFH prescriptions are still remain as the anticoagulant treatment of various clinical conditions like Acute Coronary Syndrome, Stroke and Deep Vein Thrombosis etc. APPT and INR monitoring was found to be inappropriate according to standard procedures. Also implementation of international guidelines for the use of UFH and LMWH in total population would promote the rational use of heparin analogues. Thus from the utilization evaluation, it was found that the prescription pattern of UFH and LMWH was rationalized in the hospital.

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