Hypothermic cardiopulmonary bypass in CABG surgery, it is the time to revise our protocols

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ABSTRACT

INTRODUCTION: Hypothermia during coronary artery bypass grafting (CABG) procedures using cardiopulmonary bypass (CPB) technique is a defensive maneuver. Since most surgeons worldwide are accustomed to the use of "mild" hypothermia for such procedures, this study hope to discover whether "moderate" hypothermia had a more significant impact on lowering tissue oxygen consumption during cardiac surgery, taking into account that the risks of exposing the patient to "mild" hypothermia are similar to the risks of moderate hypothermia. Furthermore, the study sought to weigh the benefits of "mild" hypothermia against those of normothermia with regards to their impact on tissue oxygen consumption.

OBJECTIVE: To evaluate the total body oxygen consumption under different ranges of body temperature during surgery performed with the aid of CPB, ending with recommendations regarding the range of temperature that yield a preferential clinical outcome as a result of lower oxygen consumption.

METHODS: between December 2014 and April 2015, 70 consecutive patients (55 males and 15 females), undergoing coronary artery bypass grafting surgery (CABG), allocated into three groups regarding the core temperature (Group 1 with normothermia 35-37°C, Group 2 with mild hypothermia 32-35°C, Group 3 with moderate hypothermia 28-32°C).

RESULTS: There were no significant changes in Group 1 and Group 2 during CPB, however, for Group 3, there was a remarkable decrease in the oxygen consumption (VO2).

CONCLUSION: Moderate hypothermia rather than mild hypothermia proves to be of more benefit to the tissues when compared to normothermic conditions, as it significantly reduces tissue oxygen consumption. Moreover, even normothermia was found to be superior to mild hypothermia due to the latter's adverse effects while maintaining similar results with regards to oxygen consumption.

Key words: Mild hypothermia, Oxygen consumption, Oxygen delivery, Normothermia, CABG, Moderate hypothermia, Cardiopulmonary bypass.

Iraqi New Medical Journal January 2016;2(1)

INTRODUCTION

Hypothermia has been a fundamental part of any cardiac surgery that involves Extra Corporeal Circulation (ECC) since the pioneer days of cardiac surgery. It was adopted to protect organs from the effects of low-flow perfusion, a consequence related to the use of precocious ECC systems that were incapable of delivering sufficient blood flow. Since its introduction in the 1950s, further improvement in ECC techniques has been achieved.[1]

Recent progress in ECC technologies has changed these circumstances. The pumps that are currently in use are more efficient and are capable of providing sufficient blood flow under normothermic Cardiopulmonary Bypass (CPB) conditions, currently used oxygenators have a greater oxygenating capacity, the biocompatibility of the whole ECC system has been improved, which leads to less adverse effects on the patient. Due to the high reliability of all components of the ECC system, a malfunction of the machine or oxygenator occurs very rarely. Such progress has altered both our concepts regarding this issue and our approach to it.[2]

Temperature management during CPB remains controversial,with gaps in our knowledge concerning a variety of aspects of temperature management.[3,4,5]

This study aims to emphasize whether the "moderate" or "mild" hypothermia have a more impact on lowering tissue oxygen consumption during cardiac surgery. Furthermore, this study is sought to weigh the benefits of "mild" hypothermia against those of normothermia concerning their impact on tissue oxygen consumption.

METHODS

Study design and settings: This is a prospective, experimental and comparative study, conducted at Iraqi Centre for Heart Diseases and Ibn Al-Bitar Specialized Cardiac Surgery Centre. The study was done on 70 patients who were admitted into these two centres to have coronary artery bypass grafting surgery (CABG) between December 2014 and April 2015. The study was done in cooperation with the department of physiology, College of medicine, Al-Mustansiriyah University in Baghdad.

The study was done according to the code of ethics and approved by the ethical committee at the Iraqi Centre for Heart Diseases and Ibn Al-Bitar Specialized Cardiac Surgery Centre. We have explained the aim, benefits and the expected risks of the study to all the participants and their signed consent forms were taken prior to the surgery.

Inclusion criteria: Any patient who was referred toIraqi Centre for Heart Diseases and Ibn Al-Bitar Specialized Cardiac Surgery Centre to have CABG during the studied period was included in this study.

Exclusion criteria: The following patients were excluded from the study:

1. Patients who were in need to have other cardiac procedures(e.g. Valve replacement).
2. Patients with (T4> 22 + T3>7) pmol/L + (TSH < 0.2) mU/L which considered as possibly hypothyroidism.
3. Patients with (T4< 8 + T3<2.5) pmol/L + (TSH > 5) mU/L which considered as possibly hyperthyroidism.
4. Patients with (S. Creatinine > 1.8 mg/dL) +(Blood Urea > 65 mg/dL).
5. Patients with (S.GPT, S.GOT) levels defined as: 20<S.GPT, S.GOT< 5U/L.
6. Patient who have Hb level as:17 <Hb< 10.(6)

The reason for excluding these patients is to avoid any factor that may affect O2 consumption/metabolism.

Randomization: Patients were allocated into three groups according to the surgeon's preferences. ***Group 1*** (normothermia 35-37 °C) included patient who were subjected to normothermia during the procedure. ***Group 2*** (Mild Hypothermia 32-35 °C) included patients who had undergone the procedure under mild hypothermia. While ***Groups 3*** (moderate hypothermia 28-32 °C) has included patients who had the procedure under moderate hypothermia protocol as in (Table 1).[7,8]

Primary end points: the endpoints of our study wereto calculate the oxygen delivery (DO2) and oxygen consumption (VO2) through measuring blood gas parameters at the start of CPB and 10 minutes after achieving the desired thermal level.

Technical Information: All patients were operated upon under general anaesthesia (opiate-based anaesthesia). We have used fentanyl 5 µg/Kg and midazolam 0.1 mg/Kg for induction and sevoflurane 1-3 MAC for maintainece. To start the CPB, heparin has been used in a dose of 300 U/kg to obtain a value of activated clotting time (ACT) of 480 seconds or more.

CPB was performed using a non-pulsatile, roller pump HLM (heart-lung machine S5, Stockert Instruments Inc. Germany, and Jostra HL 20. Germany), A membrane oxygenators (Medtronic. USA and Maquet. Germany). Blood flow rate during CPB maintained at a cardiac index of 2.4 L/min/m^2 at normothermia, and between 2.2 and 2 L/min/m^2 at mild and moderate hypothermia respectively.[9] Blood was collected from the arterial and venous ports of the oxygenator.

The samples were immediately analyzed by (OPTI cassette E-Ca for (OPTI CCA-TS Blood Gas and Electrolyte Analyzers by OPTI Medical Systems, Inc. USA, and Siemens RAPIDLab 248 Blood Gas Analyzer, Germany) according to the patient's temperature for blood gases, pH, hematocrit, hemoglobin concentration, and oxygen saturation.

Arterial and venous blood samples were collected at the baseline (sample 1) and 5-10 minutes after conducting the CPB. The controlled temperature (sample 2) after at least 10 minutes from reaching the desired temperature. Oxygen delivery (DO2) and oxygen consumption (VO2) were calculated at each experimental time using Fick principle.[10]

Statistical analysis: Data were translated into a computerized database structure. Statistical analyses were computer assisted using SPSS version 21. A multiple linear regression model was used to study the net and independent effect of a set of anexplanatory variable on a quantitative outcome (dependent) variable.All of the (70) patients were tested by unpaired t-test, and because of missing data, only fifty-nine (59) patients tested by paired t-test and ANOVA test for the blood gas analysis.Both unpaired and paired t-test had comparable values of significance. Cohen's d is a standardized measure of effect size for the difference between two means, which can be compared across different variables and studies since it has no unit of measurement. Cohen's d < 0.3 (small effect), 0.3-0.7 (medium effect), while 0.8 and higher is a (large effect).A $P<0.05$ level of significance was considered statistically significant.

RESULTS

Table 1 shows some demographic features of the participants in the three groups. Accidental higher levels of (Hb) in (Group 3) were the cause of higher levels of oxygen delivery (DO2) at (sample 1). While the results of the effect of temperature on (DO2) for the three groups was tested at (sample 2), at which the temperature was settled on plateau phase during CPB (i.e. normothermia, mild or moderate hypothermia), it was found that there are no significant differ-

Table 1: Patients features for the three groups of temperature

	Group 1 (37-35)°C		Group 2 (35-32)°C		Group 3 (32-28)°C	
	No.	(%)	No.	(%)	No.	(%)
Patients	17	24.3	36	51.4	17	24.3
	Mean	**Std. dev.**	**Mean**	**Std. dev.**	**Mean**	**Std. dev.**
Age (years)	57.3	7.5	59.2	7.6	57.6	9.9
Height (cm)	168.9	9.3	170.1	9.2	172.3	9.4
Weight (kg)	9.9	12.8	80.6	14.4	83	5.6
Body Surface Area	1.89	0.2	1.9	0.2	1.95	0.24
Ejection Fraction	57.4	8.7	56.1	13.6	57.3	8.9
Cardiopulmonary Bypass time	126	36.6	141.2	41.4	120	31.9
Cross Clamp time	79.75	31.7	93.7	31.5	55.4	12.8

Table 2: Oxygen delivery during CPB

Thermal state	Oxygen delivery (ml/min)		
	Baseline	Temperature control	Changes during bypass
Effect of Mild hypothermia compared to Normothermia			
Difference in mean	-49.1	-47.5	1.6
Cohen's d	-0.33	-0.36	0.02
P (Bonferronni t-test) for difference in mean	1	0.87	1
Effect of Moderate hypothermia compared to Normothermia			
Difference in mean	162	34.6	-127.3
Cohen's d	0.83	0.25	-1.53
P (Bonferronni t-test) for difference in mean	0.038	1	0.001
Effect of Moderate hypothermia compared to mild hypothermia			
Difference in mean	211.1	82.1	-128.9
Cohen's d	1.43	0.71	-1.43
P (Bonferronni t-test) for difference in mean	<0.001	0.12[NS]	<0.001

Table 3: Oxygen consumption during CPB

Thermal state of each operation		Oxygen consumption (ml/min) Baseline	Temperature control	changes during bypass	P (Paired t-test)	Cohen's d
Normothermia (37-35) °C	**Range**	(95.82 to 260.63)	(109.76 to 238.48)	(-69.2 to 62.1)	0.47	
	Mean	168.2	176.5	8.3		0.2
	SD	48.3	35	36.7		
	SE	14.57	10.57	11.07		
	N	11	11	11		
Mild hypothermia (35-32)°C	**Range**	(88.44 to 285.23)	(103.22 to 273.38)	(-55.4 to 91.4)	0.09	
	Mean	154	164.3	10.3		0.28
	SD	37.5	36.1	32.9		
	SE	6.62	6.38	5.82		
	N	32	32	32		
Moderate hypothermia (32-28)°C	**Range**	(51.59 to 261.74)	(84.22 to 175.92)	(-93.5 to 85.4)	<0.001	
	Mean	182	139.5	-42.5		-1.03
	SD	53.4	24.1	41.4		
	SE	13.34	6.03	10.34		
	N	16	16	16		
P (ANOVA)=		0.12	0.013	<0.001		

SD: standard deviation, SE: standard error.

Table 4: The comparison between the thermal groups regarding the oxygen consumption during CPB

Thermal state	Oxygen consumption (ml/min) Baseline	Temperature control	Changes during bypass
Effect of Mild hypothermia compared to Normothermia			
Difference in mean	-14.2	-12.2	2
Cohen's d	-0.35	-0.34	0.06
P (Bonferroni t-test) for difference in mean	1	0.89	1
Effect of Moderate hypothermia compared to Normothermia			
Difference in mean	13.8	-37	-50.8
Cohen's d	0.27	-1.28	-1.28
P (Bonferroni t-test) for difference in mean	1	0.018	0.002
Effect of Moderate hypothermia compared to mild hypothermia			
Difference in mean	28.0	-24.8	-52.8
Cohen's d	0.65	-0.76	-1.47
P (Bonferroni t-test) for difference in mean	**0.13**	**0.05**	**<0.001**

ences among them (0.11) (Table2).

The data of (Group 1) and (Group 2) showed that there were no noticeable changes in the oxygen consumption (VO2) during CPB for each group (Table 3),and by comparing between the determined groups (Table 4).While for (Group 3), there was a remarkable decrease in the (VO2) (<0.001) (Table 3).

DISCUSSION

The effect of temperature on the oxygen consumption, especially at mild hypothermia level, remains controversial issue due to insufficient published evidence.

The non-significant changes of (DO2) for group 1 and 2 during CPB indicates that flow rate was not deceased whether we used normothermia or mild hypothermia. Also it pointed out that reduction of temperature to mild hypothermia and flow rate to 2.2 L/min/m^2 did not affect the supply of the oxygen during CPB. This result may explain the determination of some references to set the cardiac index at 2.2-2.5 L/min/m^2 during normothermia.[4]

In comparison to group 1 and 2, the significant decrease of DO2 in (Group 3) can be explained by the reduction in blood flow rate that was in proportion to the decrease in temperature to the moderate hypothermia. However, DO2 for Group 3 at sample 2 were still have the same values of (Group 1). This result is in agreement with that found by Svenmarker, Pittman, and Brown 2015. [11,12,13]

The level of VO2 for Group 1 and 2 has showed that there were no noticeable changes during CPB. This result is consistent to that stated by others;[6,14] reduction of the temperature to the mild hypothermia and a flow rate to 2.2 L/min/m^2 did not affect the need of the tissues for the oxygen during CPB.

The remarkable decline in VO2 for Group 3 during CPB explained by the reduction in temperature to moderate level, which in its turn has reduced the rate of metabolism to a significant degree.This result is consistent with that of Davies, Ashmore J, Hessel, and Sgouralis.[15,16,17,18]

One of the limitations of this study was the relatively the small sample size, because of the limited time available for this study. In addition we need to measure the effect of moderate hypothermia on different organs in the body like brain, liver, kidneys, and others.

CONCLUSIONS

Moderate rather than mild hypothermia is probably the level of hypothermia that significantly reduces the tissue oxygen consumption compared to patients operated upon under normothermic conditions. Normothermia seems to be similar to mild hypothermia according to the reactions on oxygen consumption.

REFERENCES

1. Chilton V, Klein A. Equipment and monitoring. In: Florian Falter, David J Cook Sunit Ghosh, editors. Cardiopulmonary Bypass. 1st Edition. New York, Cambrigde University Press; 2009:P 1-22..
2. Slavík J, Medek K, Nesporová J, Píchovcová B, Norek R, Černý Normothermia in cardiac surgery with extracorporeal circulation, a review. *Scripta Medica (Brno)* 2003;76 (6): 331–340.
3. Engelman R, Baker RA, Likosky DS, Grigore A, Dickinson TA, Shore-Lesserson L, Hammon JW. The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of Extra Corporeal Technology: Clinical Practice Guidelines for Cardiopulmonary Bypass—Temperature Management During Cardiopulmonary Bypass. *Ann Thorac Surg* 2015;100 (2):748–57.
4. Murphy G S, Hessel E A, and Groom R C. Optimal Perfusion During Cardiopulmonary Bypass: An Evidence-Based Approach. *Anesthesia & Analgesia*, 2009; 108(5):pp 1394-1417.
5. Ho K M, Tan J A. Benefits and Risks of Maintaining Normothermia during Cardiopulmonary Bypass in Adult Cardiac Surgery: A Systematic Review. *Cardiovascular Therapeutics*, 2009;29(4): 260–279.
6. Walker SW. Laboratory reference ranges. In: Walker SW, Colledge NR, Ralston SH, Penman ID, editors. Davidson's Principles and Practice of Medicine. 22nd edition Elsevier Limited; 2014:1307-1312.
7. Crosby Ivan K, Zacour Richard K. Cardiopulmonary Bypass. In: Kron IL, Spray TL, Kaiser LR, editors. Mastery of Cardiothoracic Surgery. 3rd edition. Philadelphia: Lippincott Williams & Wilkins, a Wolters Kluwer business; 2013: 356-369.
8. Bennett JM, Shaw A, and Wagner C. Hypothermia and circulatory arrest. In: Myles Paul S, Ranucci M, and Alston R Peter. Oxford Textbook of Cardiothoracic Anaesthesia. Oxford University Press; 2015: 149-158.
9. Lich BV, Brown DM. The manual of clinical perfusion. 2nd edition. Fortmmyers, Florida: Perfusion.com publication; 2014.
10. Butterworth J, Mackey DC, Wasnick J. Morgan & Mikhail's Clinical Anaesthesiology. 5th edition. McGraw-Hill Education, LLC; 2013.
11. Svenmarker S, Häggmark S, Hultin M, Holmgren A. Static blood-flow control during cardiopulmonary bypass is a compromise of oxygen delivery. *European Journal of Cardio-thoracic Surgery* 2009; 37(1):218-222.
12. Pittman RN. Regulation of Tissue Oxygenation. *Colloquium Series on Integrated Systems Physiology: From Molecule to Function* 2011;3(3):1-100.
13. Brown JR, Parikh CR. Acute kidney injury after cardiac surgery in adults.In: Chirag R Parikh, Charuhas V Thakar, editors. Perioperative Kidney Injury: Principles of Risk Assessment, Diagnosis and Treatment. New York: Springer science+business media; 2015: 85-98.
14. Boodhwani M, Rubens FD, Wozny D, and Nathan HJ. Effects of Mild Hypothermia and Rewarming on Renal Function After Coronary Artery Bypass Grafting. *Ann Thorac Surg* 2009;87 (2): 489-495.
15. Davies, Laurie K. Temperature Management in Cardiac Surgery. In: Gravlee GP, Davis RF, Stammers AH, and Ungerleider RM, editors. Cardiopulmonary Bypass: Principles and Practice. 3rd edition. Lippincott Williams & Wilkins; 2008:155-171.
16. J. Ashmore, J. Pickett, J. Alder, R. Marks, and M. Thorniley. Whole Body Oxygen Delivery and Consumption During Cardiopulmonary Bypass Surgery. In: Bucher HU, Rudin M, Huffel SV, Wolf U, Bruley DF, Harrison DK, Wolf M, editors. Oxygen Transport to Tissue XXXIII. New York: Springer Science+Business Media; 2012:229-234.
17. Hessel II Eugene A, Hild Peter G. Pathophysiology of Cardiopulmonary Bypass. In: Hensley FA, Martin DE, and Gravlee GP (editors). A Practical Approach to Cardiac Anaesthesia. 5th edition. Philadelphia: Lippincott Williams & Wilkins; 2013:560-586.
18. Sgouralis I, Evans RG, Gardiner BS, Smith JA, Fry BC, and Layton AT. Renal haemodynamics, function, and oxygenation during

cardiac surgery performed on cardiopulmonary bypass: a modeling study. *Physiological Reports* 2015; 3(1): 1-14.

Acknowledgement: I would like to present my thanks to Dr. Ghadeer Hikmat Majid and Dr. Mohammed Shehab Al-Edani for their remarkable contribution to accomplish this work.

Abbreviation list: Extra Corporeal Circulation (ECC), Cardio Pulmonary Bypass (CPB), Coronary Artery Bypass Grafting (CABG), Oxygen Delivery (DO2), Oxygen Consumption (VO2), Activated Clotting Time (ACT), Minimum Alveolar Concentration (MAC).

Conflict of interest: Authors have nothing to declare.

Funding: Authors received no funds to complete this study a part from self funding.