Journal of Cardiovascular and Thoracic Research, 2012, 4(2), 49-52
doi: 10.5681/jcvtr.2012.012
http://jcvtr.tbzmed.ac.ir

The Effect of Cyanosis on Active Clotting Time During Diagnostic Catheterization

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ARTICLE INFO

Article Type:
Research Article

Article History:
Received: 29 Feb 2012
Accepted: 29 July 2012
ePublished: 8 Sep 2012

Keywords:
Heparin
Active Clotting Time
Cyanosis
Catheterization

ABSTRACT

Introduction: Cardiac catheterization is a common procedure which needs a careful coagulation monitoring. In our study, we aimed to find factors influencing active clotting time (ACT) following heparin therapy. **Methods**: ACT of 71 patients who were scheduled to undergo transcutaneous diagnostic catheterization and angiography were measured at baseline, 2 and 60 minutes after 50 IU/kg heparin loading. ACT in two groups of patients (cyanotic and non-cyanotic) was compared. All data were analyzed with Wilcoxon, Mann-Whitney test and Pearson in SPSS 16, *P* value less than 0.05 was considered significant. **Results**: ACT following heparin at 2nd and 60th minutes was not significantly different in cyanotic and non-cyanotic groups. At 60th minute following heparin administration, ACT decreased more dramatically in older children. **Conclusion**: Cyanosis does not affect ACT measures following heparin treatment. Moreover, after 60 minutes, heparin efficacy (ACT values) decreased more with increase in patients' age.

Introduction

Firstly discovered in 1916 by Mclean, heparin was introduced as the most common anticoagulant to have been used in clinical practice[1] especially as it is the first choice throughout cardiopulmonary bypass (CPB). It seems that different individuals response variously to different doses of heparin and therefore coagulation monitoring seems to be inevitable during operation.[2] It should be mentioned that inadequate heparinization is associated with thrombosis following blood product administration.[3-5]

Presently, activated clotting time is used as the most common method thanks to it simplicity and cost for heparinization monitoring.[6,7] In the present paper, we tried to probe the effect of a fixed dose of heparin on ACT during cardiac Catheterization. This would help to clarify the efficacy of heparin in cyanotic and acyanotic congenital heart disease patients...

Materials and methods

After obtaining ethical approval, 71 patients who were scheduled to undergo elective diagnostic angiography with non-ionic contrast solution were allocated to the present study during 1 year. Exclusion criteria were unwillingness to take part in the study, using antiplatelet therapy within previous 7 days, hereditary coagulation or platelet disorders, low platelet count, and receiving blood products during follow up period. Demographic data including age, sex, type of congenital heart disease (cyanotic or acyanotic), weight and peripheral oxygen saturation using pulse oximetry and the site of vascular access (arterial or venous) were studied.

All patients were sedated with a combination of midazolam and fentanyl. Routine monitoring included arterial blood pressure, central venous pressure, electrocardiogram, urinary catheter and nasal temperature. After establishment of the vascular access and blood sampling for baseline ACT, 50 IU/kg of heparin was injected to the patients and their ACT values were measured 2 minutes and one hour later. Target ACT was maintained between 250-350 seconds. Blood sample (2 mL) was obtained from vascular access site; and after being transferred into an ACT tube it was mixed by hand while shaking the tube steadily. After the tube was inserted into a 37C heat block chamber, it rotated inside the instrument in a magnetic field. As the blood clotted, it displaced the magnet which activates a proximity switch. The clotting time is considered as the time required the clot to displace the magnet in a given distance.[8]

All data were analyzed with Wilcoxon, Mann-Whitney test and Pearson in SPSS 16, *P* value less than 0.05 was considered statistically significant.

Results

Seventy-one patient entered the study including 15 non-cyanotic and 56 cyanotic patients with the mean age of 63

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63±5 months (minimum of 2 and maximum of 180 months). The mean ACT before heparin loading was 149 ±139 seconds which increased to 260±89 and 220±64 seconds at two minutes and one hour after injection respectively. A significant increase was observed in ACT after two minutes which significantly decreased after 1 hour (Table 1).

Ninety-six percent of the cyanotic patients had ACT less than 250 seconds at baseline. ACT was lower than 250 seconds in 65% and 77% of cyanotic patients, two minutes and one hour after heparin injection respectively. In non-cyanotic group, 100% of the patients had ACT less than 250 seconds; after heparin administration this ratio decreased to 45% in 2 minutes and 53% in 1 hour (Table 2). There was not any significant difference in ACT time between two groups at baseline, two minutes and one hour after heparin administration (Table 3).No correlation could be observed between oxygen saturation and ACT in three stages of before (P=0.9, R=0.007), two minutes (P=0.14, R=0.18) and one hour (P=0.16, R=0.18) after heparin injection.

Furthermore, no correlation could be detected between the age of patients and ACT after two minutes of heparin injection. The ACT increased in patients with no correlation to the age; however, this response is greatly varied and target ACT of 400 seconds cannot be reached mostly. ACT measures decreased with time; this decrement was more prominent at 60 minutes in older patients (Figures 1,2,3 ; P=0.015).

Table 1. Activated clotting time (ACT) changes in patients at 0,2,60 minutes

Group type	Before heparin	2 minutes later	one hour later
Cyanotic ACT(sec)	148±41	258±80	219±63
P	0.01	0.01	0.001
Acyanotic ACT(sec)	149±31	286±72	225±71
P	0.004	0.004	0.16
Total ACT(sec)	149 ±39	260±89	220±64
P	0.001	0.001	0.001

Table 2. The percentage of patients unable to reach target activated clotting time (250-350 seconds) in both groups cyanotic and non-cyanotic before, after 2 minutes and 60 minutes of heparinization

Group type (time)	Cyanotic ACT (Less than 250 seconds)	Non -Cyanotic ACT(Less than 250 seconds)
Before heparin	98	100
2 minutes after heparin	65	45
1 hour after heparin	77	53

Table 3. Comparison of Activated clotting time (ACT) between cyanotic and non-cyanotic patients

Heparin nterval	Activated clotting time Mean± SD (seconds)		P
	Cyanotic	Non-cyanotic	
Before heparin	149±31	148 ±41	0.5
After 2 minutes	286±72	258±80	0.08
After 1 hour	225±71	219±63	0.3

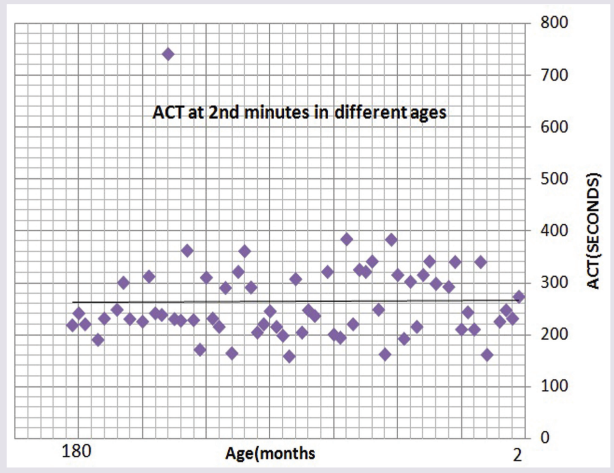

Figure 1. Active clotting time after two minutes indicating a wide range of response at dose of 50 IU/kg

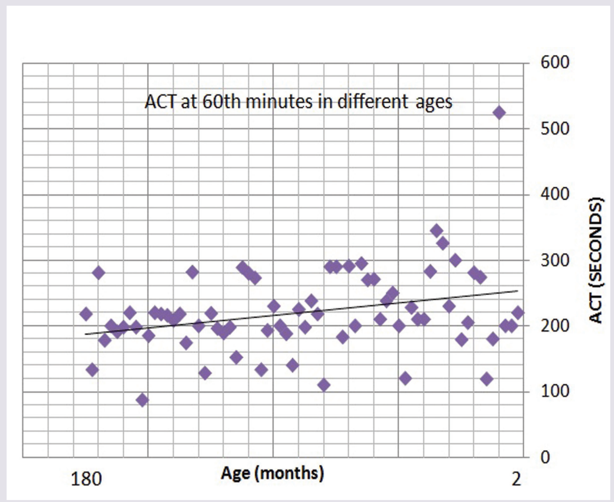

Figure 2. Correlation of activated clotting time at 60th minute after heparinization with age (P =0.015)

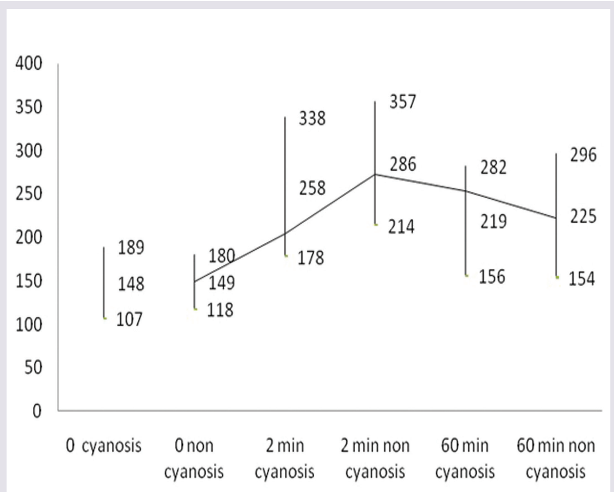

Figure 3. The mean± 95% CI of activated clotting time in cyanotic and non-cyanotic children indicating a insignificant difference between two groups

Discussion

Coagulation management undoubtedly is a complicated yet essential procedure throughout cardiac operation which could be altered by many cascades during medical procedures or cardiac operation.[5] Heparin, a key anticoagulant agent is of the ability to inactivate thrombin, factor X, and several serine proteases.[9] Furthermore, the required dose of heparin for being in a curative range is varied in different situations. Cardiopulmonary bypass, however, does require higher doses due to activation of factors following exposure of blood to any foreign surface (synthetic tubing of the CPB circuit) or subendothelial surfaces.[3,5,10]

Coagulation monitoring is a major concern as well. ACT is currently considered as the most commonly used clinical test for this purpose thanks to its simplicity and low cost.[6,7,11]

Some studies have focused on heparin efficacy during cardiac angioplasty finding no significant difference regarding response to heparin and no correlation between ischemic episodes after operation and ACT values as well. However, in ACT higher than 350 seconds, bleeding episodes tend to happen more significantly and the best ACT was reported as 250-350 in these studies.[12] Heparin is of different characteristics at different ages; preschool children are less sensitive to heparin displaying a wide range of response. Heparin 300 IU/kg prior to CPB in children older than 5 years old could rise up to 500 IU/kg in the younger patients.[13]

All these findings are suggestive of the fact that heparin is of various effects in different conditions demanding accurate doses to be set for different clinical implications. In the present study, heparin in a low dose of 50 IU/kg was used before diagnostic catheterization in two groups of cyanotic and non-cyanotic congenital heart disease patients.

The results revealed that cyanosis has no effect on heparin's clinical action; however, at this low dose, a considerable number of patients cannot get standard point of ACT target higher than 250 seconds at first hour (23% of cyanotic and 47% non-cyanotic patients). ACT increased significantly at the 2nd minute in both cyanotic and non-cyanotic groups and decreased significantly at first hour (P=0.001) in both groups. Although the mean ACT at 2nd minute in non-cyanotic is higher than cyanotic patients, decrease in ACT is lower at first hour in cyanotic group compared to non-cyanotic patients; these differences however were of no significance.

ACT decreased at first hour more significantly in older (P=0.015) but heparin action at 2nd minute was not influenced by age. This showed that heparin metabolism is accelerated with increasing age.

Conclusion

Heparin at low dose of 50 IU/kg is not probable to reach the target ACT (ACT >250 seconds) in majority of children. Following the use of heparin, the ACT is not different between cyanotic and non-cyanotic patients at 2nd minute and one hour after heparin administration. As a conclusion, a higher dose of heparin such as 100 IU/kg may be required for cardiovascular catheterization in some individuals in both cyanotic and non-cyanotic patients which also may need to be repeated after one hour from the first dose in long time procedures.

Ethical issues: The local ethics committee of Tabriz University of Medical Sciences approved the study and all patients signed informed consent.

Conflict of interests: The authors declare no conflicts of interest.

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