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Hyperthermic Intraperitoneal Chemotherapy (HIPEC) and Intraoperative Electrolyte Disturbances—Implications for Anesthetic Management

John L. Raytis, Michael W. Lew

Department of Anesthesiology, City of Hope, Duarte, USA
Email: jraytis@coh.org, mlew@coh.org

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Abstract

The administration of hyperthermic intraperitoneal chemotherapy (HIPEC) is often associated with significant intraoperative electrolyte changes. We retrospectively examined the pre-HIPEC and post-HIPEC intraoperative basic metabolic panel (BMP) values of the 20 patients who underwent HIPEC at our institution between December 2009 and January 2012. For the five patients who underwent HIPEC with oxaliplatin in 5% dextrose in water (D5W), there were statistically significant changes between the pre- and post-HIPEC values of sodium (135 to 124 mmol/L), chloride (105 to 94 mmol/L), glucose (143 to 388 mg/dl) and sodium corrected for hyperglycemia (135 to 127 mmol/L). For the 14 patients who received HIPEC with mitomycin C in normal saline (NS), there were statistically significant changes in bicarbonate (24 to 21 meQ/L), blood urea nitrogen (BUN) (10 to 9 mg/dl) and glucose (158 to 134 mg/dl). The BMP changes for the one patient who received doxorubicin/cisplatin in peritoneal dialysate are reported separately.

Keywords

Hyperthermic Intraperitoneal Chemotherapy, HIPEC, Electrolyte Disturbances, Hyponatremia, Hyperglycemia

1. Introduction

Cytoreductive reductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) is playing an increasingly important role in the treatment of patients with peritoneal malignancies. Improved survival rates for pa-

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tients undergoing the procedure versus traditional therapies have been reported [1]-[3]. Cytoreductive surgery with HIPEC often involves an extensive surgical procedure that can present multiple intraoperative challenges to the anesthesiologist [4]. In particular, the administration of HIPEC can be associated with significant intraoperative electrolyte disturbances. Depending on the specific chemotherapy agent administered during HIPEC, patients may experience considerable hyperglycemia, hyponatremia, and acidosis. Intervention by the anesthesiologist is often necessary, and readiness to appropriately treat the electrolyte disturbances associated with HIPEC facilitates the delivery of optimal anesthetic care. We set out to characterize the electrolyte disturbances seen in patients at our institution undergoing HIPEC with different chemotherapy agents.

2. Materials and Methods

2.1. Patients and Settings

After obtaining IRB approval, we retrospectively identified and included all patients who had been scheduled to undergo intraoperative HIPEC at the City of Hope National Medical Center in Duarte, CA between December 2009 and January 2012.

2.2. Data Collection and Analysis

27 patients met the inclusion criteria. Upon review, seven of the 27 patients were found not to have undergone intraoperative HIPEC and were excluded from the study. For each of the 20 patients who underwent HIPEC, the intraoperative electrolyte values closest in time prior to and after the initiation of HIPEC were recorded. The patients were grouped by the type of chemotherapy agent they received—either oxaliplatin in 5% dextrose in water (D5W), mitomycin C in normal saline (NS), or doxorubicin and cisplatin in peritoneal dialysate. The average pre- and post-HIPEC basic metabolic panel electrolyte values were calculated for each chemotherapy group. For the oxaliplatin in D5W patients, post-HIPEC sodium values corrected for hyperglycemia were also calculated using the formula (measured sodium) (0.016) (glucose-100). For each chemotherapy group, we determined the statistical significance of changes in average pre- and post-HIPEC electrolyte values using two-sided student's t-tests.

3. Results

A total of 20 patients were included in the study. Diagnoses included colorectal, primary peritoneal, appendiceal, and gastric cancers. Each patient received one of three chemotherapy agents: oxaliplatin in D5W, mitomycin C in NS or doxorubicin and cisplatin in peritoneal dialysate. The characteristics of the study population are summarized in **Table 1**.

3.1. Oxaliplatin in D5W

For the patients who underwent HIPEC with oxaliplatin in D5W, there were statistically significant decreases in

Table 1. Study population.

Average Age (Years)		55
Age Range		31 to 77
Males		9
Females		11
Primary Cancer Site	Colon	10
	Primary Peritoneal	5
	Appendiceal	4
	Gastric	1
Chemotherapy Type	Oxaliplatin in D5W	5
	Mitomycin C in NS	14
	Doxorubicin/Cisplatin in Peritoneal Dialysate	1

the pre-HIPEC vs. post-HIPEC levels of sodium, sodium corrected for glucose, and chloride. In addition, there was a statistically significant increase between the pre- and post-HIPEC serum glucose level (Table 2).

3.2. Mitomycin C in NS

The patients who underwent HIPEC with mitomycin C in NS had statistically significant decreases from pre- to post-HIPEC serum levels of bicarbonate, blood urea nitrogen (BUN) and glucose (Table 3).

3.3. Doxorubicin/Cisplatin in Peritoneal Dialysate

The pre-HIPEC and post-HIPEC basic metabolic panels (BMP) for the one patient who received HIPEC with doxorubicin/cisplatin in peritoneal dialysate are reported below (Table 4).

Table 2. Oxaliplatin in D5W

Electrolyte[a]	Pre-HIPEC average	Post-HIPEC average	P value
Sodium (mmol/L)	135	124	0.006
Corrected sodium (mmol/L)[b]	135	127	0.02
Potassium (mmol/L)	3.8	3.6	0.41
Chloride (mmol/L)	105	94	0.005
Bicarbonate (mmol/L)	24	22	0.37
BUN (mg/dL)	9	7	0.12
Creatinine (mg/dL)	0.69	0.62	0.21
Glucose (mmol/L)	143	388	< 0.001
Calcium (mg/dL)	8.0	7.3	0.60

[a]Normal values: Sodium 137 - 145 mmol/L, Potassium 3.5 - 5.1 mmol/L, Chloride 98 - 107 mmol/L, Bicarbonate 22 - 30 mmol/L, BUN 4 - 20 mg/dL, Creatinine 0.7 - 1.3 mg/dL, Glucose 80 - 128 mmol/L, Calcium 8.6 - 10.2 mg/dL; [b]Pre-HIPEC sodium (uncorrected) vs. Post-HIPEC sodium corrected for hyperglycemia.

Table 3. Mitomycin C in NS.

Electrolyte	Pre-HIPEC average	Post-HIPEC average	P value
Sodium (mmol/L)	136	136	0.61
Potassium (mmol/L)	4.0	4.0	0.95
Chloride (mmol/L)	105	101	0.51
Bicarbonate (mmol/L)	24	21	<0.001
BUN (mg/dL)	10	9	<0.001
Creatinine (mg/dL)	0.59	0.58	0.34
Glucose (mmol/L)	158	134	0.004
Calcium (mg/dL)	8.2	7.2	0.09

Table 4. Doxorubicin/cisplatin in peritoneal dialysate.

Electrolyte	Pre-HIPEC	Post-HIPEC
Sodium (mmol/L)	133	133
Potassium (mmol/L)	4.2	4.0
Chloride (mmol/L)	108	104
Bicarbonate (mmol/L)	19	21
BUN (mg/dL)	4	3
Creatinine (mg/dL)	0.49	0.48
Glucose (mmol/L)	131	233
Calcium (mg/dL)	8.1	7.1

4. Discussion

Cytoreductive surgery with HIPEC is an extensive procedure that is associated with considerable challenges for the anesthesiologist. Significant intraoperative hyperthermia, tachycardia, and acidosis can occur [4]. With respect to intraoperative electrolyte disturbances, we found HIPEC with oxaliplatin in D5W to be associated with significant hyperglycemia and hyponatremia. At our institution, oxaliplatin for HIPEC is given at 460 mg/m^2, and the degrees of hyperglycemia and hyponatremia we observed at this dose are similar to other reports [5]. Because postoperative cerebral edema has been described in patients with hyponatremia from oxaliplatin in D5W HIPEC [5] and because of the potential for worsening of cerebral edema in the setting of hyperglycemia and hyperthermia [6] [7], it is important that anesthesiologists anticipate and are prepared to treat the electrolyte disturbances that can occur with oxaliplatin in D5W HIPEC.

Although oxaliplatin itself can cause multiple toxicities, the electrolyte disturbances we observed associated with its use in HIPEC are most likely related to the fact that D5W is used as a carrier fluid for its administration. The use of D5W as the oxaliplatin HIPEC carrier fluid is based upon oxaliplatin's instability and decomposition in chloride containing solutions such as NS. However, due to the severe electrolyte disturbances seen with using D5W as a carrier fluid, future oxaliplatin based HIPEC has recently been approved at our institution to be carried out using NS as the carrier fluid instead of D5W. This policy change was made after considering the breakdown over time profile of oxaliplatin in normal saline together with the relatively short infusion time for oxaliplatin-based HIPEC used at our institution (30 minutes).

In contrast to the severe electrolyte disturbances seen with oxaliplatin in D5W, we found that the electrolyte changes associated with HIPEC using mitomycin C in NS—mild decreases in bicarbonate, BUN, and glucose—to be by comparison, lesser in severity and magnitude than those found with oxaliplatin in D5W. Our finding of a decrease in serum glucose after HIPEC with mitomycin C in NS is in contrast to the increase reported elsewhere [5].

This study characterizes the changes in electrolyte values that are associated with the intraoperative administration of HIPEC. HIPEC with oxaliplatin in D5W was found to be associated with significant hyperglycemia and hyponatremia. At our institution, a policy change has been made to eliminate the use of D5W as the carrier fluid for oxaliplatin based HIPEC. Oxaliplatin in D5W, however, is still widely used. Knowledge of the electrolyte changes associated with patients undergoing HIPEC allows anesthesiologists to anticipate and to better treat the significant disturbances that can occur.

References

[1] Cashin, P.H., Graf, W., Nygren, P. and Mahteme, H. (2012) Intraoperative Hyperthermic Versus Postoperative Normothermic Intraperitoneal Chemotherapy for Colonic Peritoneal Carcinomatosis: A Case-Control Study. *Annals of Oncology*, **3**, 647-652. http://dx.doi.org/10.1093/annonc/mdr301

[2] Elias, D., Lefevre, J.H., Chevalier, J., Brouquet, A., Marchal, F., Classe, J.M., *et al.* (2009) Complete Cytoreductive Surgery plus Intraperitoneal Chemohyperthermia with Oxaliplatin for Peritoneal Carcinomatosis of Colorectal Origin. *Journal of Clinical Oncology*, **5**, 681-685. http://dx.doi.org/10.1200/JCO.2008.19.7160

[3] Zhu, Z.G., Tang, R., Yan, M., Chen, J., Yang, Q.M., Li, C., *et al.* (2006) Efficacy and Safety of Intraoperative Peritoneal Hyperthermic Chemotherapy for Advanced Gastric Cancer Patients with Serosal Invasion. *Digestive Surgery*, **23**, 93-102. http://dx.doi.org/10.1159/000093778

[4] Schmidt, C., Creutzenberg, M., Piso, P., Hobbhahn, J. and Bucher, M. (2008) Perioperative Anesthetic Management of Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy. *Anaesthesia*, **63**, 389-395. http://dx.doi.org/10.1111/j.1365-2044.2007.05380.x

[5] Rueth, N.M., Murray, S.E., Huddleston, S.J., Abbott, A.M., Greeno, E.W., Kirstein, M.N., *et al.* (2011) Severe Electrolyte Disturbances after Hyperthermic Intraperitoneal Chemotherapy: Oxaliplatin Virus Mitomycin C. *Annals of Surgical Oncology*, **18**, 174-180. http://dx.doi.org/10.1245/s10434-010-1210-1

[6] Song, E.C., Chu, K., Jeong, S.W., Jung, K.H., Kim, S.H., Kim, M. and Yoon, B.W. (2003) Hyperglycemia Exacerbates Brain Edema and Perihematomal Cell Death after Intracerebral Hemorrhage. *Stroke*, **34**, 2215-2220. http://dx.doi.org/10.1161/01.STR.0000088060.83709.2C

[7] Sharma, H.S. (2006) Hyperthermia Induced Brain Oedema: Current Status and Future Prespectives. *Indian Journal of Medical Research*, **123**, 629-652.

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