Heated chemotherapy can help some children with cancer

July 28 2021

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Tumors that have spread to the lining of the abdomen are tough to treat. But a select number of cancer teams across the country have found success with a procedure known as HIPEC, which stands for

hyperthermic intraperitoneal chemotherapy, a method of pumping heated chemo directly into the belly instead of sending it through the bloodstream.

Michigan Medicine surgeons have used this technique for several years in adults but are just starting to provide it to children. Erika Newman, M.D., an associate professor of pediatric surgery at the University of Michigan Medical School and the associate chief clinical officer of health equity for Michigan Medicine, sat down with *Michigan Health* to explain the situations where HIPEC might be useful, what considerations are important for the procedure in kids and why Michigan Medicine's multidisciplinary team is so crucial when performing this complex technique.

What does HIPEC stand for and why would heated chemotherapy be more effective than other types of chemotherapy in certain situations?

It stands for hyperthermic or heated intraperitoneal chemotherapy or chemoperfusion.

HIPEC is administered directly into the abdomen. It's not absorbed into the bloodstream, and so it has fewer side effects on the rest of the body. That is one really important characteristic, especially for kids, because one of the aspects of cancer treatment that limits us is systemic toxicity—the total amount of harmful substances the body can endure before severe side effects develop.

Pediatric cancers that attach to the lining of the abdomen—we call that the peritoneum—and its surfaces are the best candidates because you're instilling that chemotherapy directly into the abdomen, so it can penetrate those surfaces directly as opposed to going through the

bloodstream and attacking cancer cells on the surface.

What type of cancers are appropriate for HIPEC treatment?

The most common peritoneal cancer in children and young adults that benefit from this kind of therapy is a tumor called desmoplastic small round cell tumor or DSRCT. It's a very rare but very aggressive form of cancer. The patients with this condition that have the best chance at long-term survival and have the best outcomes are the ones in which we are able to remove all of the tumor from the abdomen, including where the tumor has attached to the lining of the peritoneum, and then combine that with HIPEC. Those patients have been shown to have better outcomes than the patients that don't have HIPEC.

For this kind of cancer, HIPEC is a component of what we would now consider first-line therapy, or the first treatment given for a disease because it's widely considered the best option.

Most DSRCT patients get chemotherapy before surgery, known as neoadjuvant chemotherapy. They get anywhere from five to six cycles of chemotherapy, and then we go into what we call a local control surgery, where we remove the tumor along with giving HIPEC. And then they'll get what we call adjuvant therapy, or the chemotherapy that is given after the initial treatment and primary surgery. So essentially, the kids get really high doses of intense chemo to try to get long-term cures for some of these really tough cancers

Is HIPEC ever used as a secondary option if other treatments don't work?

It certainly can be for recurrent disease and in patients with disease that

comes back in the abdomen. It can be a treatment for other conditions, too.

Kids don't typically get colon cancer, but HIPEC can be used for metastatic colon cancer. For children, HIPEC can also be used for certain types of sarcomas that have spread to the peritoneal surfaces. In fact, the first pediatric HIPEC case we did was for a child with a sarcoma.

Another condition HIPEC can be used to treat would be malignant ovarian germ cell tumors, in which cancer forms in the germ, or egg, cells of the ovary. Those tumors can attack the peritoneal lining. So really any tumor that involves the peritoneum or the peritoneal lining would be an ideal case for HIPEC.

What's different about the procedure in kids?

First off, kids are kids—not small adults.

Second, all patients receiving HIPEC have a risk of renal failure. But children have an even more pronounced risk of renal failure with HIPEC than adults. So we do several things during our pediatric HIPEC cases to make sure that we protect their kidneys during and after the operation. This includes special medications and fluid orders.

In general, kids are smaller, so we need to ensure we have the proper pediatric-sized cannulas (tubes that are inserted into a vein or body cavity for various purposes, including to administer medication). The other things that we're thinking about are dosing—making sure we have the right doses and volumes of the chemotherapy appropriate for the size of the patient we are treating. Our chemotherapy Pharm.D. and oncology pharmacists are instrumental and are front and center in helping us navigate chemo doses and intraperitoneal chemotherapy orders.

Is that level of multidisciplinary expertise something that differentiates Michigan Medicine from some other health centers?

Absolutely! Getting us to and through the first two pediatric HIPEC cases at Michigan Medicine exemplified how phenomenally our multidisciplinary and interdisciplinary teams come together. Every service approached to assist with our initiative and ongoing efforts were excited and passionate about coming together to provide this potentially curative procedure to our pediatric population. The HIPEC pediatric procedure included:

- Pediatric oncology
- Pediatric surgery
- Pediatric anesthesiology
- The adult peritoneal malignancy program
- The pediatric intensive care unit and the pediatric critical care medicine team
- Pediatric oncology pharmacists and adult HIPEC pharmacists
- Nursing teams in the operating rooms
- Surgical technicians in the operating rooms
- Perfusionists, who specialize in bathing organs or tissues in fluid, and who helped with perfusing HIPEC

- The learners that were involved in the case, i.e., medical students
- The solid tumor program coordinator and program director

The list is huge. You need people with very specialized expertise to do this, and we have that here at C.S. Mott Children's Hospital. Our pediatric oncologists are some of the best in the country to take care of kids with cancer. And we have a full team of experts that can band together and assure that the children are getting the highest level of care in the safest and most effective way possible, so we can hopefully have a curative outcome.

What side effects do you have to consider when administering HIPEC to children?

The biggest one is renal failure in kids because of the toxicity of the chemotherapy on the kidneys. The other thing that we deal with is post-op ileus. That's when the bowels go to sleep and stop working. That's a real concern afterwards. So we don't feed the kids afterward. We just keep them hydrated with IV fluids and wait for the bowel function to return. Sometimes even five to seven days after surgery, we're still waiting.

But once we can make sure their hydration status is good, their kidneys are still healthy and working, and their ileus has resolved, then we can start ushering them back into where they were pre-operatively. By that point, they're eating and drinking and peeing and pooping and all the things are working, and then they go home.

Why did you decide to expand into HIPEC for kids this year?

HIPEC in general, even for adults, is a fairly new technique.

Up until recently, pediatric HIPEC work has been pioneered by Andrea Hayes-Jordan, a pediatric surgeon who was at MD Anderson for many years. Her area of expertise was in the benefits of HIPEC for kids with particular cancers, especially DSRCT. Her research has shown that there is survival benefit both for local occurrence and in long-term overall survival, and that work has been over the past 10 years.

It's very clear now that we can try to increase survival in kids that have really tough cancers where, if you don't attempt this, then there really are not any more treatment options. Being able to give a family hope is really important.

Over these last several years, more centers have been working toward being able to offer HIPEC. It just so happened that we had two kids in the last couple of months that were good candidates, and we thought now is the time.

What's the timeline for whether you know if the HIPEC treatment was successful or not for these two initial patients?

They're going to finish out the rest of their chemotherapy for now. Most of the time with cancer, you're doing surveillance for the first five years after. Three years and five years are the benchmarks where we'll know if it made a difference. But we already feel our efforts were successful by being able to offer our patients the option of HIPEC treatment when there were not a lot of other treatment options available.

Provided by University of Michigan