Comparison Study of the Hepcon System Four and the Hemostasis Management System

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Abstract

Milwaukee Heart Surgery Associates in affiliation with St. Mary's Medical Center was asked to be clinical investigators for a comparison study of the current Hepcon System Four (HSF) and the next generation Hemostasis Management System (HMS) manufactured by HemoTec Inc. The Hepcon System Four has been in place at St. Mary's Medical Center for the past three years in a program that performs approximately 900-1100 cardiac procedures a year. Heparin Assays and High Range Activated Clotting Times (HR-ACTs) are performed routinely on all patients placed on cardiopulmonary bypass (CPB). This comparison study will evaluate the results based upon the two systems run in tandem on a series of patients undergoing cardiac surgery with no exclusions i.e. valve repair or replacement and myocardial revascularization. The results will determine whether or not the new generation Hemostasis Management System has any distinct advantages over the Hepcon System Four and is or is not suitable for this clinical setting.

Introduction

Heparinization of the patient while on cardiopulmonary bypass regardless of the duration or for whatever reason, should be monitored in the most accurate manner possible. State-of-the-art technology exists within the market place for this very purpose. The Hepcon System Four (HSF) among other features determines the Heparin Dose Response (HDR), the response to known doses of heparin the activated clotting time (ACT) which is an effect or function test the heparin/protamine titration (HPT) which is a quantitative test for actual heparin concentration and calculates the amount of protamine needed to neutralize the circulating heparin.

It is important to realize the value of both tests in that the ACT is a test of the intrinsic clotting mechanism and tells us only how long it takes the blood to clot. The HPT relates only to the concentration of heparin and is usually not affected by factors that can alter a functional test. (Table I) By looking at both the ACT and HPT one can determine not only that adequate heparin concentrations are maintained but verify that the function of the heparin is extending the coagulation time.

The next generation device the Hemostasis Management System (HMS) combines all these features in a more efficient and user-friendly package. Cartridge filling is totally automated thereby virtually eliminating human error in measurement which is crucial in achieving an accurate result.

The intent of this investigation is to determine the comparative accuracy of the Hemostasis Management System to the Hepcon System Four as well as its ease of set up and operation.

Materials and Methods

The two HemoTec units, the HSF and HMS, were setup side by side in the O.R. and the patient data — height weight and sex — were entered into both devices. The HMS called for additional data entry such as heparin units of measure, heparin type, protamine units of measure and HDR mode. This additional data entry is stored within the computer and can be retrieved or altered and documented by use of the on-board printer.

A pre-anesthetic blood sample was obtained and an HR-ACT and HDR completed for a base line. The HDR yields a heparin amount to be used based on the individual's sensitivity to heparin (Bull) and the patients were dosed accordingly. After the heparin was allowed to circulate approximately two to five minutes and a HR-ACT was done to insure adequate anticoagulation. Our protocol for this study was set for a target time of 500 seconds. Cardiopulmonary bypass (CPB) was initiated only after an ACT result of 400 seconds.

A HPT and HK-ACT was performed approximately every 20 minutes to verify heparin concentration and clotting time throughout the pump run. After the patient was warmed and just prior to termination of CPB another HPT and HR-ACT performed in order to determine heparin concentration for calculation of protamine dosage. That amount of protamine was slowly administered after decannulation and allowed to circulate for approximately 10 minutes. A low range HPT and HR-ACT was then performed to insure neutralization and a return to baseline clotting time. If the results indicated residual heparin and

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recommended more protamine the patient was dosed accordingly. A comparative HDR and HR-ACT was drawn after neutralization was achieved in hopes of determining whether the patient had become heparin resistant as a result of prolonged cardiopulmonary bypass. (Harloff)

The perfusion circuit consisted primarily of a Bard HF-5400 oxygenator, Bard 33 micron arterial line filter and an Intersept 20 micron filtered cardiotomy reservoir. The pump was primed with 2 liters of Plasmalyte 7.4, 25 grams of Mannitol 5,000 units of porcine heparin and 50 cc of Sodium bicarbonate.

Results

Thirty (30) patients were studied and there were no exclusions. (Table 2) Of those 22(73.3%) were male and 8(26.7%) were female. Ages ranged from 29 years old to 85 years of age for a mean of 63. Average height amounted to 170.1 centimeters while weights ranged from 55 kilograms to 140 kilograms for a mean of 82. Myocardial revascularizations numbered 25(83.3%) while 5(16.7%) required concomitant procedures that included valve replacement/repair or left ventricular aneurysm resection. There were 19(63.3%) repeat revascularizations while 11(36.7%) patients were to undergo surgery for the first time. Ejection fractions ranged from .15 to .60 for a mean of .44 and pump times ranged from 110 minutes to 455 minutes for a mean of 290. All procedures were performed using intermittent ischemia at approximately 34 degrees centigrade. There were no postoperative bleeders and 1 (.03%) surgical mortality. Arterial and venous blood gases were maintained within normal physiological limits utilizing continuous on-line real-time monitoring with the aid of the CDI System 300. (Table 3)

The HDRs ranged from 1.9 mg/kg in the least resistant patients to 4.9 mg/kg in more heparin resistant patients when run on the HMS compared to 2.7 mg/kg and 4.3mg/kg respectively on HSF. ACTs were within 10% comparatively, while the HPTs were consistently 1.0 to 1.5 mg/kg lower on the HMS when compared to those same samples analyzed on the HSF.(Table 4) Comparative recommended dosages of heparin were within 7%.

Comparative preoperative and postoperative HDRs indicated that there was not enough scientific or statistically significant data to indicate that patients become more heparin resistant after prolonged CBP although clinically these investigators have observed this intraoperative decline in ACTs and HPTs after approximately 280-360 minutes into the pump run.

Discussion

Mlilwaukee Heart Surgery Associates and St. Mary's Medical Center has maintained and managed anticoagulation therapy in over 3,000 patients placed on CPB utilizing the Hemotec device. These investigators have become sufficiently convinced that anything less than monitoring ACTs and HPTs every 20-30 minutes during prolonged CPB does not constitute the minimum standard of care and narrows the margin of safety during cardiac procedures. ACTs alone cannot provide the entire clinical picture because of the many factors which affect this test; hemodilution being the critical factor. ACTs can remain high while heparin consumption continues at a rapid rate and thereby masking subclinical coagulation.

This comparative study's protocol was to include a group of 50 patients, however it became clinically apparent just after 30 patients that the HMS was more accurate in its HDR, HPT, heparin dosage and protamine dosage. ACTs were within 45 seconds ± 5 comparatively and the data began to duplicate itself. In addition there was a monetary consideration. The expense of running the same tests on two different types of disposable cartridges on the same patient became costly and it is for these reasons the study was halted at 30 patients.

Comparatively the results from HDRs HPTS and ACTs when analyzed were within 1%; the Hemostasis Management System being more consistent due to the superior nature of the upgraded clot detection method. The Hepcon System Four employs the method of clot detection by surface flow as opposed to the plunger method found in the Hemostasis Management System (Baugh). The data demonstrates that the Hemostasis Management System consistently detected strands of fibrin at a level of 1.0-1.5 mg/kg of heparin lower than the Hepcon System Four. The HMS is able to detect lower levels of heparin due to the improved reagent stability.

There are many features which distinguish the Hemostasis Management System as being a far more superior device when compared to the Hepcon System Four. The automated cartridge filling replaces manual filling (the most common cause of poor results) thereby virtually eliminating human error. Precise filling of the cartridge is critical in achieving accurate results.

In addition to the Hemostasis Management System's greater accuracy, the user-friendly on board computer data entry method allows for additional parameters that enable the operator to fine tune the device in accordance to the ever-changing needs of the patients during anticoagulation therapy. The device is far less labor intensive from not only an operational standpoint but from a maintenance aspect as well.

While the debate concerning heparin protocols rage, and opinions differ from investigator to investigator when it comes to the validity of ACTs when correlated to heparin concentrations we need to recall the statement made by Brian S. Bull, M.D.: "The potency and reversibility of the anticoagulant heparin have made possible the entire field of cardiovascular surgery as we know it today.

Familiarity with its use has lead to the assumption on the part of many that the control of heparin during and the neutralization of heparin after extracorporeal circulation are straightforward matters which can be adequately handled by means of set protocols. These protocols are

based in most cases on the weight or surface area of the patient. This sense of security has been heightened by the fact that serious errors in the control of heparin therapy may occur without there being any clinical evidence. Such evidence is often delayed until the postoperative period when merging with other causes of postoperative bleeding, the origin of the problem becomes difficult if not impossible to identify."

These investigators wish to support Bull in his statements and comment further by stating that in example the heparinization requirement of a 70 year old 50 kilogram diabetic female differs greatly from that of a 45 year old 70 kilogram non-diabetic male and to anticoagulate these two distinctly different metabolisms using the same protocol is in our opinion less than the minimum standard of care when it comes to anticoagulation therapy.

Anticoagulation therapy is an art as well as a science and state-of-the-art technology exists to aid in that science. Health care providers need to master both the science and the art if the patient is to receive the benefit of our knowledge and expertise as well as widening the operative margin of safety.

References

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Table 1
Variables Affecting an ACT

Prekallikein	Red Cell Volume
High MW Kniinogen	Platelet Count
Factor XII	Platelet Function
Factor XI	Calcium
Factor IX	Temperature
Factor VII	Heparin
Factor X	Antithrombin III
Factor V	Plasminogen
Prothrombin	Monocytes
Fibrinogen	Tissue Factor
Factor VII	Protein C
Ionic Strength	pH
Mistidine Rich Glycoprotein	Activating Agent
Platelet Factor IV	Heparin Cofactor II

Table 2

Male	22 (63.3%)
Female	8 (26.7%)
Age	29-85 (63 y/o)
Height	107.1 cm
Weight	55-140 kg (82.9 kg)
Myocardial Revascularizations	25 (83.3%)
Concomitant Procedures (MCR, AVR, MVR, or repair, LV Aneur)	5 (16.7%)
Repeat Revascularizations	19 (63.3%)
First-Time Revascularizations	11 (36.7%)
Ejection Fractions	0.15-0.60 (.44)
Pump Time	110-455 min (290)
Intermittent Ischemia	30 (100%)
Temperature	app. 34°C
Post Operative Bleeders	NONE
Operative Mortality	1 (0.03%)

n=30

Table 3

(mean values and standard deviation)

pH	PaO^2 (mm/Hg)	$PaCO^2$ (mm/Hg)	SaO^2 (%)	HCT (%)
7.41 ± .02	129 ± 17	41 ± 6	96 ± 2	22 ± 2
pH	PvO^2 (mm/Hg)	$PvCO^2$ (mm/Hg)	SvO^2 (%)	HCT (%)
7.35 ± .08	33 ± 11	47 ± 4	69 ± 3	22 ± 2

Table 4

Hepcon System Four	Hemostasis Management System (HMS)
HDR (mg/kg)	HDR (mg/kg)
2.7 heparin sensitive	1.9 heparin sensitive
4.3 heparin resistant	4.9 heparin resistant
ACT	ACT
525 seconds	588 seconds

HSF/HMS HPT Differential - 1.0-1.5 mg/kg heparin