P48

LIST OF PROCEDURES DONE

PROJECT REPORT

TITLE OF THE PROJECT: TOTAL CREATINE KINASE AND ISOENZYME MB ESTIMATION IN OPEN HEART SURGERY PATIENTS.

NAME..YEGNESWARA RAO YELLURY.....

PROGRAMME:..D.M.(Cardiology).....

MONTH & YEAR
OF SUBMISSION:...November 1989.....

Note:— (i) In the case compilation of procedures done, the contents and the subsequent pages should be made into different sections (a) Procedures done (b) Procedures assisted (c) Procedures participated (d) Procedures attended/participated etc in Other Centres. Each section should be preceded by a leaf carrying the name of the section that is succeeding.

(ii) The Contents page will carry into. as per model given under

PROCEDURES DONE

Closed Mitral valvotomy.....124 (say)
Patent ductus arteriosus-ligation.....10
Atrial septal defects.....20
.....
.....

PROCEDURES ASSISTED

Closed Mitral valvotomy.....100 (say)
.....

(iii) In the subsequent pages details of each procedure done/assisted should be given in the format given below:—

Heading: **Closed mitral valvotomy**

Date	Name of the patient	Age	Sex	Patient No.

(iv) In the case of Project Report in the page immediately following the Certificate page the under-mentioned details should be given:—

(a) Title
(b) Duration
(c) Aim and scope
(d) 50 word summary of work done

CERTIFICATE

I, Dr. Y.R. Yellury .....hereby declare that I have actually performed all the procedures listed/carried out the project under report.

Signature.....

Place: Trivandrum

Name in.... YEGNESWARA RAO YELLURY.
capital letters

Date: 5-11-1989

CONTENTS

TOTAL CREATINE KINASE AND ISOENZYME-MB ESTIMATION IN OPEN HEART SURGERY PATIENTS

Y.R. YELLURY, SUBRAMANIAM IYER, M.S. VALIATHAN AND K.G. BALAKRISHNAN.

DEPARTMENT OF CARDIOLOGY, CARDIOVASCULAR & THORACIC SURGERY AND BIOCHEMISTRY

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM -695 011, INDIA.

S U M M A R Y

Serum creatine kinase, MB isoenzyme (CK-MB) was measured at 6 hours, Ist day, 3rd and 4th day after surgery in 25 patients of Atrial Septal Defect who underwent open heart surgery. All the patients were free from clinically significant coronary heart disease and all had uncomplicated post-operative period without significant myocardial damage. The peak elevation of both total CK and CK-MB was observed on the Ist post operative day and by 4th day all the values had come down to almost baseline level. The peak value for total CK was 1,108 + 445.8 I.U/L and for CK-MB it was 64.08 + 33.7 I.U/L. The peak value of total CK was less than 1,300 I.U/L in 72% of the patients and the peak value of CK-MB was less than 80 I.U/L in 70% of the patients. This study shows that elevation of total CK to 1,300 I.U/L and CK-MB to 80 I.U/L is the normal rise that can be expected in patients undergoing open heart surgery with minimal cross-clamp time and minimal perioperative myocardial damage. Further data are necessary to make recomendations about the enzyme profile of those patients who suffer significant perioperative myocardial damage.

I N T R O D U C T I O N

Patients undergoing cardiac may suffer peri-operative myocardial infarction which may be responsible for arryhthmia, heart failure or both during post-operative period. It is quite often difficult to diagnose myocardial infarction in open heart surgery patients. Interpretation of ECG is made difficult as the pre-op ECG is often abnormal and enzymes like SGOT, LDH and total CK will be elevated to a variable degree due to tissue trauma (1). CK-MB isoenzyme is more specific and sensitive indicator of myocardial injury (2-3). The purpose of this present study is to define the upper limit of normal rise of total CK and CK-MB In patients Of Atrial Septal Defect (ASD) who had undergone open heart surgery with uncomplicated post-operative course.

MATERIALS AND METHODS

Twenty five patients undergoing open heart surgery for ASD closure have been studied. ASD closure was done under cardio-pulmonary bypass with systemic hypothermia to 26°C, topical hypothermia for cardiac cooling and infusion of 4°C crystalloid potassium cardioplegic solution to ensure cardiac arrest during the operation. All the patients were free of clinically significant coronary heart disease. Blood samples were taken from each patient before the operation and after surgery at 4 hours, Ist day, 3rd day and 4th day. Serum was separated immediately and was stored at 4°C until assay. All the samples were analysed either immediately or within 48 hours. Total CK was estimated using reagent kits from Boheringer Manheim Gmbh (4). Measurement of CK-MB was done according to the immunoinhibition method (5) using reagents from Santgen Immuno Diagnostics, Hyderabad. This method is based on the following principle:

$$\text{Creatine phosphate} + \text{ADP} \xrightarrow{\text{CK}} \text{Creatine} + \text{ATP}$$

$$\text{ATP} + \text{Glucose} \xrightarrow{\text{HK}} \text{Glucose-6-phospate (G-6-P)} + \text{ADP}$$

$$\text{G-6-P} + \text{NADP}^{+} \xrightarrow{\text{GPD}} \text{NADPH} + \text{H}^{+} + \text{6-Phosphogluconate}$$

CK catalyses the reversible transfer of phosphate group from creatine phospate to Adenosine diphosphate (ADP) forming Adenosine triphospate (ATP). The rate of ATP formation is measured through two coupled reactions catalysed by Hexokinase (HK) and Glucose-6-phospate dehydrogenase

(G-6-PD). The rate of reduction of Nictotinamide adenine dinucleotidephospate (NADP) to NADPH is measured by increase in asborbance at 340 nm. The rate of change in absorbance is directly related to the CK-B activity in the specimen.

The normal values for total CK was 24 to 170 I.U/L in males and 24 to 150 I.U/L in females. For CK-MB, the normal range was 0 to 18 I.U/L.

R E S U L T S

There were total 10 males and 15 females in the age group of 9 to 38 years with mean age of 19.6 ± 9.2 years.

All the patients had uncomplicated post-operative recovery without any significant hemodynamic problems. None of the patients had post-operative hypotension requiring inotropic support, low cardiac output and cerebrovascular accidents. Comparison of pre-op and post-op ECGs did not reveal any evidence of myocardial infarction.

Total CK was normal in all the patients before surgery (82.6 ± 37.2. I.U/L). In all the patients elevation of total CK was observed in the immediate post-op period. The peak elevation was observed on the Ist post-op day. The maximum elevation was found to be 1,108 ± 445.8 I.U/L (Fig-I). In 18 patients, the peak values were below 1,300 I.U/L. In the remaining 7 patients, they were above 1,300 I.U/L. There was decline from the peak on the 3rd post-op day and by 4th post-op day, they were mildly elevated above the upper limit of normal range (Fig-II). CK-MB was normal in all the patients prior to surgery (9.6 ± 6.6 I.U/L). In the immediate post-op period, all the patients had elevation of CK-MB. The maximum value of of 64 + 33.7 I.U/L was observed on the Ist post-op day (Fig-III). In 9 patients the peak values were below 80 I.U/L and in the remaining 6 patients, they were above 80 I.U/L. On the 3rd post-op day, the values have declined,

D I S C U S S I O N

In the post-operative period after open heart surgery, the diagnosis of myocardial infarction is quite difficult. Post mortem studies have shown that ECG greatly underestimates the incidence of myocardial necrosis in this setting (3,5). Eventhough serum total CK is relatively a specific marker of myocardial damage, after open heart surgery, it may be elevated due to skeletal muscle damage, ventriculotomy or bypass itself (6-8). In all our patients, total CK was elevated in the immediate post-op period. The other possible causes for the increase may be due to the manipulation of chest wall muscles, injury of the heart and due to manipulation and sewing of atrium (8-9). CK-MB has been found to be specific indicator of myocardial injury in patients of myocardial infarction unrelated to cardiac surgery (3,10). However, its value in the diagnosis of peri-operative infarction following CPB operations is more controversial. The mere presence of CK-MB may not suffice since it is detected in all patients undergoing cardiac surgery (11,12). In the present study, the peak elevation of both total CK was found to be 1,108 $\pm$ 445.8 I.U/L and for CK-MB it was 64.08 $\pm$ 33.7 I.U/L. on the first post-operative day. In 72% of patients, the peak total CK was less than 1,300 I.U/L. In 76% of patients, the peak value for CK-MB was less than 80 I.U/L. The cause of the elevation may be due to ventriculotomy, atriotomy and minimal myocardial damage due to cardio-pulmonary bypass itself,

Graeber et al (13) have studied CK-MB profile in post-operative ASD, MVR and CABG patients. They postulated that elevation of CK-MB of more than 50 I.U/L on the Ist and 2nd post-operative samples indicates acute ventricular injury. Baur et al (14) reported peak elevation of CK-MB of 20 I.U/L at 5 hours after surgery in a group of patients of ASD and mitral valve disease. According to them, higher elevation and delayed and sustained rise of CK-MB was observed in those patients of CABG with myocardial infarction.

The extent of increase of total CK and CK-MB after open heart surgery varies from centre to centre depending on the efficiency of myocardial preservation, surgical technique and amount of intra-operative myocardial injury. It is necessary to define the normal rise in each centre. Since all our patients of ASD had no evidence of coronary artery disease and since all of them had uncomplicated recovery, total CK of 1,300 I.U/L and CK-MB of 80 I.U/L is the minimal increase that can be expected in general, in patients undergoing open heart surgery without significant peri-operative myocardial damage. This data will be useful in the interpretation of the enzyme values in those patients who suffer from peri-operative myocardial damage. Other workers also have studied the enzyme profile of the patients undergoing ASD, MVR and CABG surgery which involves no ventriculotomy. Hence, it may be worthwhile studying patients in whom ventriculotomy is done like VSD closure and Intracardiac repair for TOF or DCRV where resection of

myocardium is necessary and whether such procedures further augment the release of CK enzymes. Only if such estimation is done in CABG patients as a routine and compare the clinical profile of post-operative hemodynamics, one can establish the normal expected rise and differentiate peri-operative infarctions.

REFERENCES

1. Codd JE, Sullivan RG, Weins RD, Barner HB, Kaiser GC, Willman VL, Myocardial injury following myocardial revascularisation; detection by isoenzyme analysis. Circulation. 56 Suppl 2:49-53, 1977.

2. Shell WE, Sobel BE: Biochemical markers of ischaemic injury. Circulation 53:Suppl : 98-105, 1976.

3. Wagner GS, Roe CR, Limbird LE et al: The importance of identification of the myocardial specific isoenzymes of creatine phosphokinase (MB form) in the diagnosis of acute myocardial infarction: Circulation 47:263-269,1973.

4. Szasz et al: Clin.Chem 22:650, 1976.

5. Neumeir D, Prellwitz W, Wurzburg U et al: Retermination of creatine kinase isoenzyme MB activity in serum using immunological inhibition of creatine kimase M subunit activity. Activity kinetics and diagnostic significance in myocardial infarction clein.Chem Acta. 73:445-451, 1976.

6. Brewer DL, Bilbro RH, Bartel AG: Myocardial infarction as a complication of coronary bypass surgery; Circulation 47:58-64, 1973.

7. Nickell WK, Allbrittan, FF, JR:Serum t ransaminase content related to tissue injury: Surgery 42:240, 1957.

8. Fraser RS, Rosall RE, Black W Dvorkin J: Serum transaminase response to cardiac surgery using cardio-pulmonary bypass: J. Thorac & Cardiovasc. Surg 43 : 810, 1962.

9. Graeber GM, Cafferty PJ, Wolf RE, Cohen DJ, Zatjtchuk R: Concentrations of creatinine kinase and lactate dehydrogenase in the muscles encountered during median sternotomy and in the wall of cardiac chambers: Surg. Forum 34 : 337-339, 1983.

10. Schultheiss HP, Bispink G, Neuhoff V, Botle HD, Myocardial lactate dehydrogenase isoenzyme distribution in the normal heart. Basic Res Cardiol 76:681-689, 1981.

11. Anumada G, Robers R, Sobel BE: Evaluation of myocardial infarction with enzymatic studies: Prog. Cardiovasc. Dis 18:405-420, 1976.

12. Tonkin AM, Lester RM, Guthrow CE, Roe CR, Hackel DB, Wagner G.S: Persistance of MB isoenzyme of creatine phospokinase in the serum after minor iatrogenic cardiac trauma. Circulation 51:627-631, 1975.

13. Coleman RE, Klein MS, Roberts R, Sobel BE: Improved detection of myocardial infarction with technitium-99m stannous pyrophosphate and serum MB creatine phosphokinase: Am J Cardiol 37:732-735, 1976.

14. Graeber GM, Shawl FA, Harold D et al: Changes in serum creatine kinase and lactic dehydrogenase caused by acute perioperative myocardial infarction and by transatrial cardiac surgical procedures. J.Thorac. Cardiovasc. Surg. 92:63-72, 1986.

15. Baur HR, Steele BW, Preimesberger KF, Gober FL: Serum myocardial creatine kinase after coronary arterial bypass surgery. Am.J. Cardiol 44:679-685, 1979.

APPENDIX i

T A B L E - I

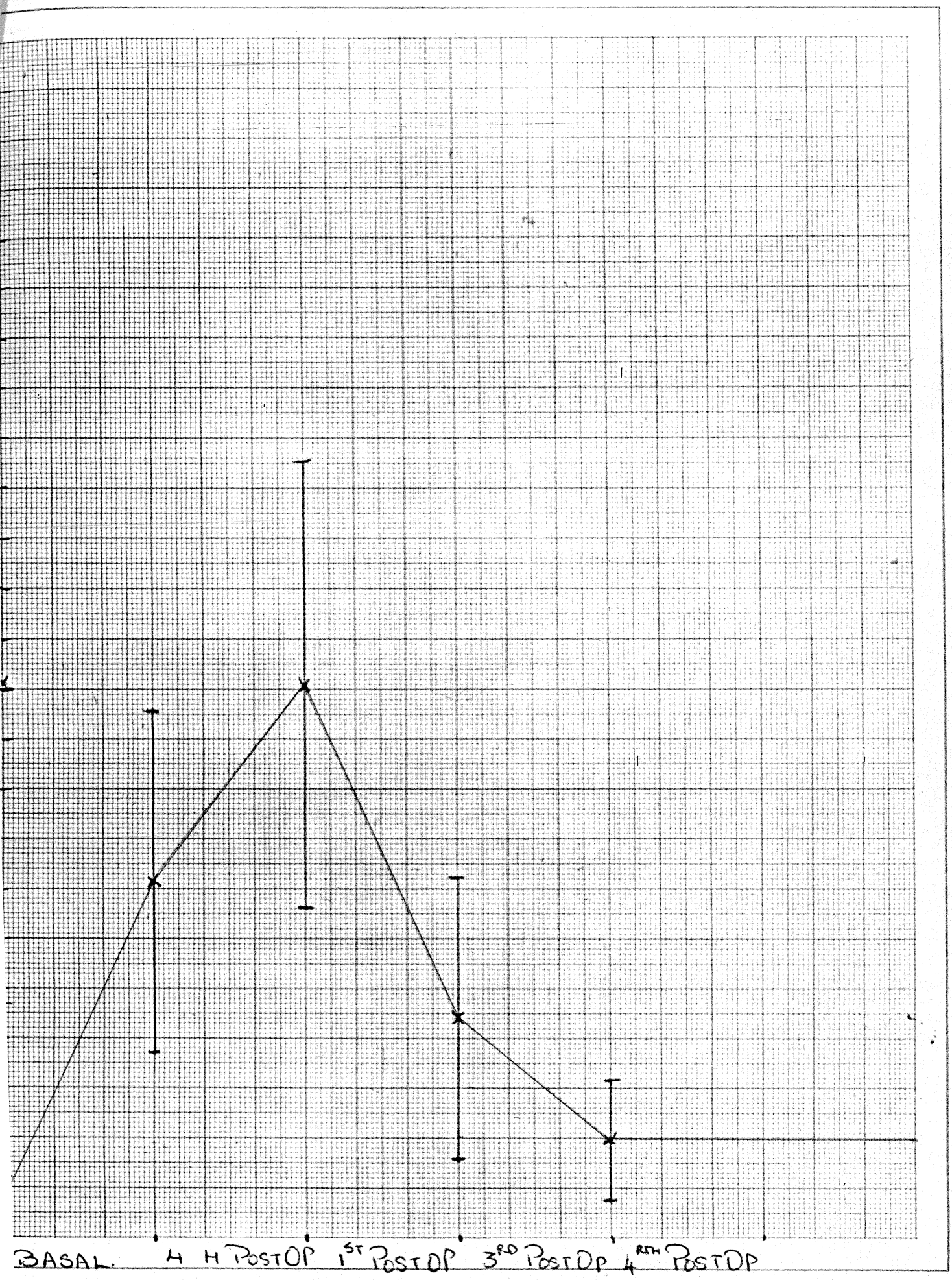
Total CK And CK - MB Values After Open Heart Surgery

(IU/L)

Enzyme	Basal	4Hour. Post-op	Ist day	3rd day	4th day
Total CK	82.6 ± 37.2	113.8 ± 41.9	1,108.08 ± 445.8	440.5 ± 281.6	198.2 ± 120.2
CK - MB	9.6 ± 6.6	42.2 ± 22.2	64.08 ± 33.7	29.4 ± 18.5	18.3 ± 7.5

Fig 1

AL SERUM CK VALUES IN [redacted] 25 POST OPERATIVE ASD PATIENTS.



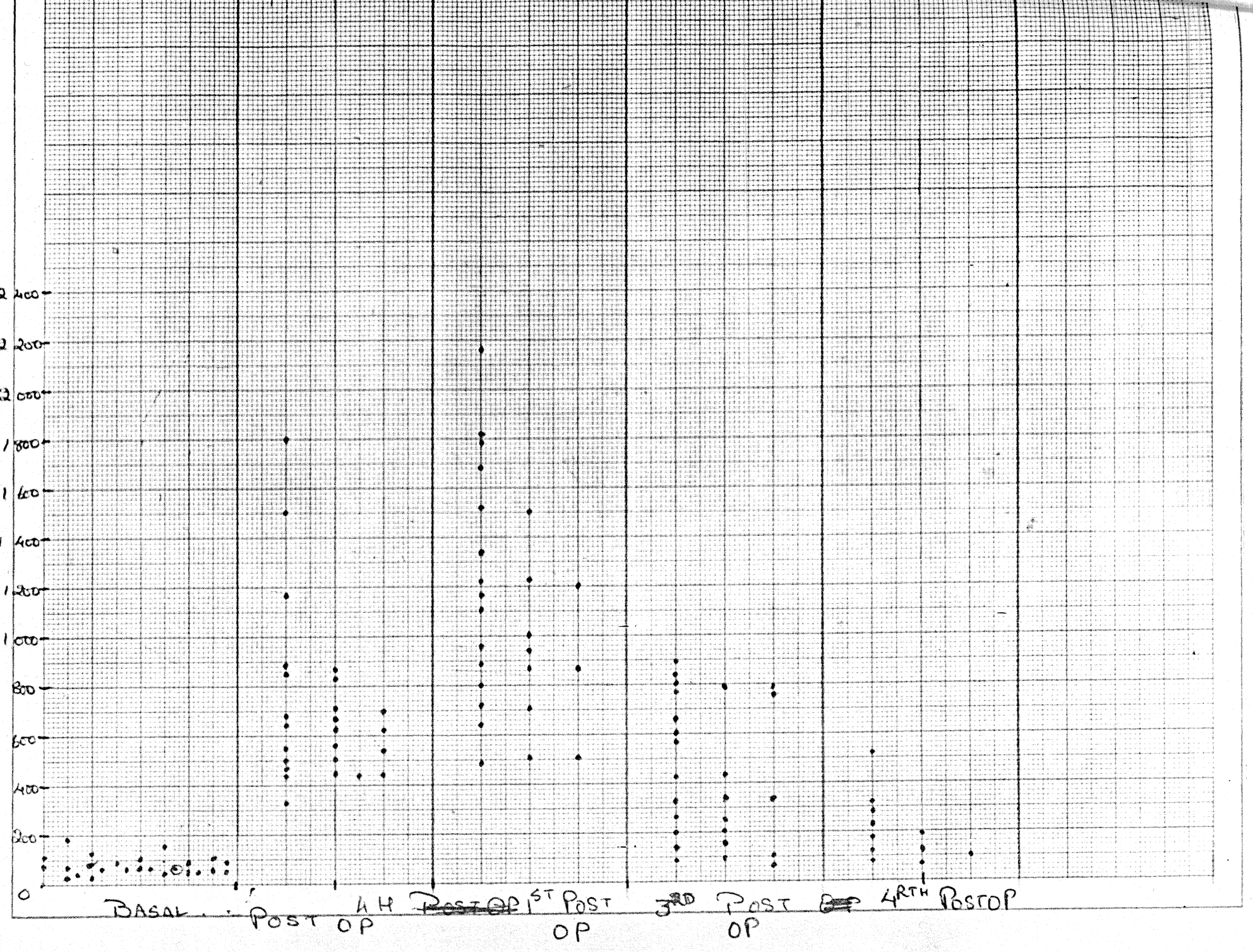
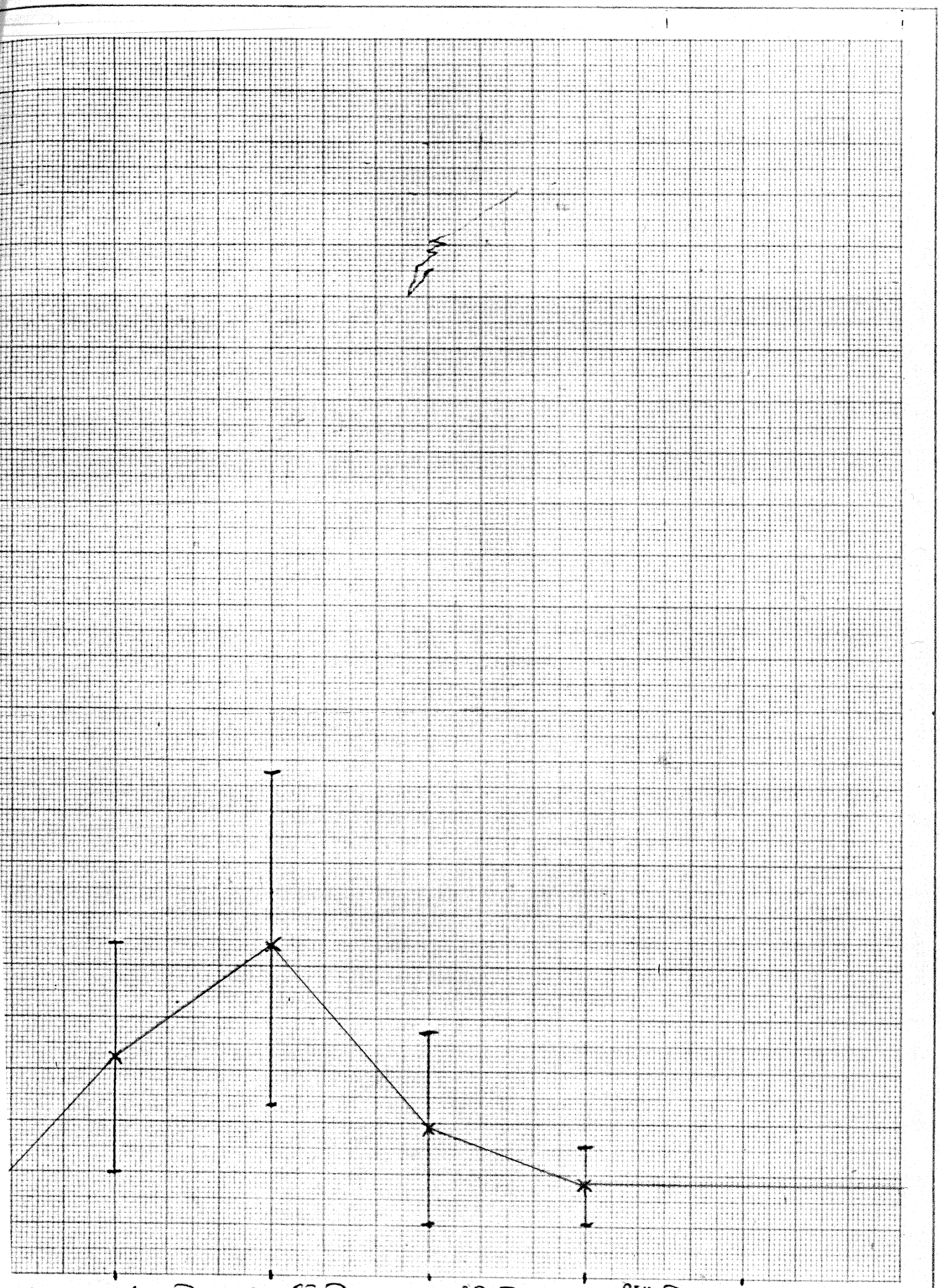

TOTAL CK VALUES
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
BASAL
POST OP
4H POST OP
1ST POST OP
3RD POST OP
4RTH POSTOP

Fig III

CK-MB VALUES IN 25 POST OPERATIVE ASD PATIENTS



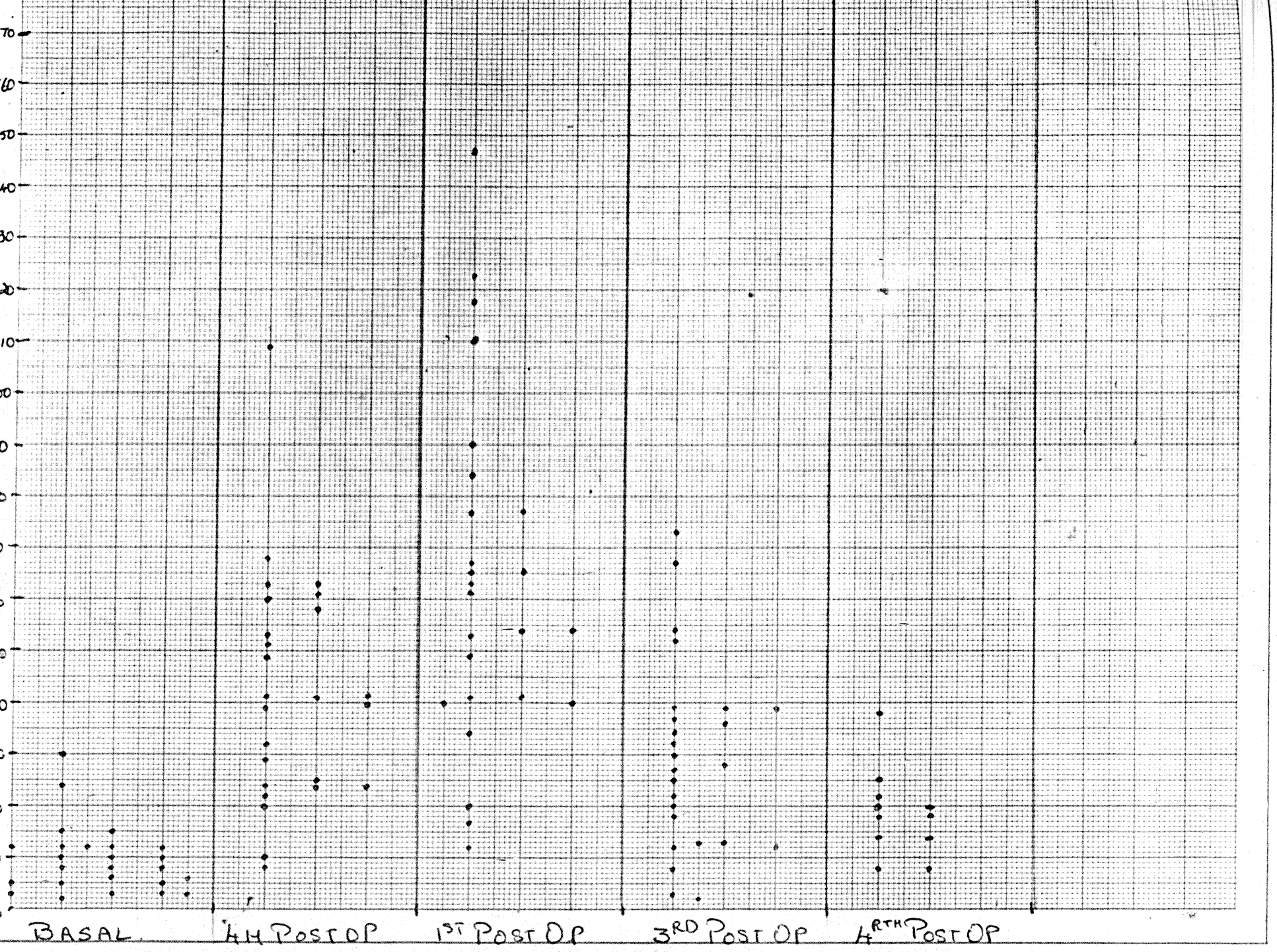

BASAL
4H POST OP
1ST POST OP
3RD POST OP
4RTH POST OP

Fig 5

TOTAL CPK.

CPK - MB

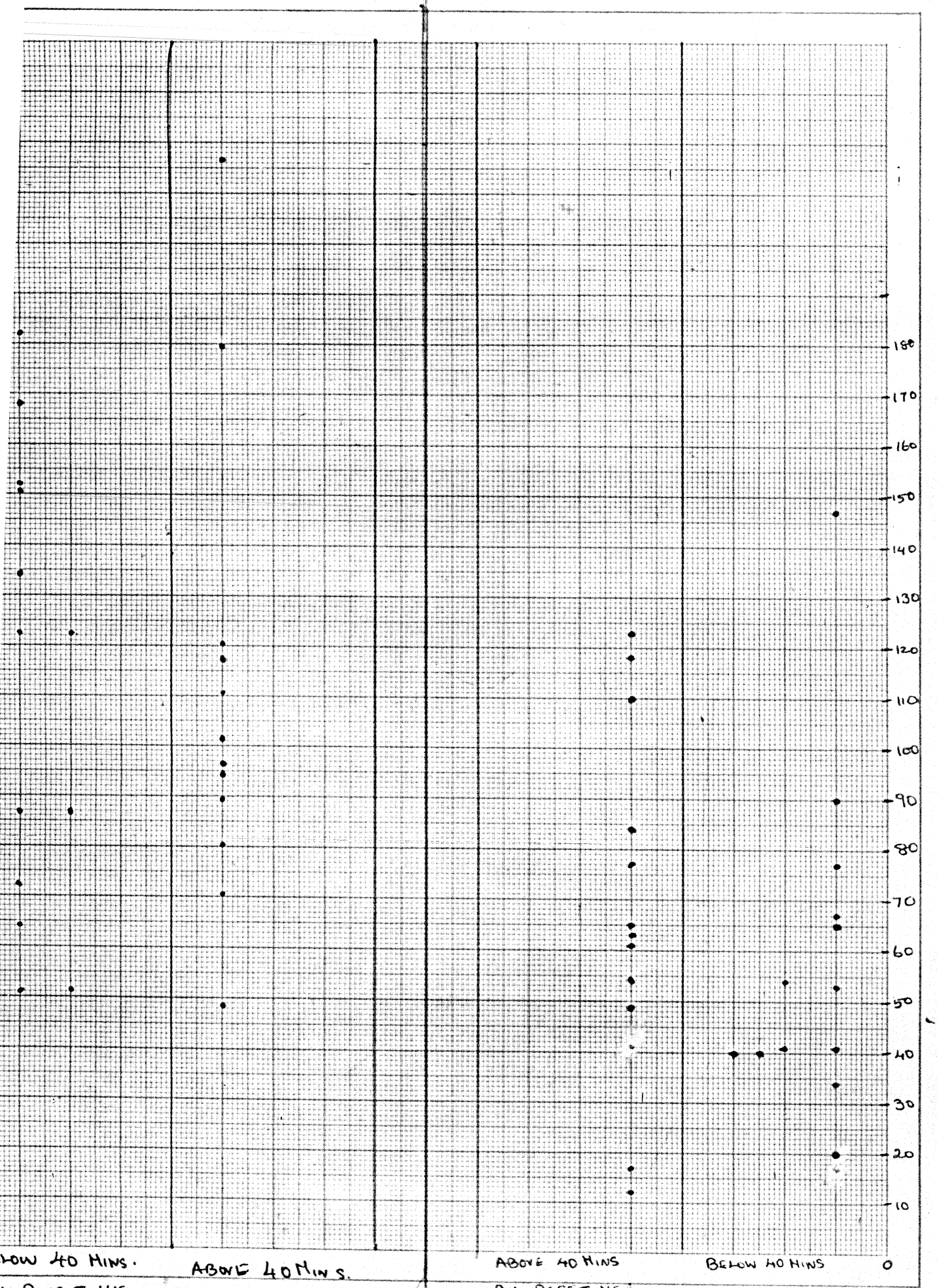


Fig 6

TOTAL CPK — MB.