MEASUREMENT OF CARDIAC STROKE VOLUME USING AN INTERNAL COINCIDENCE COUNTING SYSTEM AND ALBUMIN TAGGED COBALT - 58

Study Objectives:

This study will be a clinical evaluation of the method of measuring the cardiac stroke volume by means of precordial coincidence counting utilizing albumin tagged Cobalt - 58. Techniques for measuring cardiac output and stroke volume using precordial counting and albumin tagged isotopes have been thoroughly investigated (1). However, it is felt that coincidence counting techniques made possible by the more recent development of coincidence counting apparatus will make this method of measuring cardiac output a much more reliable and efficient clinical procedure. The study will attempt to:

A. Compare the values obtained with other standard non-isotopic means of measuring cardiac output.

B. Evaluate the theoretical advantages of this technique in measuring cardiac output during non-steady states such as during exercise.

C. Evaluate the technique as a means of obtaining instantaneous and repetitive measurements of cardiac output over short intervals of time.

These studies are to be performed to determine the feasibility of using this technique in the routine clinical evaluation of outpatients with known or suspected cardiac disease. The applicability of using this method in the cardiovascular evaluation of normal subjects such as those undergoing various conditioning and deconditioning studies will also be determined.

Plan of Investigation:

A. The procedure involves the initial intravenous injection of approximately 0.1 μc/Kg of albumin tagged Cobalt - 58 into the subject followed by a 10 - 15 minute period to allow the isotope to equilibrate in the intravascular compartment.

The subject is then positioned in such a way that the coincidence pair of scintillation crystals are alligned directly anterior and posterior to the heart. Precordial count rates are then recorded simultaneously with the recording of an electrocardiogram. The differences in count rates during systole and diastole can then be determined. By determining the activity of the Cobalt - 58 isotope from a blood sample drawn during this time, the differences in systolic and diastolic count rates over the heart can be expressed in terms of volume changes in the heart.

B. Other methods for determining the diastolic and systolic intervals of the heart such as by carotid pulse or apex cardiogram tracings will be evaluated also.

C. In each subject the minute stroke volume obtained by this method will be compared with:

1. the minute cardiac output determined by a standard dye dilution technique;

2. multiple determinations of the cardiac output will be carried out on the same subject to study the reproducibility of the method. In some subjects cardiac output will be measured on several occasions during sustained rest. In others, the cardiac output will be determined after repeated periods of graded exercise using the same workload;

3. the accuracy of the calculated stroke volume over intervals considerably shorter than one minute and during exercise will also be determined.

Complementary Drugs and Isotopes

No complementary drugs or radioisotopes will be administered.

Fate of the Isotope

The fate of albumin tagged Cobalt - 58 in the body is governed primarily by the fate of the albumin carrier. Albumin has a biological half life of 17 days during which time it remains confined to the intravascular space. Once degradation of the albumin occurs in the body the free Cobalt is rapidly excreted in the urine with only minor amounts being taken up by body organs. After intravenous injection of a Cobalt isotope, only 5% will remain in various body organs after 4 days (2).

A. Not applicable.

B. Albumin tagged Cobalt - 58 remains localized to the intravascular space after intravenous administration, its distribution being passive to the physiologic distribution of albumin. As noted above, Cobalt is rapidly cleared from the body in its free inorganic form. (2). Therefore, the biological half-life of albumin tagged Cobalt - 58 will be essentially that of albumin or 17 days. Since the physical half-life of Cobalt - 58 is 71 days, the effective half life would be 13.8 days.

Since small amounts of Cobalt - 58 do remain in the body after degradation of the albumin carrier, the maximal radiation dose can best be expressed by utilizing the physical half-life of 71 days. Using this figure the highest possible total body radiation dose received by a 70 Kg subject after administration of 0.1 μc/Kg of Cobalt - 58 would be 0.2 roentgens (reference enclosed).

Description of Human Subjects

A. A total of 30 patients without manifest disease will be studied. These subjects will be volunteers obtained from the United States Air Force

Training Command Basic Training Program at Lackland AFB, Texas, for specific participation in this study.

These subjects will be exclusively males between the ages of 18-25 years and will be selected on the basis of a negative history and physical for cardiovascular disease.

B. A total of 10 subjects with manifest cardiac disease will be studied. These patients will be selected from the USAF Consultation Service patients with the prerequisite being the presence of cardiomegaly. The subjects will be studied in the same manner as the normal subjects to determine if variations in heart size and geometry appreciably alter the reliability of the technique. The age range of these subjects will be between 30 and 60 years.

C. Women will not be involved as subjects in any part of this study.

Specific consent of all human subjects used in this study will be obtained. All normal subjects will be obtained by solicitation of volunteer participants.

The Cobalt - 58 isotope will be administered intravenously as a pyrogen free, albumin tagged solution. The maximum dose will be 0.1 uc/Kg.

A. Albumin tagged Cobalt - 58 is distributed in the body in the same manner as physiologic albumin and thus remains within the intravascular compartment. The biological half life of albumin tagged Cobalt - 58 administered intravenously will be essentially that of albumin which is 17 days. Upon biological degradation of albumin, free inorganic Cobalt is rapidly excreted from the body with less than 5% remaining after 4 days.

B. For a 70 Kg man the retained Cobalt - 58 isotope will be 7 uc having an effective half life of 13.8 days based on the biological half-life of 17 days for albumin. In relationship to the permissible body burden for occupational exposure for Cobalt - 58 of 30 uc, this dosage is quite small. Since the tissue requirements for cobalt ions is extremely small and only minute amounts of the ions are retained, (2) the body radiation received from the eventually albumin-free cobalt - 58 will be negligible.

C. The dose selected is that which can be expected to give a statistically significant difference in count rates over the heart as a result of the relatively small changes in intracardiac blood volume occurring between the systolic and diastolic intervals. In selecting this dose, geometric and density factors of the body and heart were taken into account.

D. Not applicable.

All of the physical facilities necessary for storing and handling the isotope are presently available through the Radiology Branch, Aerospace Medical Sciences Division, USAFSAM.

Funds have been allocated for the purchase of the necessary coincidence counting equipment and its procurement is anticipated within 90 days.

Normal subjects will be obtained after approved by the Human Volunteer Use Committee, USAFSAM, through Air Training Command, Lackland Basic Training Center from basic trainees on a voluntary basis. Abnormal subjects will be obtained from the USAF Aeromedical Consultation Service, USAFSAM, on a voluntary basis. Approximately 60% of all patients seen in this service have some cardiac diagnosis.

Consultation is available from Radiobiology Branch, Basic Sciences Division, USAFSAM, and also from Department of Radiology, Wilford Hall USAF Hospital, locally.

A. Major Malcolm C. Lancaster, Chief of the Internal Medicine Branch, will be the principle investigator. Major Lancaster is a Diplomate, American Board of Internal Medicine and Associate Fellow, American College of Cardiology. Isotope experience includes: (1) One year (1955) - Studies in transport of Na^{22} across blood brain barrier - University of Texas, Southwestern Medical School, Department of Physiology, Dallas, Texas. (2) Three years (1953-1956) - Clinical experience in diagnostic and therapeutic use of I^{131}, Co^{60} and P^{32}, Maxfield Clinic, Dallas, Texas. (3) Four years (1956-1960) - Clinical experience in use of I^{131}, Fe^{59}, and Cr^{51} diagnostically, Fitzsimons General Hospital, Denver, Colorado. (4) One year (1964) - Clinical experience in diagnostic use of Risa-I^{131} lung scans with precordial scans, Fitzsimons General Hospital, Denver, Colorado. (5) Eighteen months (1965-66) - Clinical experience in diagnostic use of I^{131}, Triosorb T-3, Fe^{59}, Cr^{51}, Risa-I^{131}, Wright-Patterson USAF Hospital, Wright-Patterson AFB, Ohio and (6) One year (1966-67) Research experience Fe^{59}, Cr^{51}, Triosorb T-3 and Tritium, USAFSAM.

B. Captain Paul L. McHenry, Internal Medicine Branch, will also be directly involved with this project. Captain McHenry has had two years of clinical research experience in the measurement of coronary blood flow using coincidence counting techniques and Rubidium 84, University of Indiana School of Medicine.

The entire study would be projected to require 12 months for completion.

Data reporting is not required since AEC licensing is not required. However an initial report of data would be expected in 6-8 months with a final report upon completion of the study.

REFERENCES

1. MacIntyre, William J., Pritchard, Walter H. and Moir, Thomas W. The determination of cardiac output by the dilution method without arterial sampling. Circulation 18:1139-1154, 1958.
2. Goodman, and Gilman. The pharmacological basis of therapeutics, 2nd Edition.