RETROSPECTIVE EVALUATION OF CORRELATION OF POST EXTRACTION HEMORRHAGE AND ANTI COAGULANT THERAPIES IN YOUNGER POPULATION: A PREVALENCE BASED CLINICAL STUDY

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Abstract- Background and Aim: Post operative bleeding is very common post operative complication seen in extraction cases. Anti coagulant therapies are employed to manage several clinical conditions. Patients those who are already on anti coagulant therapy, can show different patterns of post extraction hemorrhage. Anti coagulant makes blood flow via veins more easily. So, blood will be less likely to make a dangerous blood clot (like thrombosis

or embolism). The sole endeavor of present study was to evaluate the correlation of post extraction hemorrhage and anti coagulant therapies in younger population. This study was retrospectively performed to assess the related prevalence also in the studied population. Materials & Methods: Patients case history, follow up case sheet and discharge summaries were explored. Younger age group patients those had undergone single tooth atraumatic extraction for different reasons, were selected for study. Patients who reported to be on anticoagulant therapy for more than one year, were studied in group one. Patients who reported to be on anticoagulant therapy for six to twelve months, were segregated in group two. Patients who reported to be on anticoagulant therapy for less than six months, were studied in group three. Patients not receiving this therapy were served as control group or group four. Post operative bleeding was studied under five categories in each group. These were mild, moderate, severe, uncategorized and no bleeding. Statistical Analysis and Results: Statistical analysis was done by statistical software Statistical Package for the Social Sciences (SPSS). P ≤ 0.05 was considered as statistically significant. Total 84 male and 36 female patients were studied in this study. Therefore, majority of the studied patients were male. In group I, 9 out of 30 patients had no bleeding. However, 8 patients showed severe post operative bleeding. 5 patients showed only mild bleeding. In this group (group I), P value was significant for all five severities of bleeding. In group IV, 23 patients had no post operative bleeding. Nevertheless, only 1 patient showed severe post operative bleeding. Only 1 patient showed mild bleeding. In this group (group IV), P value was significant for patients with no post operative bleeding (0.03). Conclusion: Within the limitations of the study, authors concluded that anti coagulant therapies are significantly affecting post operative bleeding in extraction cases. The relative severity and prevalence of bleeding are also exaggerated by time period of anti coagulant therapy. Patients those who were on anti coagulant therapy for more than one year, showed maximum prevalence and severity of bleeding.

Key Words: Warfarin, Anticoagulant Therapy, Prevalence, Bleeding

1. INTRODUCTION

Literature has well substantiated that warfarin based anticoagulant therapies commonly utilized by more than 5 million patients in North America for clinical managements of atrial fibrillation, mechanical heart valve and venous thrombo embolism.[1,2] It's well known that Warfarin anticoagulant therapy drastically diminishes the developmental risk of arterial thrombo embolism. This thrombo embolism can eventually turn into life threatening events like stroke. Warfarin has been shown to reduce these risks by at least 65%. This anticoagulant has also been demonstrated to reduce the clinical risk of thromboembolism by 88%.[3,4] Because of these clinical and remedial benefits, the treatment of patients on anticoagulant therapy who necessitate surgery or another invasive procedure is a severe dilemma. This is because practitioners should evaluate the relative risk of thromboembolism exaggerated by warfarin therapy. In the researches all over the world related to anticoagulant therapy, warfarin therapy been comprehensively explored and

developed as potential therapeutic agent for successful avoidance and treatment of arterial and venous thrombosis.[5,6] Despite of these clinical superiorities, warfarin therapy frequently associated with post operative bleeding and related complications. Since post operative hemorrhage is a critical clinical problem, few clinicians and researchers suggest the patient to stop the warfarin therapy for at least 3 days before any oral surgical event. Nevertheless, stopping the use of these drugs poses the patient to potential atrial and venous vascular problems. The ultimate objective of any anticoagulant therapy is to proficiently prevent unwanted and dangerous clot formation.[7,8] Warfarin is an antagonist of vitamin K, a constituent essential for production of clotting factors II, VII, IX and X. Warfarin has two major functioning; anti-coagulant activity and anti-thrombotic effect.[9,10] This study was attempted to evaluate the correlation of post extraction hemorrhage and anti coagulant therapies in younger population. The study was retrospectively performed to assess the related prevalence also in the studied population.

2. MATERIALS & METHODS

This study was designed, deliberate and conducted in the department of oral surgery of the institute. The study was solely based on the data archives of the department. Predominantly, patients case history, follow up case sheet and discharge summaries were explored to meet our objectives. Data exploration of last two years was attempted. We have targeted only younger age group patients those had undergone single tooth atraumatic extraction for different reasons. Both male and female patients were selected randomly. Pure randomized sampling procedure was employed in the selection procedure. Inclusion criterion included non traumatic extraction, absence of any soft tissue deformity, absence of any pathology in the jaws, absence of any other systemic medication, accepted salivary flow. Exclusion criterion included any gross anomaly associate with maxillofacial structures, mentally retarded patients and smokers. Patients were grouped as per their history of anticoagulant therapy (warfarin). Warfarin is an antagonist of vitamin K, a constituent essential for synthesis of clotting factors II, VII, IX and X, as well as the naturally occurring endogenous anti-coagulant proteins C and S. Warfarin has two functions: anticoagulant activity and antithrombotic effect. Those who reported to be on anticoagulant therapy for more than one year, were segregated in group one. Patients who reported to be on anticoagulant therapy for six to twelve months, were segregated in group two. Patients who reported to be on anticoagulant therapy for less than six months, were studied in group three. Patients not receiving this therapy were served as control group or group four. Post operative bleeding was studied under five categories in each group. These were mild, moderate, severe, uncategorized and no bleeding. After comprehensive data evaluation and analysis, total 120 patients were filtered out for study. We have accurately assorted the patients in all four study groups depending upon their criterion. Each group has thirty patients. Fourth group served as control group wherein no history of warfarin uptake was reported. Frequencies of post extraction bleeding in all four study groups were also noticed. Study inferences was kept complete confidential. The privacy and other incorporated rights of the patients along with their freedom

of expression were not disclosed. Results thus received was compiled in table and subjected to basic statistical analysis. P value less than 0.05 was considered significant (p< 0.05).

3. STATISTICAL ANALYSIS AND RESULTS

In the current study, all obvious findings and data were gathered in logical manner. Compiled data was sent for statistical analysis using statistical software Statistical Package for the Social Sciences version 21 (IBM Inc., Armonk, New York, USA). The processed data was subjected to suitable statistical tests to obtain p values, standard deviation, chi- square test, standard error and 95% CI. Table 1 and Graph 1 showed that second age group of 25-29 years has maximum patients (47). P value was significant for this age group (0.01). Total 84 male and 36 female patients were studied in this study. Therefore, majority of the studied patients were male. Patients of more than 39 years of age were not included in the study. Minimum 21 patients were reported in the fourth age group of 35-39 years. P value was significant for this age group (0.02). Table 2 showed fundamental statistical descriptions for group I; evaluated for more than 12 months of Warfarin usage. Maximum 9 out of 30 patients had no bleeding. However, 8 patients showed severe post operative bleeding. 5 patients showed only mild bleeding. In this group (group I), P value was significant for all five severities of bleeding. Table 3 showed fundamental statistical descriptions for group II; evaluated for more 6-12 months of Warfarin usage. 11 out of 30 patients had no post operative bleeding. Though, 6 patients showed severe post operative bleeding. 4 patients showed only mild bleeding. In this group (group II), P value was significant for patients with severe post operative bleeding (0.01). P value was also significant for patients with no post operative bleeding (0.02). Table 4 showed basic statistical descriptions for group III; evaluated for less than 6 months of Warfarin usage. More than half (16) patients had no post operative bleeding. Nevertheless, 5 patients showed severe post operative bleeding. 2 patients showed only mild bleeding. In this group (group III), P value was significant for patients with no post operative bleeding (0.01). Table 5 showed basic statistical descriptions for group IV; evaluated for patient with no Warfarin usage. Maximum 23 patients had no post operative bleeding. Nevertheless, only 1 patients showed severe post operative bleeding. Only 1 patient showed mild bleeding. In this group (group IV), P value was significant for patients with no post operative bleeding (0.03). Table 6 showing comparison of prevalence among the 4 study groups using one-way ANOVA [for group I, II, III,IV]. P value was significant for patients (0.002).

Table 1: Age & gender wise allocation of patients

Age Group (Yrs)	Male	Female	Total	P value
20-24	21	8	29 [24%]	0.09
25-29	34	13	47 [40%]	0.01*
30-34	14	9	23 [19%]	0.10
35-39	15	6	21 [17%]	0.02*
>39	-	-	-	-
Total	84	36	120 [100%]	*Significant

Table 2: Fundamental statistical description [for group I: evaluated for more than 12 months of Warfarin usage]

Severity [for all 30 patients]	n	Mean	Std. Deviation	Std. Error	95% CI	Pearson Chi-Square Value	Level of Significance (p value)
Mild	5	1.830	0.834	0.336	1.92	1.627	0.00*
Moderate	7	2.736	0.342	0.024	1.91	1.203	0.01*
Severe	8	1.535	0.849	0.928	1.83	2.426	0.04*
Uncategorized	1	0.378	0.938	0.933	1.35	1.425	0.02*
No Bleeding	9	1.928	1.536		1.72	1.792	0.01*

*p<0.05 significant

Table 3: Fundamental statistical description [for group II: evaluated for more 6-12 months of Warfarin usage]

Severity [for all 30 patients]	n	Mean	Std. Deviation	Std. Error	95% CI	Pearson Chi-Square Value	Level of Significance (p value)
Mild	4	1.225	0.627	0.638	1.82	1.738	0.08
Moderate	6	1.920	0.278	0.092	1.02	1.928	0.05
Severe	6	1.829	0.039	0.528	1.32	2.426	0.01*
Uncategorized	3	1.029	0.930	0.029	1.49	1.039	0.09
No Bleeding	11	1.728	1.573	0.928	1.54	1.763	0.02*

*p<0.05 significant

Table 4: Fundamental statistical description [for group III: evaluated for less than 6 months of Warfarin usage]

Severity [for all 30 patients]	n	Mean	Std. Deviation	Std. Error	95% CI	Pearson Chi-Square Value	Level of Significance (p value)
Mild	2	1.356	0.834	0.022	1.90	1.738	0.70
Moderate	5	1.837	0.342	0.526	1.42	1.939	0.50
Severe	5	1.438	0.849	0.627	1.12	2.432	0.09
Uncategorized	2	0.038	0.938	0.933	1.63	2.835	0.06
No Bleeding	16	1.638	1.536	0.928	1.96	1.932	0.01*

*p<0.05 significant

Table 5: Fundamental statistical description [for group IV: no warfarin usage: control group]

| Severity [for all 30 patients]	n	Mean	Std. Deviation	Std. Error	95% CI	Pearson Chi-Square Value	Level of Significance (p value)
Mild	4	0.637	0.629	0.837	1.63	1.039	0.40
Moderate	1	1.029	0.309	0.003	1.90	1.535	0.09
Severe	1	0.102	0.037	0.530	1.73	2.536	0.08
Uncategorized	1	0.837	0.031	0.039	1.32	1.039	0.50
No Bleeding	23	0.983	1.049	0.028	1.83	1.536	0.03*

$p < 0.05$ significant

Table 6: Comparison of prevalence among the 4 study groups using one-way ANOVA [for group I, II, III,IV]

Parameters	Degree of Freedom	Sum of Squares $\sum$	Mean Sum of Squares m$\sum$	F	Level of Significance (p value)
Between Groups	4	4.948	1.536	2.452	0.002*
Within Groups	35	12.836	0.938	-	
Cumulative	73.37	8.538	-		

$p < 0.05$ significant

Graph 1: Age & gender wise allotment of patients
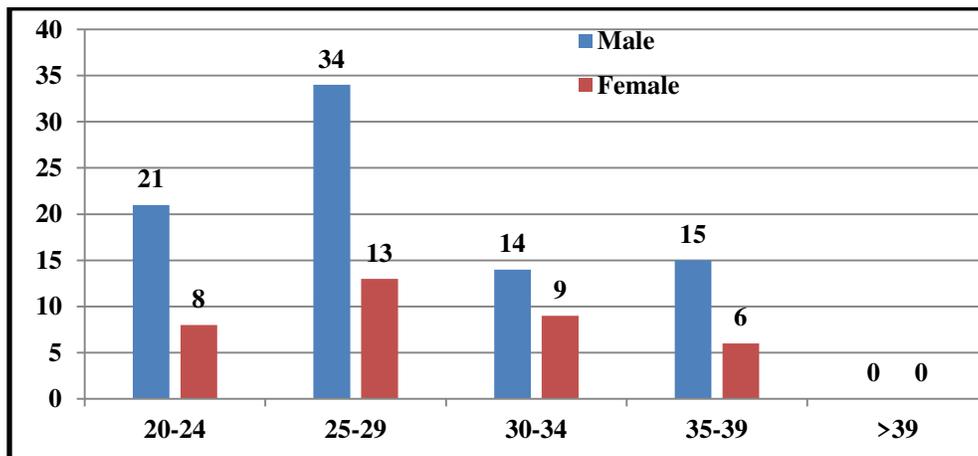
4. DISCUSSION

Literature has revealed extensive work on warfarin therapy since decades. Many of the pioneer workers have shown significant clinical correlations in post operative bleeding and warfarin therapy. Many of the related clinical guidelines and protocols have been published in this regards time to time.[11,12] However, most commonly practiced method is to stop warfarin therapy few days before surgical procedure. Warfarin, a potent anticoagulant is frequently used to indulgence of undue blood clots. These blood clots are usually venous thrombosis or pulmonary embolism.[13,14] This anticoagulant is also used to stop new clots formation. By reducing the formation of unwanted clots inside the blood vassals, anticoagulant also diminishes the potential risk of stroke induced cardiac arrest. In researches, warfarin is usually called a blood thinner; however the more exact term is anticoagulant.[15,16] Warfarin helps to keep blood flowing effortlessly in the body. It is because of its ability to reduce the amount of few imperative substances in blood. These crucial elements are primarily proteins in the form of clotting factors. Warfarin is clinically utilized for atrial fibrillation, venous thromboembolism, prosthetic valve replacement, myocardial infarction, stroke, valvulopathy.[17,18] Such patients seeking oral surgical procedure must be handled cautiously. The curative effect of warfarin is deliberated as prothrombin time and communicated as the international normalized ratio (INR).[19,20] The common dental practitioners in the hospitals and private setups should regularly provide treatment in these critical circumstances. The dentist must include a discussion of the risks of postoperative bleeding as part of routine preoperative consent.[21] The present study was primarily focused to evaluate the correlation of post extraction hemorrhage and anti coagulant therapies in younger population. Several significant correlations were drawn in these regards.

5. CONCLUSION

Authors have drawn some very noteworthy conclusions from this study. Within the limitations of the study, authors concluded that anti coagulant therapies are significantly affecting post operative bleeding in extraction cases. The relative severity and prevalence of bleeding are also exaggerated by time period of anti coagulant therapy. Patients those who were on anti coagulant therapy for more than one year, showed maximum prevalence and severity of post operative bleeding. Patients those were under control group, showed minimum prevalence and post operative bleeding. Authors noticed no gender predilection in these regards. Our study inferences should be considered as indicative for presuming prognosis for similar clinical conditions. Nonetheless, we expect some other large scale studies to be performed that might further establish certain standard and concrete guidelines in these perspectives.

6. REFERENCES

1. Kwak EJ, Nam S, Park KM, Kim SY, Huh J, Park W. Bleeding related to dental treatment in patients taking novel oral anticoagulants (NOACs): a retrospective study. Clin Oral Investig 2019;23:477–484.

2. Shaw J, de Wit C, Le Gal G, Carrier M. Thrombotic and bleeding outcomes following perioperative interruption of direct oral anticoagulants in patients with venous thromboembolic disease. J Thromb Haemost 2017;15:925–930.

3. Abayon M, Kolokythas A, Harrison S, Elad S. Dental management of patients on direct oral anticoagulants: case series and literature review. Quintessence Int 2016;47:687–696.

4. Firriolo FJ, Hupp WS. Beyond warfarin: the new generation of oral anticoagulants and their implications for the management of dental patients. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;113:431–441.

5. Berton F, Costantinides F, Rizzo R, Franco A, Contarin J, Stacchi C, Maglione M, Visintini E, Di Lenarda A, Di Lenarda R. Should we fear direct oral anticoagulants more than vitamin K antagonists in simple single tooth extraction? A prospective comparative study. Clin Oral Investig 2019;23:3183–3192.

6. Rocha AL, Oliveira SR, Souza AF, Travassos DV, Abreu LG, Ribeiro DD, Silva TA. Bleeding assessment in oral surgery: a cohort study comparing individuals on anticoagulant therapy and a non-anticoagulated group. J Craniomaxillofac Surg 2019;47:798–804.

7. Hair JF Jr, Black WC, Babin BJ, Anderson RE. Multiple regression analysis: Pearson new international edition, 2014, 7th edn. Pearson Education Limited, Essex.

8. Brennan Y, Gu Y, Schifter M, Crowther H, Favaloro EJ, Curnow J. Dental extractions on direct oral anticoagulants vs. warfarin: the DENTST study. Res Pract Thromb Haemost 2020;4:278–284.

9. Lababidi E, Breik O, Savage J, Engelbrecht H, Kumar R, Crossley CW.Assessing an oral surgery specific protocol for patients on direct oral anticoagulants: a retrospective controlled cohort study. Int J Oral Maxillofac Surg 2018;47:940–946.

10. Mauprivez C, Khonsari RH, Razouk O, Goudot P, Lesclous P, Descroix V. Management of dental extraction in patients undergoing anticoagulant oral direct treatment: a pilot study. Oral Surg Oral Med Oral Pathol Oral Radiol 2016;122:e146–e155..

11. Yagyuu T, Kawakami M, Ueyama Y, Imada M, Kurihara M, Matsusue Y, Imai Y, Yamamoto K, Kirita T. Risks of postextraction bleeding after receiving direct oral anticoagulants or warfarin: a retrospective cohort study. BMJ Open 2017:15:952-60.

12. Lopez-Lopez JA, Sterne JAC, Thom HHZ, Higgins JPT, Hingorani AD, Okoli GN, Davies PA, Bodalia PN, Bryden PA, Welton NJ, Hollingworth W, Caldwell DM, Savovic J, Dias S, Salisbury C, Eaton D, Stephens-Boal A, Sofat R. Oral anticoagulants for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis, and cost effectiveness analysis. BMJ 2017;59:5058-64.

13. Hanken H, Grobe A, Heiland M, Smeets R, Kluwe L, Wikner J, Koehnke R, Al-Dam A, Eichhorn W. Postoperative bleeding risk for oral surgery under continued rivaroxaban anticoagulant therapy. Clin Oral Investig 2016;20:1279–1282.

14. Bensi C, Belli S, Paradiso D, Lomurno G. Postoperative bleeding risk of direct oral anticoagulants after oral surgery procedures: a systematic review and meta-analysis. Int J Oral Maxillofac Surg 2018;47:923–932.

15. Morimoto Y, Yokoe C, Imai Y, Sugihara M, Futatsuki T. Tooth extraction in patients taking nonvitamin K antagonist oral anticoagulants. J Dent Sci 2016;11:59–64.

16. Cabral KP. Pharmacology of the new target-specific oral anticoagulants. J Thromb Thrombolysis 2013;36:133–140.

17. Miller SG, Miller CS. Direct oral anticoagulants: a retrospective study of bleeding, behavior, and documentation. Oral Dis 2018;24:243–248.

18. Kyosaka Y, Owatari T, Inokoshi M, Kubota K, Inoue M, Minakuchi S. Cardiovascular comparison of 2 types of local anesthesia with vasoconstrictor in older adults: a crossover study. Anesth Prog 2019;66:133–140.

19. Miclotte I, Vanhaverbeke M, Agbaje JO, Legrand P, Vanassche T, Verhamme P, Politis C. Pragmatic approach to manage new oral anticoagulants in patients undergoing dental extractions: a prospective case-control study. Clin Oral Investig 2017;21:2183–2188.

20. Inokoshi M, Kubota K, Yamaga E, Ueda K, Minakuchi S. Postoperative bleeding after dental extraction among elderly patients under anticoagulant therapy. Clin Oral Investig. 2020 Sep 1. Epub ahead of print.

21. Available From: United Nations (2019) Department of Economic and Social Affairs, population division. World population ageing. https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2019-Highlights.pdf. Electronically Accessed on 4 Jan 2021.