Vehicles of Heparin Management: A Comparison

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INTRODUCTION

The following study deals with the inherent problem in determining a suitable protocol for monitoring heparin therapy for patients undergoing cardiopulmonary bypass surgery.[1,2,3,4] To assist perfusionists in the clinical setting of the operating room, two automated devices have been engineered to help monitor a safe heparinization level during cardiopulmonary bypass procedures. The two vehicles—the Hemotec Hepcon A-10* and the International Technidyne Hemochron Model 400**—were compared to clinically assess heparin management. The following research data was compiled on seventy-six open heart surgical patients. In order to assist perfusionists, whose concern for optimum clinical care is dependent upon instrumentation, this paper hopes to assess which of these two devices are the most reliable, consistent, and reproducible.

PROTOCOL

The seventy-six clinical patients all underwent cardiopulmonary bypass surgery, and samples were simultaneously compared by both devices. The initial heparinizing dosage was determined by the Hepcon A-10, which is based on T. H. Allen's[4] equation, which is calculated by height, weight and sex. The perfusionist manually programs the information into the Hepcon which calculates the blood volume. The amount of the priming volume of the oxygenator is added and the result is the amount of heparin needed to attain a desired level of heparin maintenance. From this total heparin dosage, we subtracted 20 milligrams of heparin, which was equal to the amount used in our prime solution. All seventy-six patients strictly followed this protocol for determining the initial heparin dosage.

Prior to systemic heparinization, all patients were sampled and measured by the Hemochron for a base line figure, according to the manufacturer's guidelines. After the initial heparinizing dosage was administered, a period of twenty-five minutes elapsed, to allow for adequate circulation and mixture of the heparin, before simultaneous samples were drawn and measured for pre-bypass determinations. Once bypass was initiated,

* Hemotec, Hepcon A-10, Critikon, Irvine, CA 92714.
** Hemochron, International Technidyne, Edison, NJ.

a period of twenty-five minutes elapsed before samples were drawn and measured. Thereafter, samples were drawn and measured every forty minutes until the conclusion of bypass, with simultaneous samples measured continuously.

Just prior to the discontinuance of bypass, samples were drawn from the oxygenator, measured and compared, and a neutralizing dose was determined by the Hepcon for protamine neutralization, based on a ratio of a 1:1.1 of heparin to protamine. Approximately fifteen minutes after the protamine dose was administered, simultaneous samples were again drawn and compared for a return of the base line figure.

The Hemochron pre-manufactured coagulation test tubes were used exclusively throughout the study. The Hepcon heparin assay test cartridges used for pre-bypass and during bypass determinations were the silver cartridges with an assay range of 2.0-3.5, and for post-bypass determinations the yellow cartridges with an assay range of 0.0-1.5 were used, according to the manufacturer's specifications.

The extracorporeal circuit was comprised of a prime of 1500 ml. of lactated Ringers, to which was added 20 milligrams of sodium heparin, 44 milliequivalents of sodium bicarbonate and one gram of ascorbic acid. During all cardiopulmonary bypass procedures, moderate hypothermia was used to approximately 25°C, aortic root cardioplegia was administered, electrolytes, hemoglobin and hematocrit, blood gases, fluid input and urine output were measured.

RESULTS

The pre-bypass/pre-heparin samples determined by the Hemochron had a mean average of 130.8 seconds, with the samples varying in ranges of a high of 189 seconds and a low of 96 seconds, with eighty per cent falling into the 100-150 second range.*** These samples were used as base line figures which would be compared to the post neutralization samples of the patient.[5,6]

Strictly following the Hepcon protocol for heparin management, the patient was heparinized. Allowing for adequate circulating mixture of approximately twenty-five minutes, simultaneous samples were drawn from the patient and compared. Regardless of the Hepcon range, the average of all pre-bypass Hemochron samples was 731.4 seconds, with the range varying from 230-2000 seconds. All Hemochron samples were placed in their corresponding Hepcon level. (TABLE I) The figures in Table I show no corresponding trend to each other. A patient at a 2.0 Hepcon range could have a corresponding Hemochron sample any where from 232-1613 seconds, and the same comparison could be made for the remaining three Hepcon maintenance levels.

When a comparison was drawn between the two pre-bypass studies, pre- and post-heparin Hemochron samples, the average was 5.64 times the base line figure. The range varied from 1.56 times to 17.5 times the base line figure.

Once on bypass, and the patient's blood and the extracorporeal circuit were adequately mixed, the first during-bypass sample was drawn from the oxygenator and compared. The average of all Hemochron samples was 1010.6 seconds, with the range

*** Whenever samples were drawn from patients, the first 8-10 cc's withdrawn were discarded, and the next sample was used for determinations.

TABLE I
Pre-Bypass Samples

Hepcon Range	2.0	2.5	3.0	3.5
	509	681	1131	540
	1105	1192	498	801
	740	487	699	564
	1045	454	645	625
	734	588	647	357
Hemochron	567	982	512	830
Seconds	924	507	686	522
	259	381	540	551
	1613	2000	755	621
	851	946	363	413
	400	570	591	579
	847	576	230	369
	473	779	269	842
	807	408	439	1279
	907	1800	962	1300
	792	1200		379
	278	1034		1411
	232	694		1700
		516		456
		620		560
		1280		721

TABLE II
1st Sample During Bypass

Hepcon Range	2.0	2.5	3.0	3.5
	574	1220	817	1322
	656	1242	964	1700
	1041	1026	1614	531
	1553	610	618	1499
	1112	1131	2400	874
	925	1456	982	1593
Hemochron	567	505	1800	1170
Seconds	806	1213	1074	864
	531	863	832	624
	2000	1185	639	895
	797	825	1619	412
	1235	823	962	824
	1629		1502	1515
	1163		727	1166
	1127		989	402
	417		1390	1167
	1028		805	447
	334		1078	476
	782		324	350
	958		217	1323
	911		822	
	2176			
	1060			

TABLE III
Post Bypass Samples

Hepcon Range	Hemochron Secs	Average % Difference: Initial
0.0	Average 134.1	10.05 per cent Range– High—22 per cent Low— 0 per cent
0.5	Average 134.3	12.35 per cent Range– High—28 per cent Low— 0 per cent
1.0	Average 124.5	10.44 per cent Range– High—25 per cent Low— 1 per cent
1.5	Average 135	10.33 per cent Range– High—22 per cent Low— 1 per cent

varying from 217–2400 seconds. Once again all corresponding Hemochron samples were placed in their respective Hepcon maintenance levels and compared. (TABLE II) The figures in Table I compared similarly to those in Table II, in that the Hemochron samples showed no trend in consistency or reproducibility. A patient with a Hemochron of 800 seconds could appear in any of the Hepcon levels from a 2.0–3.5 range. At this point, when these samples are being measured, the patient's temperature is approximately 25°C, on bypass, with a hematocrit of approximately 23.5, caused by hemodilution.

All remaining bypass samples were measured, approximately one hour after the initiation of bypass. The average of all total Hemochrons at this point was 880.7 seconds with contrasting ranges from 300–1700 seconds.

During bypass, the Hemochron has limitations, noticeably temperature, which will adversely affect Hemochron test results, and long run times. Test results of 600 or more seconds imply a slow rate of fibrin formation. In such cases the time required for end point identification may be increased, with a corresponding decrease in accuracy and precision. It is, therefore, recommended that Hemochron test results in excess of 600 seconds be interpreted qualitatively only.[7] In looking back at the pre-bypass/post-heparin Hemochron samples, fifty-three (53) per cent exceeded 600 seconds, and when examining the first during-bypass samples, eighty-two (82) per cent exceeded 600 seconds.

The Hepcon determined the dosage of protamine needed to neutralize the active heparin in each patient, based on a level of a 1:1.1,[8] heparin:protamine. After the protamine was allowed to act for approximately fifteen minutes, comparative samples were again drawn from the patient. The average of all Hemochron samples was 131.9 seconds. As compared to the average of all pre-heparin samples, the comparison is equitable, 131.9 seconds to 130.8 seconds, giving the appearance of effective neutralization. Table III shows that regardless of the Hepcon range, from 0.0–1.5, the Hemochron averages were similar and their difference from their own respective initial samples was slightly more than ten (10) per cent. A patient who could appear as being in the neutral range of 0.0, as per the Hepcon, could range from zero (0) to twenty-two (22) per cent higher in his Hemochron samples, based on his own initial sample.

HEPCON vs. PROTOCOLS

In comparing the Hepcon vs. the standard method of determining the initial heparin dose of 3mg./kg., in ninety-four (94) per cent of our cases, fifteen (15) per cent more heparin was needed to maintain a 3mg./kg. level. In the remaining six (6) per cent of our cases, only two (2) per cent less heparin was needed to maintain a 3mg./kg. level.

In comparing the Hepcon protocol of protamine neutralization of 1:1.1 of existing heparin vs. a protocol of 1.5 times the total heparin administered, the advantage of knowing calculated figures based on qualitative sampling appears to be superior to dosage guesswork. When comparing the Hepcon protocol vs. a protocol of 1.5 times the initial heparin dose plus the twenty milligrams of heparin in the extracorporeal circuit; (1) in 10 cases, sixteen (16) per cent protamine was given based on the Hepcon; (2) in 59 cases, twenty-nine (29) per cent less protamine was given based on the Hepcon; and (3) in seven cases the dosage was equal.

When comparing the Hepcon protocol vs. a protocol of 1.5 times the initial heparin dose plus the twenty milligrams in the extracorporeal prime and a 1:1 of additional heparin given during bypass: (1) in four cases we would have given only five (5) per cent more protamine based on the Hepcon; (2) in 64 cases we would have given forty-four (44) per cent *less* protamine based on the Hepcon; (3) in eight cases there would have been no change; (4) seven cases, still less with the Hepcon; and (5) in one case five (5) per cent more.

CONCLUSION

In comparing the Hemochron vs. the Hepcon during cardiopulmonary bypass, the results clearly show that the Hepcon is the more reliable vehicle for measuring specific heparinization of the patient and for monitoring safe heparinization levels during bypass. The Hemochron test results vary from patient to patient with no consistent reliability due to adverse reactions of varying temperatures and hemodilution. In looking at the twenty-five per cent of the cases where blood was administered during bypass, it was noted that the Hemochron number was seventy per cent lower than the preceeding test result regardless of the Hepcon range, representing another variable in the Hemochron test results. In operating the Hepcon, the manipulation is exactly the same, offering little technical error, and no operator bias.

When studying the neutralization of each heparinized patient, the Hepcon again was the more reliable for reversal, showing a significant step forward for technology. The Hemochron test results represented a close return to a coagulative base line state, but an actual representation of neutralization of all existing heparin was not definitive, based on this study's results.

When knowing the precise amount of heparin that is needed based on the perfusionist's requirements and the patient's needs, the Hepcon would appear to be the vehicle of choice.

Heparin Sodium Injection, USP, Upjohn, Kalamazoo, Michigan.

Protamine Sulfate Injection, USP, Eli Lilly and Company, Indianapolis, Indiana.

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