The Effect of Interruption, Adjusting and Continuing of Warfarin on Bleeding after Tooth Extraction

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Abstract: Sodium Warfarin is one of the oral anti coagulant drugs that is used by some patients to avoid thromboemboli. For these patients one of the problems after the surgery is hemorrhage. These patients should be checked and evaluated before the surgery. The aim of this study, was to determine and compare the effect of interruption, adjusting and continuing warfarin on bleeding after tooth extraction. In an experimental study we surveyed the effect of warfarin on bleeding for 17 patients with 81 extractions. On the basis of the received results from lab and the amount of Pro-Thrombin time (PT), The kind of problem and consulting with cardiovascular specialist on interruption, adjusting and continuing the use of drug were decided 0.37 extractions in group one (continuing the drug), 33 extractions in group 2 (drug adjustment) and 11 extractions in group 3 (discontinuing the use of the drug). All the patients underwent a bilateral symmetrical extraction of the teeth. The findings were analyzed by correlation coefficient, chi-square (χ^2) and t-tests. The average amount of INR was 2.25±0.55 in all 3 groups (SD = 0.55). The results showed average amount of PT in patients with no bleeding was 19.7±2.3, while in mild bleeding it was 19.3±4.7. In 3 groups no hemorrhage was observed after extraction in the first 30 min. During the first 24 h, only 8 of the extractions, who did not notice the post operative orders, showed signs of mild bleeding. The difference between group 1 and the other groups was not significant statistic cally (p>0.5). There was no hemorrhage in the 3 groups 48 h and 5 days after extraction. There was no significant relationship between hemorrhage and the type of systemic disease either clinically or statistically. It was concluded that continuing Warfarin if International Normalized Ratio (INR) is in the Normal Range (INR<4) poses no danger for the patient and if the patient is at risk of thrombo-emboli, continuing the drug is advised. In cases of INR>4 adjusting the drug should be taken into consideration. It is not advised to stop the medication if the consequences are irreparable.

Key words: Warfarin, anticoagulant, bleeding, tooth extraction

INTRODUCTION

Among those, who need oral surgery, some are affected with systemic diseases including artificial heart valve, myocardial infarction, cerebro-vascular accidents, deep vein thrombosis. To avoid thrombo-emboliy, they use anticoagulant drugs such as warfarin (Cohen and Warman, 1989; Whal, 2000). Warfarin (cumadin) affects the ability of the liver to produce vitamin K-dependent factors II, VII, IX and X. (Kwon and Laskin, 2001). Liver and kidneys change warfarin into active metabolites with half life ranging from 25-60 h, with a mean of about 40 h.

Warfarin has a duration of action ranging from 2-5 days and its maximum plasma concentration is about 2-8 h after oral administration. Warfarin can be detected in plasma within 1 h of its oral administration (Goodman *et al.*, 1996).

The action of warfarin can be assayed using PT test. warfarin therapeutic range is between 1.5 and 2 times the normal control time. Assuming a control time of 12 sec, This leads to a therapeutic reage of warfarin as 18-24 sec (Donoff, 1997). One of the problems in patients, who take anticoagulant drugs is hemorrhage so that sometimes blood transfusion is necessary and on the other hand,

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stopping or changing the dose of warfarin might cause the risk of thromboemboli (Cohe and Warman, 1989). Consultation with patient's physician and cooperation between physician and dentist could be useful for patients taking warfarin and also, need elective oral surgery (Peterson *et al.*, 2003).

The problems of controlling bleeding is important less than thromboembolism and Vascular occlusion after alteration of anticoagulant therapy (Aldous and Olson, 2001). So, these patients should be checked and evaluated concerning the use of the needed drugs before surgery (Cohen and Warman, 1989).

Some protocols for surgery and extracting the teeth in these patients are as follows:

- To replace heparin for warfarin
- To decrease anticoagulant drugs before extraction
- To stop prescribing and using warfarin temporarily
- Not to change the medication (Wahl, 2000; Devani *et al.*, 1998)

In this research, we have tried to have an exact and controlled clinical evaluation and suggest a practical way for the patients who taking warfarin. Therefore, the aim of this study was to determine and compare the effect of cessation, adjusting and continuing the use of warfarin on bleeding after tooth extraction.

MATERIALS AND METHODS

This experimental study was performed on 17 patients (with 81 tooth extractions) who had systemic problems (artificial heart valve, heart disease, vein thrombosis) in the Department of Maxillofacial Surgery, Faculty of Dentistry, University of Qazvin, Iran. These patients were 6 women and 11 men with an age average of 50.2 ± 10.3 years who were referred by cardiovascular specialists. All these patients underwent bilateral and almost symmetrical teeth extraction. The patients with liver problem were excluded from the study. Each patient was sent to a laboratory for the primary evaluation. On the basis of the received results from the lab and the amount of, Pro-Thrombin time (PT), the kind of problem and consulting with cardiovascular specialists on cessation, adjusting and continuing, the use of drug were decided. To prevent bacterial endocarditis the prophylaxis was used before the surgery if necessary. From among the 81 cases of tooth extraction, 37 individuals continued the drug (group 1), 33 individuals had drug adjustment (group 2) and the other 11 individuals stopped using the drug (group 3).

All the patients were treated under local anesthesia (Mepivastesin, Cristalia Co., Brazil) on an outpatient basis and local measures (consisting of surgical pack gelatamp + wet gauze and suture) were used in all cases to control post operative bleeding. All were operated by the same surgeon and had similar conditions for the 2 operations as much as possible. Three teeth were extracted on one side. The patients were asked not to open their mouth for 30 min. After this time if there was no bleeding, the area was sutured. The patient was discharged after placing a wet gauze on the wound. The patients were advised to refer to an assigned hospital if there was any sign of bleeding, otherwise in 24, 48 h or 5 days after the surgery they should have come back to the surgical ward of the Faculty (hemorrhage was indicated in 3 periods using A, B and C codes).

A = No hemorrhage (no blood was seen on the wet gauze)
B = Mild hemorrhage (hemorrhage was seen on the wet gauze)
C = Severe hemorrhage (hemorrhage required removal of clot and suture replacement in which the whole area needed to be examined)

The patients were advised to avoid eating, drinking or speaking for 3 h after the operation, avoid smoking for 5 days, go on a diet which contained soft cool food and liquids and do no heavy exercise. For hygienic considerations after 8-12 h, they had to wash their mouth with tepid water. The findings were analyzed by correlation coefficient, chi-square (χ^2) and t-tests.

RESULTS

In this study the effect of cessation, adjusting and continuing the use of wafarin on bleeding after minor mouth surgeries were studied and the following results were obtained: In evaluating pro-thrombin time, the amount of PT was 19.68 ± 2.8 sec in the 3 groups (SD = 2.8). The maximum of PT, was 23 sec (14.8%) (Table 1). The average amount of INR was 2.25 ± 0.55 in all 3 groups (SD = 0.55) (Table 2).

Age, pro-thrombin time and INR in the 3 groups are shown in Table 3. The results from Pearson correlation coefficient express that there is a reverse relationship between age and pro-thrombin time; with increasing of age, pro-thrombin time is reduced. The results of t-test showed the pro-thrombin time in patients with no bleeding was 19.7 ± 2.3 while in mild bleeding it was 19.3 ± 4.7. The difference between group one and the other

Table 1: Frequency distribution of PT

Amount of PT	Number	(%)
14.00	4	4.9
14.50	3	3.7
16.50	5	6.2
17.00	6	7.4
17.50	3	3.7
18.00	6	7.4
18.50	4	4.9
19.00	3	3.7
19.50	7	8.6
20.00	11	13.6
22.00	6	7.4
22.30	1	1.2
22.50	6	7.4
23.00	12	14.8
24.00	3	3.7
25.00	1	1.2

Table 2: Frequency distribution of INR

Amount of INR	Number	(%)
1.10	4	4.9
1.20	3	3.7
1.50	5	6.2
1.60	3	3.7
1.70	8	9.9
1.80	4	4.9
2.00	3	3.7
2.10	11	13.6
2.20	11	13.6
2.40	1	1.2
2.50	5	6.2
2.70	11	13.6
2.80	8	9.9
3.10	3	3.7
3.30	1	1.2

Table 3: Mean of age, PT and INR in all 3 groups

Group number	No bleeding (73)	Mild bleeding (8)	Result of test
Age			
Mean	48.90	56.10	T = 3.53
Variant	9.80	10.60	p = 0.013
PT			
Mean	19.70	19.30	T = 0.53
Variant	2.30	4.70	p = 0.6
INR			
Mean	2.15	2.13	T = 0.2
Variant	0.43	0.90	p = 0.9

Table 4: Frequency distribution of bleeding in the first 24 h after extraction

Kind of treatment	No bleeding	Mild bleeding	Severe bleeding	Total
Group 1	33	4	-	37
	89.2%	10.8%	-	45.7%
Group 2	32	1.0	-	33
	97%	3%	-	40.7%
Group 3	8	3	-	11
	72.8%	27.2%	-	13.6%
Total	73	8	-	81
	90.1%	9.9%	-	100%

did not followed the post operative orders, showed signs of mild bleeding. There was no hemorrhage in the 3 groups 48 h and 5 days after extraction.

DISCUSSION

This study showed that continuing warfarin when the INR is within the normal range INR ≤ 4 and using local measures to control post operative bleeding, do not put the patients in danger. If the patients are at risk of thromboemboli continuing the drug and in cases of INR > 4 adjusting of drug should be taken into consideration. It is not advised at all to stop the medication if the consequences are irreparable. In a survey by Devani *et al.* (1998), on 65 warfarin users who needed an extraction, they concluded that if INR is between 2-4, surgical pack, suture was enough to stop bleeding and there is no need to change the amount of warfarin before an extraction. In an another study Ferrieri *et al.* (2007) reported that atraumatic operation and post extraction appropriate orders can influence post operative complications.

It has been expressed, in several researches patients that therapeutically anticoagulated with warfarin whose INR is within the normal range, can be treated without interruption when proper local measures are used (Blinder *et al.*, 2001; Carter *et al.*, 2003; Halfpenny *et al.*, 2001; Patatanian and Fuguate, 2006; Randall, 2005; Salam *et al.*, 2007). Similarly at present study During the first 24 h Only 8 of the Extractions, who did not followed the post operative orders, showed signs of mild bleeding.

Halfpenny *et al.* (2001) the use of fibrin adhesive, Blinder *et al.* (2001) (gelatin spong + suture), Salam *et al.* (2007) (absorbable oxycellulose + suture), Randall (2005)

groups was not significant (p>0.05). On the other hand, age had no significant effect on the use of warfarin. According to Chi-square (χ^2) test, there was no significant relationship between hemorrhage and the type of systemic disease (p>0.05). Based on the regression line equation there was a general relationship between INR and prothrombin time:

$$INR = -1.25 + 0.186\,PT$$

Out of the 37 extractions in group one (continuing the drug), 33 extractions were without hemorrhage (89.2%) after the surgery and in 4 of them (10.8%), mild hemorrhage was observed in the first 24 h. In the 33 operations in group 2 (adjustment of the drug), 32 were without hemorrhage and in one case (3%) there was a mild bleeding. In the 11 operations in group 3 (discontinued the drug) 8 extractions (72%) were without hemorrhage and in 3 operations (27.2%) mild hemorrhage was observed (Table 4).

None of the patients had any immediate post operative bleeding in the thirty minutes after extraction. During the first 24 h, only 8 of the Extractions, who

(haemostatic dressing + suture + local pressure), Patatanian and Fuguate (2006) (haemostatic mouth washes) and Della *et al.* (2003) (platelet-rich plasma) have reco mmended.

On the basis of another research by Wahl (2000), it is proposed that if INR is in the normal range, there is no need to stop warfarin for dental extraction and if INR is more than the normal range, the dentist should decide on the type of treatment considering the type of dental problem.

Following a randomized controlled clinical trial by Evan and colleagues, they concluded that the incidence of bleeding complication in the intervention group (warfarin continued) was higher (15/57, 26%) than in the control group (7/52, 14%) but this difference was not significant. They found that continuing warfarin when the INR is <4.1 could lead to an increase in minor post extraction hemorrhage. They, however, found no evidence of an increase in clinically important bleeding (Evans, 2001).

The present study proposes that, if the INR is within the normal range of (INR ≤ 4) and local measures are used to control post operative bleeding, there is no justification for altering warfarin treatment prior to dental extraction in these patients, which has the same conclusion as other reached in their research (Blinder *et al.*, 2001; Carter *et al.*, 2003; Devani *et al.*, 1998; Halfpenny *et al.*, 2001; Patatanian and Fuguate, 2006; Randall, 2005; Salam *et al.*, 2007).

In another study done by Webster and Wilde (2000) it was mentioned that the amount of INR needed for extraction and gingival surgery is 3.5 and the acceptable amount is 3-4 and concluded that if INR is <4, no change in medication is advised and if INR is >4 warfarin should be discontinued and the operation should be carried out when, INR is in the treatment range. In another study by Beirne and Koehler (1996) in, it has been proposed that the extraction of teeth can be performed with INR, of 4 or less. They also, suggested that with proper local measures, teeth can be safely extracted and the development of thrombo emboli in high-risk patients can still be avoidec. However, dosage of warfarin may need to be modified if the risk of bleeding is too high (Beirne and Koehler, 1996). In the basis of another study by Okado *et al.* (2004). It is proposed that in addition to PT-INR level, warfarin manipulation and size of wound could be effective to control the post extraction hemorrhage in patient on warfarin.

In a study conducted by Malden *et al.* (2007) reported that INR in patients with multiple extraction

increases post extraction. The results showed that there was relation ship between severity of surgery and anticoagulation, so INR should be assayed post extraction.

In this research, bleeding was not seen in the first thirty minutes after the extraction that is the same as the results obtained by Devani *et al.* (1998). In the present study, results confirm the use of wet gauze with normal saline, gelatamp and suture to control bleeding that is the same as the results obtained by Beirne and Koehler (1996). There was no relationship between hemorrhage and the type of cardiovascular diseases. In the first 24 h in the 3 groups, 8 mild bleedings occurred because the patient did not take the physician's advice after the operation. In this study, the result does not confirm the hypothesis of reducing or stopping the drug to preserve the health of patient.

CONCLUSION

Consultation with the patient's physician is necessary. Reducing or stopping the use of sodium warfarin for more safety does not seem necessary. With proper local measures, continuing warfarin if INR is within the normal range (<4) poses no danger for the patient and reduces the harmful effects of bleeding after the extraction.

The type of treatment depends on the kind of cardiovascular disease and the amount of prescribed warfarin.

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