Toxicity of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy, (HIPEC) in Pediatric Sarcomatosis

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Sarcomatosis in Children

- Intra-abdominal metastasis secondary to soft tissue sarcoma is a rare form of tumor dissemination in children.
- Complete surgical resection is often deemed impossible.
- Children are frequently offered palliative care only.
HIPEC in Children

• An aggressive approach
• Surgical excision of dozens to hundreds of tumor nodules
• Perfusion of the abdominal cavity with hyperthermic intraperitoneal chemotherapy (HIPEC) with a curative intent.
HIPEC in Children

- We have done 47 HIPEC procedures (1st N. America)
- We evaluated the toxicity and outcome of 23 children and young adults undergoing 27 HIPEC procedures using Cisplatin. (6mo follow-up)
  - Rhabdomyosarcoma (RMS)
  - Fibrosarcoma
  - Desmoplastic small round cell tumor, (DSRCT)
  - Mesothelioma
  - Wilms’ tumor
  - Melanomatosis
  - Adenocarcinoma
WHAT IS HIPEC?
HIPEC set up
WHAT TYPE OF PATIENTS MAY NEED HIPEC?
Histiocytic Sarcoma  2yo
DSRCT 5yo
DSRCT 5yo
WHAT IS CYTOREDUCTIVE SURGERY?
DSRCT Pelvic
DSRCT Diaphragm
DSRCT Omentum
DSRCT Omentum
DSRCT Omentum
Sarcoma Mesentery
Why Hyperthermic Cisplatin?

• No local peritoneal toxicity

• No cross resistance to drugs previously given systemically

• Neutralizing or binding agent sodium thiosulfate given IV for 24 hours to minimize systemic toxicity (renal, hearing)
Methods HIPEC Children

- All patients underwent cytoreductive surgery
- 100mg/M2 of Cisplatin at 40.5-41 degrees Celsius, for 90 minutes
- A subset were enrolled on our phase 1 study dose escalation cohort received 150mg/M2 Cisplatin HIPEC.
- All toxicities were recorded.
Pediatric HIPEC Phase 1 Trial

• Surgical removal of all tumors (up to 400+) in abdomen (3-18yo)
• Excellent performance status
• Cisplatin chemotherapy for 90 minutes at 40-40.5°C
• Dose escalation 100-150mg/M2
Toxicity HIPEC Children

• 27 HIPEC in 23 children
• Follow up 6 to 60 months
• Operation time 9-15 hours
• Average hospital stay 10 days
• QOL back to normal ~2 months
Toxicity HIPEC Children

- In the phase 1 study, the maximum tolerated dose was 100mg/M2.
- Dose limiting toxicity was grade 3 renal failure.
- Five of 27, 18%, had grade 3 or higher renal failure.
- 10% required dialysis.
Toxicity HIPEC Children

• 1 subclinical decrease in hearing
• 2 grade 3 hematologic toxicities
• 2 grade 3 hepatic toxicities
• 1 grade 3 ileus.
Morbidity of HIPEC

- No mortality
- DLT creatinine increase by 2x, 1 temp. dialysis, returned to normal range 1-2 weeks
- 1 cardiomyopathy from tumor burden reversed with beta blockers
- Partial small bowel obstruction
- No post op bleeding or ‘take back’ to OR
Outcomes

- Surgical complications occurred in 5/27 (18%) of patients.
- 7 patients (26%) had no recurrence.
- CR 0 patients had an 83% survival probability.
Complete Resection HIPEC

Probability of OS vs Time (Months)

- No (E/N = 1/8)
- Yes (E/N = 5/13)

P-value = 0.071
Conclusion HIPEC Children

- Toxicity of HIPEC in children is low
- No mortality
- Renal toxicity is major
- Surgical morbidity lower than adult HIPEC
- Phase 2 trial ongoing