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Research Paper

Sialic Acid in Low Risk and High Risk Patients Undergoing off Pump Coronary Artery Bypass Graft – A Comparative Study

Medical Science

KEYWORDS : Coronary artery bypass grafting; coronary artery disease; Protein bound sialic acid.

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ABSTRACT

Back ground: Coronary artery bypass graft (CABG) may be associated with inflammatory response and myocardial damage. The study compared pre-operative and post-operative sialic acid levels in both, low risk and high risk patients, undergoing CABG.

Materials and Methods: Pre-operative and 24 hours post-operative blood samples were collected in low risk and high risk coronary artery disease patients scheduled for CABG and sialic acid was estimated.

Results: Although post-operative protein bound sialic levels were significantly higher in both low and high risk patients undergoing CABG (pre-operative vs post-operative p<0.01), the increase was more significant in high risk group when compared to low risk group (low risk vs high risk group - pre-operative p<0.001 and post-operative p<0.001)

Conclusion: Increased post-operative SA suggests that it might be useful in assessing inflammation and myocardial damage in patients undergoing CABG. SA may help in differentiating the high risk from the low risk varieties undergoing CABG.

Introduction

Coronary artery bypass grafting (CABG) is the surgical treatment for coronary artery disease (CAD) (Nagpal et al, 2006). CABG was found to be associated with an intense inflammatory response (Larmann et al, 2004). Although the systemic inflammatory response is recognized to contribute to patient morbidity and mortality after CABG, there is paucity for studies linking specific mediators with a defined adverse outcome (Landis, 2007). Sialic acid, (SA), a family of acetylated derivatives of neuraminic acid that increases in inflammatory response has been recognized as an independent marker for predicting cardiovascular risk (Nigam et al, 2006). Moreover perioperative myocardial infarction is a major problem during CABG, in high risk patients (Stanton et al, 2003). With regard to this, considerable interest has been shown in evaluating SA as a unique and novel marker which could be particularly useful in assessing myocardial cell damage in patients undergoing CABG and the rate of increase for SA found to be significantly higher than the traditional cardiac markers (Berkan et al, 2002). But research done so far for evaluating the usefulness of SA in CABG patients are very limited and documents reported have failed to compare their levels in the high risk and low risk undergoing CABG, which would throw some insight into whether this marker could differentiate the selected risk groups, that form important determinants in adding on to the burden of CABG complications.

Hence, the present study was taken up to estimate and compare the pre-operative and post-operative levels of SA in both, low risk patients and high risk patients, undergoing CABG.

Materials and Methods

Study design

The study protocol was approved by the Institutional Ethics Committee. 100 patients with CAD referred to the cardiothoracic department of a tertiary care hospital from August 2012 till January 2013 was included in the study. The study group included patients aged between 40 - 75 years, undergoing CABG. A written informed consent was obtained from all patients the day before the surgery. The patients undergoing CABG were subjected to coronary angiography and echocardiography. The left ventricular function was assessed by echocardiography. The patients were divided into two groups - Group I and Group II.

Group I included low risk CAD patients (n=50) undergoing CABG with either one of the following criteria - good left ventricular function, i.e. ejection fraction > 40%, no major risk factors for surgery, having stable angina and no history of previous infarct.

Group II

included high risk CAD patients (n=50) undergoing CABG in the study centre. Patients identified with low ejection fraction (< 40%) were included in this group.

Exclusion criteria

Patients with valvular heart disease, ventricular aneurysm, heart failure, lung disease, cirrhosis, renal disease were excluded from the study.

Biochemical measurements

Blood samples were drawn for biochemical analysis from the cubital vein, 12 hour before operation and 24 hours post-operative. The blood was transferred to plain bottles, shaken well and then centrifuged at 3000rpm for 5 min, and the serum was separated. The serum thus collected was stored at -20°C until further analysis. 100µl of serum was precipitated using 5ml ethanol and centrifuged at 500rpm for 5min. Supernatant was separated from the precipitate. Protein bound SA was analyzed by the ninhydrin method proposed by Yao et al. (1989) Precipitate was dissolved in 1ml of 0.1N NaOH. In the standard test tube 100µl of standard SA was taken and in blank test tube 100µl of distilled water was taken, 1ml of glacial acetic acid and 1ml of ninhydrin reagent were added to all the test tubes and kept in boiling water bath for 10 min and cooled under tap water and absorbance was measured at 470nm in a spectrophotometer(thermo scientific) against blank set at zero.

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Statistical analysis:
Data was analysed with the statistical package for social science version 11 (SPSS-11). The level of significance of the difference in the mean between groups and their comparison was done using Student's t-test. SA was expressed as mean ± SD values. P value ≤ 0.05 was considered to be statistically significant.

Results
The mean age of the patients in group I (low risk patients) was 53.06 ± 7.7 years and group II (high risk patients) was 58.1 ± 6.7 years.

Table 1: The post-operative levels of serum SA, were significantly increased compared to pre-operative levels in both the low risk ($p<0.01$) and high risk ($p<0.01$) patients undergoing CABG

Table 2: Pre-operative levels of serum SA in the high risk group, showed a significant increase ($p<0.001$) compared to low risk group.

Table 3: Post-operative levels of serum SA in the high risk group, showed a significant increase ($p<0.001$) compared to low risk group

Discussion
Despite the fact with evidence that coronary artery bypass grafting surgery (CABG) prolongs life and reduces symptoms in patients with severe coronary artery diseases, these benefits are accompanied by increased risks (Stanton et al, 2003). Surgery leads to the amelioration of ischemia, and an improvement in symptoms in the long term. However, the operative period is highly important as a determinant of short- and long - term outcome (Gillies et al, 2005). Morbidity associated with CABG can be attributed to the generalized inflammatory response. During CABG, surgical trauma may be one of the factors that can elicit a systemic inflammatory response (Butler et al, 1993). Serum sialic acid, an inflammatory marker has been shown to be a strong predictor of cardiovascular mortality (Sriharan et al, 2002).

In the recent years the role of SA as a predictor of cardiovascular events has gained considerable interest (Sriharan et al, 2002). Several studies have reported elevated levels of SA in coronary artery disease (Crook et al, 1998). It has been reported that in coronary artery disease elevated serum SA is due to some type of acute –phase reaction. Elevated serum SA levels might also be due to either shedding or secretion of SA-containing glycolipids and/or glycoproteins into plasma from myocardial cells (Süer et al., 2006).

In the present study we observed that protein bound SA in CABG patients was significantly increased post-operatively than preoperative levels. The increase in SA levels may be as a result of mechanical damage occurring during operation or due to the inflammatory response of surgical trauma (Wysocka et al, 2005).

On comparing the low risk and high risk groups, the pre-operative SA showed a statistically significant increase in the high risk group. This may suggest that preoperatively, inflammatory response is more exaggerated in high risk group when compared to the low risk group. This necessitates the need for better care to lower the inflammation in such group, which may have an impact on the surgery. Similarly the post-operative protein bound SA in the high risk group was significantly higher than the post -operative levels in the low risk group. This increase in the high risk group postoperatively indicates higher amount of perioperative myocardial damage and inflammatory response in high risk patients undergoing CABG when compared to the low risk patients. Studies done by Lindberg et al. (1991), observed that serum SA is a strong predictor of cardiovascular mortality. Crook et al. (1997), has earlier reported raised myocardial SA levels in high risk patients. SA might be useful in assessing myocardial damage in patients undergoing CABG. However the present study has its limitations that it has not simultaneously estimated the SA along with other traditional cardiac markers in selected groups undergoing CABG.

In conclusion, increased serum sialic acid in the post-operative condition suggests that it might be useful in assessing inflammation and myocardial damage in patients undergoing CABG. The pre and post operative levels of SA in both these groups may help in differentiating the high risk from the low risk varieties undergoing CABG. Further research is necessary to clarify whether intervention strategies to attenuate inflammation and myocardial damage will have an effect on SA levels in high and low risk groups undergoing CABG.

1: Comparison of pre- and post-operative levels of sialic acid in serum of low risk and high risk patients of CABG (Mean ± SD)

	Study Groups					
	Low Risk Group of OPCABG (n=50)			High Risk Group of OPCABG (n=50)		
Parameters	Preoperative	Postoperative	p value	Preoperative	Postoperative	p value
Sialic acid (mg/dl)	35.7 ± 2.1	36.9 ± 2.9	<0.01	44.2 ± 2.6	45.6 ± 2.07	<0.01

Table 2: Comparison of pre-operative levels of sialic acid in serum of the study groups (Mean ± SD)

	Study Groups		
Parameters	Low risk OPCABG (n=50)	High risk OPCABG (n=50)	p value
Sialic acid(mg/dl)	35.7 ± 2.1	44.2 ± 2.6	<0.001

Table 3: Comparison of post-operative levels of sialic acid in serum of the study groups (Mean ± SD)

	Study Groups		
Parameters	Low risk OPCABG (n=50)	High risk OPCABG (n=50)	p value
Sialic acid (mg/dl)	36.9 ± 2.9	45.6 ± 2.07	<0.001

REFERENCE

1. Nagpal AD, Bhatnagar G, Cutrara CA, et al. Early outcomes of coronary artery bypass with and without cardiopulmonary bypass in octogenarians. Can J Cardiol 2006 22(10):849-853. | 2. Larmann J, Theilmeier G. Inflammatory response to cardiac surgery: Cardiopulmonary bypass versus non-cardiopulmonary bypass surgery. Best Pract Res Clin Anaesthesiol 2004 Sep; 18(3):425-38. | 3. Landis C. Why the inflammatory response is important to the cardiac surgical patient. J Extra Corpor Technol 2007 Dec; 39(4):281-4. | 4. Nigam PK, Narain VS, Ajay Kumar. Sialic acid in cardiovascular diseases. Indian Journal of Clinical Biochemistry, 2006, 21 (1) 54-61. | 5. Stanton K. Shernan, MD. Perioperative myocardial ischemiareperfusion injury. Anesthesiology Clin N Am 21 (2003) 465– 485. | | 6. Berkan O, Sagban M. Sialic acid or troponin T to detect perioperative myocardial damage in patients undergoing elective coronary artery bypass grafting. Circ J. 2002 Nov; 66(11):1019-23. | | 7. Yao K, Ubuka T, Masuoka N, Kinuta M, Ikeda T. Direct determination of bound sialic acids in sialoglycoproteins by acidic ninhydrin reaction. Anal Biochem. 1989 Jun; 179(2):332-5. | | 8. Gillies M, Bellomo R, Doolan L, et al. Bench-to-bedside review: inotropic drug therapy after adult cardiac surgery: a systematic literature review. Crit Care. 2005;9(3):266-279. | | 9. Butler J, Rocker GM, Westaby S. Inflammatory response to cardiopulmonary bypass. Ann Thorac Surg. 1993 Feb;55(2):552-9 | | 10. Sriharan M, Reichelt AJ, Opperman MR, Duncan BB, Mengue SS, Crook MA, et al. Total sialic acid and associated elements of the metabolic syndrome in women with and without previous gestational diabetes, Diabetes Care, 2002 25: 1331-1335. | | 11. Crook M, Lumb P, Andrews V .Serum total sialic acid, a reputed cardiovascular risk factor, and its relationship to lipids, plasma fasting insulin, blood pressure and body mass index in normal individuals. Clinical Science. 1998; 95:53–57. | 12. SüerGökmen S, Kazezoğlu C, Sunar B, Ozçelik F, Güngör O, Yorulmaz F et al. Relationship between serum sialic acids, sialic acid-rich inflammation-sensitive proteins and cell damage in patients with acute myocardial infarction. Clin Chem Lab Med. 2006; 44(2):199-206. | 13. Wysocka A, Korycińska A, Dragan M, Berbeć H, Roliński J, Stazka J. Apoptosis of lymphocytes and sialic acid plasma level in patients undergoing cardiac surgery. Folia Biol (Krakow). 2005; 53(3-4):223-8. | 14. Lindberg G., Eklund G.A., Gullberg, Bo, Rastam L. 1991. Serum sialic acid concentration and cardiovascular mortality. Br. Med. J. 302, 143-146. | 15. Crook JR, Jonathan HG, Brendan M.D. Increased Ventricular Sialylation in Patients with Heart Failure Secondary to Ischemic Heart Disease. Clin. Cardio1997; 20:455-458. |