Comparative Analysis of Compliance between Rivaroxaban with Heparin and Warfarin in the Management of Deep Vein Thrombosis at Tertiary Care Hospital, Larkana

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ABSTRACT
Objective: The objective behind this study is to evaluate the compliance and noncompliance, between standard therapy with latest oral anticoagulants (NOACs) with each other so as a head-to-head comparison will ever be available.

Methodology: A descriptive observational study was conducted at SMBBMUH Larkana. The questionnaire (specially designed) was filled up to monitor the non-compliances associated with drugs used for the management of Deep Vein Thrombosis (DVT). The study was conducted on the 100 patients who were reported with DVT at tertiary care hospital SMBBMUH Larkana. A series of questions were asked from reported patients regarding symptoms and side effects. Finally the results were analyzed by using descriptive statistics.

Results: Results show that out of 100 patients, male patients (79%) observed more than female (21%) and mostly patients perform indoor jobs (39%). Prevalence of DVT is high about 53% patients were suffering from DVT during 03 months. It was found that mostly patient non compliance observed with Warfarin (n=26) as compare to heparin (n=19) and Rivaroxaban (n=07).

Conclusion: The study concluded that the more compliance achieved with Rivaroxaban as compared to warfarin and heparin. Mostly noncompliant factors are cost; prolong therapy, adverse drug reaction were common factors of non compliance in DVT patients.

Keywords: Deep vein thrombosis, Heparin, Pulmonary embolism, Coagulation.

INTRODUCTION
With the improvement of new generation oral anticoagulants like factor Xa inhibitors gives us new available choice. This study will also help us in determining the best alternatives in DVT with, Cost, Side effects, Drug-drug Interactions (DDI), Drug food Interactions (DFI), chances of major bleeding, Coagulation monitoring [1]. DVT is a frequent complication which can affect both genders i.e. male
and female. Although incidence with male is relatively higher [2]. It not only affects surgical patients but also acutely ill hospitalized patients. It may also affect persons who remain static for a longer period or having long flights [3]. For many years, Heparins and Warfarin have been used as first line therapy in Venous Thromboembolism (VTE).

The Thrombosis can be defined as “process in which the blood cells clumps together to form aggregates inside the blood vessels and causes resistance in flow of blood inside the circulatory system is called as thrombosis”. Thrombosis occurs when the walls of blood vessels damaged. The body utilizes platelets and fibrin so they stick together to form aggregates to stop the blood loss. If the thrombosis occurs in the vein then it is called as Venous Thrombosis. Venous thrombosis may cause the blockage of vein. If the thrombosis occurs in the artery, than it is called as Arterial Thrombosis [4,5]. The arterial thrombosis is just mild or moderate rarely it becomes sever. Whereas the venous thrombosis may influence the blood supply results damage of tissue which is supplied by that artery. When the blood clot which dislodged from other site in the circulatory system obstructs the blood vessels is called as Thromboembolism. When blood clot obstructs blood vessels in lungs called as Pulmonary Embolism. If blood clot obstruct blood vessels in brain than it is called as Stroke. It may also obstruct the blood vessels in gastro intestinal tract, kidney or legs. The drugs such as warfarin, heparins are prescribed to cure the Thrombosis [6,7].

Deep Vein Thrombosis occurs when the thrombus formation occurs in one or more than one veins which are much more away in the body or in a deep vein in the body most commonly in legs. It can also occur if a person cannot move for a longer period of time due to any reason. Deep Vein Thrombosis can be travel through your circulation system and enter in the lungs, blocking blood stream (Pulmonary Embolism)[8].

There are two fundamental classes of DVT, and they depend on how long the blood coagulation is available. Acute DVT can be defined as “When a blood clot develops and has been around for 14 days or less, at that point it is called acute DVT”. Chronic DVT can be defined as “When the blood clot continues for 28 days or more, than it is called chronic DVT” [9,11].

The main causes of a blood clot in a deep vein thrombosis (DVT) are, slowed blood stream, abnormal coagulating issues, medical procedure or a physical issue to the veins, malignancy can likewise cause DVT [13]. DVT ordinarily frames in a single leg or one arm. Not every person with a DVT will have indications, yet side effects can include; Swelling of the leg or arm, Pain or delicacy in the leg, The affected area of the leg or arm that is swollen or damages might be hotter than expected, Skin that is red or stained, The veins close to the skin’s surface might be bigger than normal [14].

If a person, have deep vein thrombosis (DVT), such person, have to take a medication, for example, Anticoagulants: Heparin, Warfarin, Rivaroxaban, Vena cava channels, Compression stockings, Exercise. Heparin is an anticoagulant (blood thinner agent) that inhibits the development of blood clusters. It creates its significant anticoagulant impact by inactivating thrombin and initiated factor X (factor Xa) through an antithrombin (AT)- dependent mechanism. Heparin ties to AT through a high-partiality pentasaccharide, which is available on about 33% of heparin atoms [13] Warfarin is an anticoagulant agent typically used to inhibit blood clump development just as relocation. Warfarin hinders the vitamin K synthesis of biologically active form of the calcium dependant clotting factors II, VII, IX and X, just as the administrative elements protein C, protein S, and protein Z [15]. Rivaroxaban is an anticoagulant and the primary orally dynamic direct factor Xa inhibitor. In contrast to warfarin, routine lab checking of INR is not important. Rivaroxaban restrains both free Factor Xa and Factor Xa bound in the prothrombinase complex. It is an exceptionally particular direct Factor Xa inhibitor with oral bioavailability and fast onset of action[16,17].

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**METHODOLOGY**

A hospital based descriptive observational study was conducted on the 100 patients who were reported with Deep Vein Thrombosis at tertiary care hospital SMBMUH Larkana. Before collection of data permission was obtained from Medical Superintendent of teaching hospital of SMBMUH Larkana via office letter No.D.Ph/847. Only those patients were included in the study whose age from 18 years to 65 years. Only those patients were included in the study which was reported with DVT.
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children were not included in the study. The study not comprises on same gender of patients. This research analysis was carried for 06 months.

This study has been conducted by filling up the questionnaires (specially designed) to monitor the compliance, non compliance and factors of non compliance for the patients associated with drugs used for the management of DVT. A series of questions were asked from reported patients regarding symptoms, compliance and side effects.

Finally the results were analyzed through descriptive analysis by using descriptive statistics.

**RESULTS**

In Table 1, Compliance and non compliance with Rivaroxaban was given, out of 33 patients, 25 patients were compliant with Rivaroxaban only 08 patients were non compliant with Rivaroxaban.

| S. No | Variables | Frequency | Percentage |
|-------|-----------|-----------|------------|
| 1     | Compliance| 25        | 75.8%      |
| 2     | Non compliance| 08      | 24.2%      |
| 3     | Total     | 33        | 100%       |

In Table 2, factors of non compliance were given, it was observed that among non compliant factor majority of patients were non compliant with Rivaroxaban due to prolong therapy, where as less common non compliant factor with Rivaroxaban were cost and polypharmacy.

| S.No  | Factors   | Frequency(n=8) | Percentage |
|-------|-----------|----------------|------------|
| 1     | Cost      | 1              | 12.5%      |
| 2     | Poly pharmacy| 1           | 12.5%      |
| 3     | Side effects| 2            | 25%        |
| 4     | Prolong Therapy| 4         | 50%        |

In Table 3, Compliance and non compliance with heparin was given, out of 22 patients only 03 patients were compliant where as majority of patients were non compliant with heparin.

| S. No | Variables | Frequency | Percentage |
|-------|-----------|-----------|------------|
| 1     | Compliance| 03        | 3.6%       |
| 2     | Non compliance| 19        | 86.4%      |
| 3     | Total     | 22        | 100%       |

In Table 4, non compliance factors with heparin were given. It was observed that most common non compliant factor with heparin was availability in Injectable form, where as less common non compliant factor was diet restriction.

| S.No | Factors              | Frequency(n=19) | percentage |
|------|----------------------|-----------------|------------|
| 1    | Monitoring           | 5               | 26.3%      |
| 2    | Diet Restriction     | 2               | 10.4%      |
| 3    | Injectable           | 7               | 37%        |
| 4    | Adverse drug reactions| 5           | 26.3%      |
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In Table 5, Compliance and non compliance with warfarin was given, out of 45 patients only 19 patients were compliant, where as 26 patients were non compliant with warfarin.

Table 5. Compliance and Non Compliance in Warfarin Taken Patients.

| S. No | Variables       | Frequency | Percentage |
|-------|-----------------|-----------|------------|
| 1     | Compliance      | 19        | 42.2%      |
| 2     | Non compliance  | 26        | 57.8%      |
| 3     | Total           | 45        | 100%       |

In Table 6, factors of non compliance were given, it was observed that most common non compliant factor was cost, where as less common noncompliant factor was adverse drug reaction.

Table 6. Factors of Non-Compliance.

| S.No | Factors of non Compliance | Frequency (n=26) | Percentage |
|------|----------------------------|------------------|------------|
| 1    | Cost                       | 09               | 34.7%      |
| 2    | Poly pharmacy              | 08               | 30.8%      |
| 3    | Adverse drug reactions     | 04               | 15.3%      |
| 4    | Prolong Therapy            | 05               | 19.2%      |

**DISCUSSION**

Deep vein thrombosis (DVT) is one of the most important manifestation of venous thromboembolism. It is also an important reason of increasing the morbidity and mortality especially in hospitalized patients. It is very difficult to diagnose that not only increases its rate of mortality but also increase the uncertainty of its prevalence throughout the world [12]. Although, different studies reported the lower incidence of DVT in Asian countries in contrast to western countries but lack of recent researches on DVT in Asian countries is one of the major reason of reporting lower incidence of DVT. Lack of research on DVT patients increases the chances of poor diagnosis, prognosis of diseases, increasing morbidity and mortality.

Therefore, current descriptive observational research was designed in setting of tertiary care hospital of Larkana, where diagnosed patients of DVT were enrolled from medicine department and evaluated for commonly reported clinical sign and symptoms of DVT, patients drug compliance with Heparin, Warfarin and Rivaroxaban drugs and associated non-compliance factors with these antithrombotic drugs.

In this research study 100 patients of DVT were assessed, among which greater part of DVT patients were male (79%) patients and remaining were female (21%) patients. Comparable examination by Amiwero, C., et al., additionally detailed the 62.5% male DVT patients and 37.9% female DVT patients [10]. Another comparative investigation led in Pakistan by Zamir, Q., et al., additionally announced the 59% male DVT patients and 41% female DVT patients. Another Pakistani investigation by Arsh, An., et al., additionally announced the a lot higher 75.7 male DVT patients and lower 24.3% female DVT patients [12]. The entirety of the comparative investigations are indicating that male patients are for the most part experiencing DVT when contrasted with female patients.

In current research the drug compliance with rivaroxaban was present in (54.5%) patients followed by warfarin drug compliance in (42.5%) and drug compliance with heparin was (0.0%) DVT patients and patients. A similar study by Kang, J. M., et al., reported the overall drug compliance 93.8% with antithrombotic drugs, whereas drug compliance with rivaroxaban was 100.0% and warfarin drug compliance was 93.8% [18]. Similarly, different other studies such as; Lazo-Langner, A., et al., compared the heparin and rivaroxaban, Deitelzweig, S., et al., compared the warfarin and rivaroxaban [20], Al Khateep, Y. M., et al. (2019) compared the warfarin and rivaroxaban [19] and Piati, P. K., et al. (2019)
compared the heparin, warfarin and rivaroxaban [21] and reported the higher drug compliance with rivaroxaban followed by heparin and warfarin.

CONCLUSION

The study concluded that out of 100 patients, male patients observed more than female and mostly patients perform indoor jobs. Prevalence of DVT is high, about 53% patient were suffering from DVT during 03 months. It was found that mostly patient non compliance observed with heparin as compare to warfarin and rivaroxaban. The cost, prolong therapy, adverse drug reaction, diet restriction and monitoring are more common factors of non compliance in DVT patients. Over all the compliance rate of Rivaroxaban was more as compared to warfarin and heparin.

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