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RESEARCH ARTICLE

PROTHROMBIN TIME AND INTERNATIONAL NORMALIZED RATIO PREDICT BLEEDING COMPLICATIONS AMONG CARDIAC VALVE REPLACEMENT PATIENTS UNDERGOING CARDIOPULMONARY BYPASS

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ABSTRACT

Background: Hemorrhage after cardiopulmonary bypass (CPB) remains a clinical problem. Many risk factors associated with excessive blood loss have been identified, but postoperative bleeding remains poorly explained because of the complexity of the hemostatic process and the technical difficulties imposed by operative procedures. It suggests a need for patient testing to determinate hemostatic disorder after CPB and to be able differentiate a surgical cause for abnormal bleeding.
Objectives: The study objective was to determine the prothrombin time (PT) and international normalized ratio (INR) in predicting bleeding in Sudanese patients among Mechanical valve replacement undergoing cardiopulmonary bypass.
Design: Descriptive Cross sectional study
Methodology: A prosthetic valve was implanted in 150 patients between July 2013 to January 2014.The age of patients ranged between 20 to 80 years with mean of 41years. The PT and INR were determined using coagulation analyzer model Spinreact- (BIOBAS10). One hundred and fifty patients underwent valve replacement: 60 patients(40%) had isolated mitral valve replacement (MVR), 46 patients(30.7%) had isolated aortic valve replacement (AVR), 26(17.3%) had duple valve replacement(DVR) and 18 (12%) had coronary artery bypass graft (CABG), and 50 healthy individuals were recruited as control group.
Results: The mean of prothrombin time(PT) was (34.5±14.02) seconds and there was significant variation (p.value < 0.05) between the patients and controls(13.1±1.8)seconds. The mean international normalized ratio(INR) was (3.2±1.6) however there was a significant variation (p.value < 0.05) between the patients and controls(1.0±0.25). Among Sudanese patients with prosthetic heart valve, bleeding was the major complications rather than thromboemboloism. About 129(86%) patients from 150 had prothrombin time more than 20 seconds and about 44(29.3%) patients show international normalized ratio more than 3.5. The mean PT-INR was 2.4±0.6 in the cases without hemorrhage complications, and 4.2±1.5 in the patients associated with excessive bleeding. There was significant difference in mean PT-INR between the bleeding complication group and non complication group (p.value < 0.05). More than 72% of patients with hemorrhage complications showed the PT-INR more than 3.97.
Conclusion: PT and INR had high sensitivity and specificity in predicting blood loss among patients with valvular replacement and represent good indicators of platelet and fresh frozen plasma transfusion in these patients. The Prothrombin time and INR correlated with blood loss and transfusion requirements for predicting excessive blood loss after cardiopulmonary bypass.

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INTRODUCTION

Hemorrhage after cardiopulmonary bypass (CPB) remains a clinical problem. Many risk factors associated with excessive blood loss have been identified (Wolfe *et al.,* 2007), but postoperative bleeding remains poorly explained because of the complexity of the hemostatic process and the technical difficulties imposed by operative procedures. It suggests a need for patient testing to determinate hemostatic disorder after CPB and to be able differentiate a surgical cause for abnormal bleeding. (Wolfe *et al.,* 2007) A common cause of bleeding following CPB is a localized defect in surgical hemostasis. However, it may be difficult to distinguish bleeding due to an acquired systemic coagulopthy from a localized surgical problem unless the patient has obvious evidence of a generalized bleeding tendency such as epistaxis or oozing from catheter sites. In the absence of a coagulopathy, bleeding that exceeds 10 mL/kg in the first postoperative hour or an

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average of ≥ 5 mL/kg in the first 3 postoperative hours has been suggested as a guideline for reoperation. Any sudden bleeding after chest tube drainage has stopped is also considered an indication for reoperation. (Edmunds and Addonizio 1987)

Risk factors for bleeding include high intensity of anticoagulation (INR > 4.0), age 65, highly variable INRs, history of gastrointestinal bleeding, hypertension, cerebrovascular disease, serious heart disease, anemia, malignancy, trauma, renal insufficiency, concomitant drugs and long duration of warfarin therapy. Regular monitoring of INR should be performed on all treated patients. Those at high risk of bleeding may benefit from more frequent INR monitoring, careful dose adjustment to desired INR, and a shorter duration of therapy. Patients should be instructed about prevention measures to minimize risk of bleeding and to report immediately to physician's signs and symptoms of bleeding. (Wadelius *et al.,* 2005) Cardiopulmonary bypasses (CPB) have placed a great problem in the clotting system mechanism and some of coagulation clotting factors affected. Bleeding associated with cardiac surgery procedures is a one of the big problem take place and blood loss reduces the adaptative of clotting factors capacity of cardio vascular system. Complications following heart valve replacement are not common, but can be serious. All valves made from animal tissue will develop calcium deposits over time. These deposits interfere with the function of the valve, it must be replaced. Blood clots may form on the surface of the supplying blood to the brain, kidney and legs. These blood clots may cause fainting spells, stroke, kidney failure, or loss of circulation to the legs. These blood clots can be treated with drugs or surgery. (Brister *et al.*, 1993; Boisclair *et al.*, 1993) The infection of heart muscles affects up to 2% of patient who have heart valve replacement. If the infection persists, the new value may have to be replaced. The prothrombin time (PT) and International normalize ratio (INR) are useful for identifying coagulation factor deficits after cardiopulmonary bypass (CPB). (Dela Cadena *et al.,* 1994) However, long processing times and the need for fresh frozen plasma (FFP) to be thawed cause delays in factor replacement. We hypothesized that, by treating with warfarin, blood sampled toward the end of CPB can provide PT results that help to determine the requirement for follow up after CPB. Laboratory delays can be eliminated with point-of-care Compared with PT measurements done after CPB, the mean bias for laboratory PT and INR measurements taken during CPB seemed to be minimal, suggesting a moderate degree of agreement. Nonetheless, the limits of agreement around PT during CPB exceeded our threshold of -1.0 second, with the largest discrepancy seen with larger PT measurements. In choosing this threshold, we did not find any previously published data to guide us. (Wachtfogel *et al.,* 1989; Rivers *et al.,* 1975; Woodman and Harker 1990) Although it is stringent, a more relaxed threshold such as -2.0 seconds seemed too wide to be clinically meaningful. (Tabuchi *et al.*,1993)

However, using the prothrombin time-international normalized ratio (PT-INR) has been proposed in recent years. (Kazami 1985) The guideline of the American Heart Association (AHA) in 1992 set the optimal clinical range of warfarin for patients with artificial valve replacement at 2.5-3.5 in terms of the PT-INR value, and further recommended that slightly lower PT-INR values of 2.0-3.0 should be used for the management of the patients with a high risk of bleeding. (Hirsh *et al*., 1992)

MATERIALS AND METHODS

This is a descriptive Cross sectional study done during the period of July 2013 to January 2014 in Alshaab teaching hospital and Ahmed Qasem teaching hospital in Khartoum state to measure prothrombin time (PT) and international normalized ratio(INR) and to determine their values in predicting bleeding in Sudanese patients among Mechanical valve replacement undergoing cardiopulmonary bypass. 150 patients with mechanical valve replacement undergoing cardiopulmonary bypass and 50 healthy individuals were recruited as control group.

Preparation of platelet poor plasma (PPP)

The blood samples were collected from patients and controls in tri-sodium citrate (3.2%) anticoagulant (ratio1:9). platelet poor plasma sample were prepared by centrifugation at 2000g for 15 min. The samples were being kept at room temperature for PT and INR estimation using the coagulometer model spinreact biobas 10.

Data analysis

All data are presented as mean±SD using Statistical Package for the Social Sciences, unless otherwise noted. Statistical comparisons were performed using unpaired student's t-test with $p<0.05$ considered as significant.

RESULTS

One hundred and fifty patients of either sex underwent valve replacement: 60 patients (40%) had isolated mitral valve replacement (MVR), 46 patients (30.7%) had isolated aortic valve replacement (AVR), 26(17.3%) had double valve replacement (DVR) and 18(12%) had coronary artery bypass graft (CABG) (Table 1).

Table 1. The frequency of patients under valve replacement:

Case	Frequency	Percent
MVR	60	40%
AVR	46	30.7%
DVR	26	17.3%
CABG	18	12%

Table 2. The mean of the prothrombin time in patients and controls

	Count	Mean	STD Deviation
Patients	150	34.5	14.02
Control	50	13.1	1.8

Table 3. The mean of the international normalized ratio in patients and Controls

	Count	Mean	STD Deviation
Patients	150	3.2	1.6
Control	50	1.0	0.25

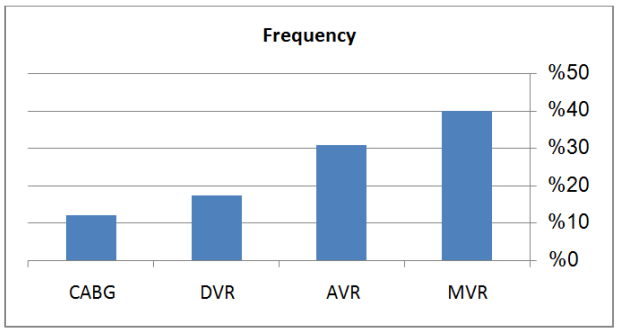

Figure 1. The frequency of patients underwent valve replacement according to the type of valve

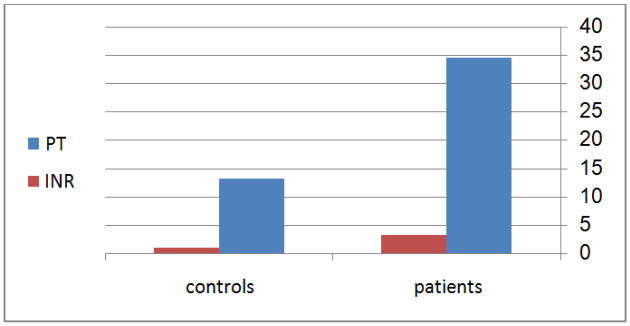

Figure 2. The mean of prothrombin time and international normalized ratio in patients and controls

The controls were normal individuals of either sex. 52% of the patients were male and 48% of them were female. The age of patients ranged between 20 to 80 years with mean of 41years and the controls have the same age range. The results showed that 54.7% of patients were in age group of 20-40 years, 31.3% of the patients were between 41-60 years and 14% were between 61-80 years. The mean of prothrombin time (PT) was 34.5±14.02 seconds and there was significant variation (p.value < 0.05) between the patients and controls(13.1±1.8) seconds (Table 2). The mean international normalized ratio(INR) was 3.2±1.6 however there was a significant variation (p.value < 0.05) between the patients and controls (1.0±0.25) (Table 3). Sudanese patients with prosthetic heart valve, bleeding was the major complication rather than thromboemboloism. About 129(86%) patients from 150 had prothrombin time more than 20 seconds and about 44 (29.3%) patients show international normalized ratio more than 3.5. The mean PT-INR was 2.4±0.6 in the cases without hemorrhage complications, and 4.2±1.5 in the patients associated with excessive bleeding. There was significant difference in mean PT-INR between the bleeding complication group and non complication group (p.value < 0.05). More than 72% of patients with hemorrhage complications showed the PT-INR more than 3.97.

Conclusion

PT and INR had high sensitivity and specificity in predicting blood loss among patients with valvular replacement and represent good indicators of platelet and fresh frozen plasma transfusion in these patients.

The Prothrombin time and INR correlated with blood loss and transfusion requirements for predicting excessive blood loss after cardiopulmonary bypass. During the study period, hemorrhage complications were noted in 44 (29.3%) of 150 patients with a prosthetic heart valve. The mean PT-INR was 2.4±0.6 in the cases without hemorrhage complications, and 4.2±1.5 in the patients associated with excessive bleeding. There was significant difference in mean PT-INR between the bleeding complication group and non complication group (p.value < 0.05). More than 72% of patients with hemorrhage complications showed the PT-INR more than 3.97.

REFERENCES

Boisclair MD, Lane DA, Philippou H, Sheikh S, Hunt B. Thrombin production, inactivation and expression during open heart surgery measured by assays for activation fragments including a new ELISA for prothrombin fragment F1+2. Med Thromb Haemost. 1993;70:253-258.

Brister SJ, Ofosu FA, Buchanan MR. Thrombin generation during cardiac surgery: heparin the ideal anticoagulant? Med Thromb Haemost. 1993;70:259- 262.

Dela Cadena RA, Wachtfogel YT, Colman RW. Contact activation pathway: inflammation and coagulation. In: Colman RW, Hirsh J, Marder VJ, Salzman EW, eds. Hemostasis and Thrombosis: Basic Principles and Clinical Practice. 3rd ed. Philadelphia, Pa: JB Lippincott Co; 1994:219-240.

Edmunds LH Jr, and Addonizio VP Jr: Extracorporeal circulation, in Coleman RW, Hirsh J, Marder VJ, Salzman EW (eds): Hemostasis and Thrombosis (ed 2). Philadelphia, PA, Lippincott, 1987, p 901.

Hirsh J. Oral anticoagulant therapy. Urgent need for standardization. Circulation 1992; 86: 1332–5.

Kazami M. Guideline for oral anticoagulant therapy. Blood & Vessel 1985; 16: 431–40.

Rivers RPA, Hathaway WE, Weston WL. The endotoxin-induced coagulant activity of human monocytes. *Med Br J Haematol*. 1975;30:311-315.

Tabuchi N, Haan J, Boonstra PW, van Oeveren W. Activation of fibrinolysis in the pericardial cavity during cardiopulmonary bypass. *J Thorac Cardiovasc Surg*. 1993;106:828-833.

Wachtfogel WT, Harpel PC, Edmunds LH Jr, Colman RW. Formation of C1s-C1-inhibitor, and plasmin- 2-plasmin inhibitor complexes during cardiopulmonary bypass. Blood. 1989;73:468-471.

Wadelius M, Chen LY, Downes K, *et al*. Common VKORC1 and GGCX polymorphisms associated with warfarin dose. *Pharmacogenomics J*. 2005;5:262-270.

Wolfe R, Bolsin S, Colson M, Stow P. Monitoring the rate of reexploration for excessive bleeding after cardiac surgery in adults // Quality and Safety in Health Care, 2007; 16:192–196.

Woodman RC, Harker LA. Bleeding complications associated with cardiopulmonary bypass. Blood. 1990;76:1680-1697.

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