### Pre-operative Considerations

In this series, two patients with a history of adverse reaction to injection of Melphalan (L-phenylalanine mustard) directly into the retinal artery were studied. This approach to delivery of chemotherapy has many advantages, which include avoidance of intravenous chemotherapy and the associated adverse effects of systemic delivery (myelosuppression, GI toxicity, failure to thrive) as well as ability to use Melphalan, which is the most effective agent against retinoblastoma, but cannot be used systemically due to its high toxicity at therapeutic doses.1

After the second Melphalan injection, both patients experienced a transient period of decreased tidal volume and ETCO2, which was followed by a transient decrease in BP with subsequent injections. In both patients, these episodes typically lasted 30-60 seconds. To further characterize this reaction, when each patient returned for repeat Melphalan injection, both an arterial line and trans-esophageal echo probe were placed following mask induction and intubation. Both patients were premedicated with glycopyrrolate.

### References


### Intra-operative Management

The first patient, a two year old female with no pre-existing cardiopulmonary issues, responded to the injection with an immediate increase in heart rate, followed by decreases in both blood pressure and ETCO2. However her TEE exam was unchanged, and her blood pressure and ETCO2 returned to baseline after 60 seconds following an IV fluid bolus of 10cc/kg. Throughout this episode, the patients tidal volume and airway pressure remained unchanged.

The second patient, a three year old with no significant cardiopulmonary issues, displayed hemodynamic changes within one minute of injection. Initially the patient's tidal volume rapidly decreased from 80ml to 20mL, and her pulse oximeter reading and ETCO2 significantly decreased. She was manually ventilated with 100% oxygen with noticeable difficulty and decrease in lung compliance. Upon auscultation, the patient had decreased breath sounds but no wheezing. After 30 seconds of this reaction, a decrease in blood pressure without a change in heart rate was noted. This drop in BP did not respond to a single dose of phylephrine, but did respond to two small boluses of epinephrine (0.1mcg/kg each).

Midesophageal 4-chamber view demonstrated a decrease in right ventricular contractility and bowing of the ventricular septum to the right, both of which improved with the epinephrine. The heart rate remained at baseline and the oxygen saturation, ETCO2 and tidal volumes all improved within two minutes of the Melphalan injection. The blood pressure did improve, but remained low-normal until the end of the case.

### Post-operative Course

Both patients were extubated at the end of the procedure and had unremarkable post-operative courses. In both cases, tryptase levels were not elevated. Initially thought to be related to an anaphylactic picture, this reaction appears to be secondary to an autonomic reflex, similar to the trigeminocardiac or oculo-pulmonary reflex. Premedication with an anticholinergic would be thought to lower the risk of this reflex from occurring and attenuate the reaction, but we did not find this to be the case. In a retrospective study, Phillips et al. had similar findings to our own.2 This reaction occurs in two phases: first, it is likely that an acute increase in pulmonary arterial pressure causes the changes in ventilation. Second, it is likely that this acute increase in PA pressure causes depression of the right ventricle, eventually leading to the decrease in blood pressure. Due to a lack of data regarding this reaction and the relative novelty of Melphalan injection directly into the retinal artery, this reflex has yet to be well defined. At this point, Cleveland Clinic Children's is the only institution to have echocardiographic evidence of this reaction and the effect it has on the right ventricle specifically. Additional research is required to further characterize this life-threatening reaction and determine if there is a means of eliminating its occurrence or reducing patient response to it.

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**Case Series: Adverse cardio-respiratory reaction following direct intra-arterial chemotherapy injection for treatment of retinoblastoma.**

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