Intestinal Failure Associated Liver Disease - Pediatric Grand Rounds-20240913_082940-Meeting Recording-Sept. 13, 2024

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46m 2s

Kamat, Deepak M started transcription

Kamat, Deepak M 0:27

Good morning and welcome to pediatrician round 7:30 in the morning and it's time to start our grand rounds.

The CME code is in the chat box and will keep repeating it every 10-15 minutes.

Quick request for all of you. Please complete the variations at the end of the grand rounds, which daily Asse after the grand rounds.

It is very helpful to me to send feedback to the speaker, so please do feel the evaluations which daily ascends after the grand rounds.

Introduced this morning. Scram on speaker doctor Srina Patel, who is a clinical assistant professor of Pediatrics and medical director of Children's Hospital of Los Angeles intestinal and rehabilitation program in the division of Gastroenterology, Hepatology and Nutrition at Children's Hospital of Los Angeles at ESC Keck School.

patherndon 1:18

Given.

Kamat, Deepak M 1:19

Of medicine.

Doctor Patel received her MD from the University of Miami, Leonard Miller School of Medicine and did her PhD.

patherndon 1:24

Can't sleep?

Kamat, Deepak M 1:28

Residency Fellowship in gastroenterology, as well as fellowship in Transplant

hepatology at the Baylor College of Medicine in Texas Children's Hospital. She received advanced nutrition training at the Children's Hospital of Los Angeles.
Her clinical and research interest includes intestinal failure, associated liver disease, and she's going to discuss this topic with us this morning.
Doctor Patel, thank you very much.
I know this is very early for you. 5:30 in the morning in LA. And thank you for accepting our invitation.
We are looking forward to your presentation. Thank you.

PS **Patel, Shreena** 2:05
Thank you so much.
So I'm I'm very excited to talk to you guys about intestinal failure, associated liver disease or eiffelld. I I think it nicely melds both of my intestinal failure and hepatology interests.
So I will go ahead and start by saying I have no disclosures to make.
Before we can really talk about intestinal failure, associated liver disease, or I failed, I'll briefly review what intestinal failure is so intestinal failure is defined as having a small bowel and or colon with an inadequate ability to absorb nutrients for proper growth and development.
So intestinal failure is the umbrella term, and we generally consider there to be two types of intestinal failure.
There's surgical intestinal failure, which we common.
Refer to a short bowel syndrome or short gut syndrome and this occurs when there's bowel resection that leaves less than 50% of what we would normally see in place.
There's also functional intestinal failure, which is the improper nutrient absorption occurring despite having an adequate and normal length of bowel.
So I've listed the some of the most common reasons for either of these things in this table to the right.
But it's important to note that necrotizing enterocalytic litis are neutraliser.
NEC is still actually the most common reason for intestinal failure.
So looking at what is intestinal failure, associated liver disease, or eiffeled, the term has really replaced parenthal nutrition associated cholo stasis and perennial nutrition, associated liver disease, and we'll sort of talk about why that is.
There isn't really a formal, standardized diagnostic criteria that defines Eiffel Tow, but we estimate that it occurs in about 20 to 30% of infants and children with intestinal

failure who require prolonged PN and then, as is suggested by the group at Colorado Children's and generally well.
Accepted nationally.
The presence of Cholestasis and elevated liver enzymes to 1 1/2 times the upper limit of normal.
Generally indicates the presence of Eiffel Tow as we talk about.
Or, as we'll talk about, there are now a few studies that show patients with Eiffel tend to actually have persistent and sometimes even progressive fibrosis even after their TPN is discontinued.
It was described by these two groups that I felt clinical course tends to be different in the pediatric and adult patient populations.
So in children, we tend to see that there is an inflammatory and cholestatic picture that can be rapidly progressive.
But in adults, we see an inflammatory picture that is much more indolent. And as I alluded to before, PN is no longer or. Tpn is no longer considered to be the only factor that contributes to eifld.
Rather, we know that Ifeld is a separate entity.
And it occurs in patients with intestinal failure.
So it's important to remember that preterm infants without intestinal failure or without intestinal disease will likely have complete resolution of their Cholestasis that occurs while they're on PN. Once the PN has been discontinued.
The obvious caveat there is that you've completely ruled out other etiologies of Cholestasis.
So as a pediatric pathology of eiffelld has been described even further to consist of two separate phases. Phase one is where you have active inflammation or active Cholestasis and this is really when you see the elevated serum direct or conjugated bilirubin, that's greater than one to two and.
Or is greater than 20% of the total bilirubin and you can see this.
Even on patients who have been on TPN for only 14 days.
Typically, phase one will resolve just like in the preterm. Non intestinal failure patients, once patients have been weaned off of TPN.
But as I mentioned earlier, the outcome of Eiffel Tow can be persistent or even progressive fibrosis in the liver even when TPN is discontinued.
And that's what's really happening in this phase two of the disease.
So I'm showing you data from this finished group in 2013 that looked at 38 intestinal

failure patients, sixteen of whom were on PN and 22 who were off PN who had undergone a liver biopsy and they found.
That 94% of on PN patients and 77% of off PN patients had an abnormal liver Histology on these biopsies. So as you would expect and given our understanding of these two phases of Eiffel, when you look at the specific abnormalities that they saw in.
The IT as depicted in these graphs you can see that on the left.
There was a reduction and or resolution of portal inflammation.
And Cholestasis.
In the off PN group, but a persistence of fibrosis and steatosis in the group that's off in these right graphs.
So that's despite being off of PN for an average of eight years in the off PN group. At the time that these liver biopsies were done.
So this is another, much smaller study that was done by the group in Nebraska in 2013.
They took six.
They took liver biopsies from six kids who were getting a fish oil based lipid emulsion, which we'll talk about and they did a blind evaluation and scoring of these sequential liver biopsies and they found that hyperbilirubinemia and synthetic function was preserved or reversed in all cases but that.
They saw fibrosis persisting in two patients.
Fibrosis that was progressive in three and and regressed in only one of the patients.
So knowing that there can be persistent or even progressive hepatic fibrosis and I felt patients, it's then important to think take it one step further and think about what the clinical implication is. And in the case of intestinal failure patients we're talking about transplantation specifically when you have.
Eiffel D.
The type of transplantation patients will receive is a combined liver and intestinal transplant, and historically, that's led to more transplants than recurrent sepsis.
Or the loss of central vascular access has led to isolated small belt transplants and in 22,000 and one, the American Society of Transplantation put out a position paper regarding the indication for pediatric intestinal transplants and based on transplant trends, they estimated that Eiffel becomes irreversible pro.
And leads to transplant in about 13.
Sorry, three to 19% of intestinal failure, children.

So in 2014, the group at Georgetown looked at UNOS wait list data from 1993 and 2012, and specifically at the number of new registrants for isolated small bowel transplant and combined liver small bowel transplant.
And that's what I'm showing you in these 4/4 graphs.
They divided it out into four different age groups.
The hashed line represents those that were combined liver, intestinal transplant, new registrants, and the solid representing.
Intestinals transplant alone.
And you can see that four patients that are less than 18 in these first three graphs combine liver small bowel transplant has historically been more common than isolated small bowel transplant. As I just stated.
But they did find that in 2012 there was an overall decrease in the number of patients listed for combined liver small bowel transplant, a trend that was driven mostly by the kids that were less than one year of age.
And a trend that had a significant shift at about 2006.
And we'll talk about, you know.
Why? What contributes to the disease and how we management?
How we manage it and sort of the 2006 time point will become a little bit more obvious. So it is reassuring that while still some patients still have this progressive fibrosis arm management in general of intestinal failure has positively progressed.
So with that said, we can now look at what I felt now that we know what I felt is an its potential.
We can shift gears and look at etiology.
So as I've already mentioned, the term Eiffel Tow has replaced P nailed and P NAC because the disease is not just related to the TPN, but it's likely multifactorial in nature.
And proposed contributors include infection like small intestinal bacterial overgrowth or SIBO central line infections and recurrent sepsis.
Excuse me. Lack of enteral nutrition. In addition to the actual perennial nutrition prescription surgical factors like.
Leaving the bowel in discontinuity that disrupts enterohatic circulation and can lead to a loss of intestinal mucosal length and patient factors like prematurity.
So we'll talk about all of these a little bit more in detail.
So starting with small intestinal bacterial overgrowth, or sibo, the proposed mechanism by which you get liver injury is such that with small bowel dilation, SIBO

develops.
That leads to bacterial translocation of bacteria from the gut into the bloodstream.
That bacteria then go on to activate a pro inflammatory environment in the liver.
That in turn leads to Cholestasis.
For this group from Finland, looked at 50 short bowel syndrome kids, all of whom had been on TPN for at least three consecutive months.
And that had an upper GI between 2002 and 2016.
And specifically, they analyzed liver biochemistry and Histology and relationship to the degree of small bowel dilation.
They found that the greater small bowel diameter group had a higher GGT and that this was statistically significant.
They also found that if they measure.
Within six months of a blood stream infection caused by an intestinal bug that this measured bilirubin was higher. And then in terms of liver Histology, there was also a higher grade of Cholestasis, a higher grade of portal inflammation and fibrosis in those biopsies that were taken within six.
Months of a bloodstream infection caused by intestinal bacteria, so again supporting the thought that SIBO and bacterial translocation as a result can lead to liver.
Pathology.
In addition to SIBO, Clapses also seem to contribute.
So klapsse here I'm referring to central line, associated bloodstream infections such that the greater the number of clabse's and the earlier the onset of clapsies, the more severe the liver disease.
OK. So switching gears to nutritional factors and sort of starting with the hottest topic in the bunch.
Intravenous lipid emulsions.
It's important to understand that the reason we give intravenous lipid emulsions is twofold.
It provides a calorically dense macronutrient, but also provides essential fatty acids that we know are really important for nutritional.
Growth and proper neural developmental growth, especially in our neonatal population.
There are really two aspects of the IV lipid emulsion that have been proposed to be harmful.
The first is the Omega 6 polyunsaturated fatty acid content.

Linoleic acid. While it is an essential fat, which is important to remember, is also a precursor to arachidonic acid production of which can lead to a pro inflammatory milieu.
So we know that plant based or soybean oil based lipid emulsions.
Tend to have a high Omega 6 content, whereas fish oil based lipid emulsions or what we traditionally refer to as omegaven are abundant in omega-3 polyunsaturated fatty acids, which are in opposite anti-inflammatory in nature.
So the second harmful component is phytosterols and phytosterols are found in plants.
They're minimally absorbed from the human diet.
Umm. And we know that all IV lipid emulsions have phytosterols, but that the highest amount of phytosterols are found in soybean oil based lipid emulsions and specifically it's the phytosterol called stigmasterol that is an FXR antagonist or a farnesoid X receptor antagonist, which leads to a down Reg.
Of bile acid and bilirubin transporters, and thus Cholestasis in the long term.
So while soybean based oil lipid emulsions.
Have the highest amount of phytosterols fish oil based lipid emulsions have the least amount of phytosterols present?
The Boston Group put out a nice chart in their 2021 paper that depicts the major lipid products. And as you can see, they've divided the motions into pure soybean oil based composite emulsions and pure fish oil based or omegaven.
I'll note that while we've been using smooth well before since well before 20/22, it was actually just approved for pediatric use in March of 2022.
And there's a lot of info in this.
Table but I will highlight the two things that we just talked about, the Omega 6 content and phytosterol content. As I previously stated, the soybean based oil lipid emulsions of which we typically use intra lipid.
Has the highest Omega 6 to omega-3 ratio and the highest phytosterol content.
So now to think about other impactful nutritional factors other than the type of lipid.
We know that dextrose given at high glucose infusion rates can lead to hyperglycemia. And when that occurs, hyperinsulinemia resulting in hepatic steatosis which can be harmful in the long run.
There's also been some emphasis placed on the amount of vitamin E in TPN and the different emulsions have varying amounts of vitamin E.
But there isn't at present.

Sufficient data to really strongly suggest that we should be supplementing this in rtpn, and there's also important to know that there are components of the PN that require photo protection and without it can lead to light oxidation and free radical formation.
The other large nutritional component and eiffeld is the lack of enteral feeding.
We know that not feeding the gut can lead to a poorly stimulated bowel in terms of motility can lead to small intestinal bacterial overgrowth. As we talked about, Racebo can also lead to decreased entropy, circulation, and biliary flow, as well as a decreased release of intestinal trophic fact.
That are needed for the long term small bowel adaptation that occurs in these patients.
From a surgical standpoint, bowel that's left in discontinuity similar to is the case in lack of enteral feeding, can also disrupt enteropathic circulation, and that really can lead to a loss of the negative feedback mechanism that controls bile acid synthesis.
Even more small bowel that's left in discontinuity can result in a reduced overall absorptive capacity, and is the case where small and in the case where small bowel is not connected to the colon.
Fluid and electrolyte management may be more difficult because absorption of these things is actually the primary job of the colon.
So now that we know what contributes the disease process, we can talk about how we can intervene.
The one way is to treat CBO when it presents.
Typically, presenting symptoms include bloating, gassiness, looser stools and in extreme cases, de lactic acidosis.
We typically use alternating antibiotics to treat the SIBO, but I will point out that it's literature really hasn't supported.
The use of prophylactic antibiotics or empirically initiating antibiotic therapy just because a patient has a SIBO risk factor in regards to clabse, really the focus is on prevention.
And caregiver education is probably one of the most important factors of prevention because we rely on caregivers to take care of the central line at home and to administer the TPN at home.
But the other thing we can do is use ethanol locks.
And Paul Wales, Group at Sick Kids did a systematic review to compare the efficacy and safety of ethanol locks with heparin locks in the rate of clapses and the rate of

catheter replacements.
And they found that they saw with ethanol locks the klav C rate was actually decreased by 81% and the catheter replacement rate decreased by 72%, which is significant.
So now to look at how we manage the use of intravenous lipid emulsions.
Because we know that soybean oil based lipid emulsions have a high Omega 6 and high phytosterol content, it makes sense that lipid minimization has been proposed as a preventative strategy.
So when I say lipid minimization, I'm talking about a dose of 1G per kilo per day or less.
As typically the standard dose of four lipid emulsion is 2 to 3 grams per kilo per day.
In retrospective, studies have shown a reduced incidence of Cholestasis in lipid restricted groups.
But really, when this has been looked at from a prospective.
Standpoint randomized control studies aren't consistent with this finding, and that's actually been shown more than once. But in contrast, when a patient has already developed eiffeled or have already shown signs of Cholestasis, there are guidelines that suggest that dose reduction is certainly acceptable.
And this is the position statement from the 2018 S begun S Pen group in the guideline for pediatric parental nutrition that states as part of a measure to reverse eifeld and pediatric patients, a discontinuation of soybean oil based lipid emulsion, a reduction of other lipid emulsion do.
And or the use of a composite emulsion with fish oil should be considered along with treatment and management of other risk factors.
But I will caution that.
It's important to note that when you reduce the dose of lipid or restrict the dose of lipid, you can see poor growth and or you can see essential fatty acid deficiency with lipid restriction.
So it's important to remember that we talked about too much Omega six can be being pro inflammatory, but linoleic acid, which is an Omega 6 polyunsaturated fatty acid, is still an essential fat.
An EFA deficiency can have a negative effect on neurodevelopment.
Again, especially in our neonate population.
So because fish oil based lipid or omegaven has the lower Omega 6 and phytosterol content, it makes sense to use a fish oil based lipid emulsion as monotherapy.

But it's important to remember that when we're using omegaven, it's for really for the treatment of eiffeld that has already developed. So there really aren't any prevention studies looking at omegaven.
For preventing eifeled and the FDA package insert, which is what I'm showing you here is.
Pretty explicit in this in that sense that you should only be using it in patients who have developed Cholestasis.
So in contrast, there are many studies that have shown that use of a fish oil based lipid emulsion is efficacious in the case that ifelt has already developed and the start of the string of studies that really showed this efficacy was with the Boston Group paper in P.
Pediatrics that they published in 2008 where they showed that there there was reversal of cholecystasis after the switch to a fish oil based lipid emulsion.
Specifically, they compared the safety and efficacy outcomes of fish oil based lipid emulsion in 18 infants with Cholestasis that developed while they were getting soybean oil based lipid emulsion with those from a historical cohort of 21 infants who also developed Cholestasis while getting only soybean based oil.
Lipid emulsion. So their primary endpoint was looking at the time to reversal of Cholestasis.
Which they defined as having three consecutive direct bilirubins that were less than or equal to 2 and on the left.
Here I'm showing the curves.
That show you the proportion of subjects who reversed Cholestasis at different time points for both the fish oil and historical cohorts.
So this dashed line is the fish oil group and the solid line, the soybean historical cohort, the median time to reversal of Cholestasis in the fish Oil group was about nine weeks versus 44 weeks.
The soybean historical cohort.
And that's about five times faster.
So pretty significant.
It was important to note that in this study, they did not see in the patients who got omegaven any essential fatty acid deficiency. They did not see worsened Coagulopathy or increased infection or growth delay.
And then in these two graphs to the right.
Labeled A and B, you're seeing the direct bilirubin trajectories over time.

Asia is the fish oil group and B is the soybean oil cohort.
The box plots represent the distribution of direct Billy levels that were taken during two week intervals that are indicated here and the number of observations during each of those two intervals is shown in parentheses below and you can see that in the fish oil group the direct B.
Improved with time.
Or even normalized, but in the soybean historical cohort, the direct Billy Ruben actually went up and worsened with time.
There are several studies that subsequently confirmed the efficacy and short term safety of fish oil monotherapy in the use of treatment for EIFLD that includes again the Boston Group demonstrating a 50% Cholo stasis resolution.
The group at Texas children showing in 2013 prospectively and almost 83% Cholestasis resolution, and the group at UCLA showing a 75% closeasis resolution with use of fish oil lipid emulsion.
Boston also went on to conduct a longer term use study of OMEGAVEN, and they did not find that there was any sort of increased mortality, increased rate of transplantation or recurrence of liver Cholestasis in the omegaven group.
So all of these studies really helped lead to the 2018 FDA approval of OMEGAVEN use in pediatric patients.
The use of omegaven has certainly made an impact on the way we manage TPN and intestinal failure associated patients. But when you think about the two phases of ifald and specifically phase two of eiffeled and the persistence of fibrosis, beyond the correction of your conjugated bilirubin, the Len.
Of therapy question arises, meaning what's the ideal length of fish oil monotherapy use even after you've seen an improvement in your labs?
It's also important to note that there is a subset of patients where Omegaven doesn't necessarily work to reverse Cholestasis, and this table is listing risk factors for that subset of patients. And really, these make sense. These kids tend to be sicker.
So the last aspect of lipid management that we'll look at is the use of a composite lipid emulsion. And for us in the US that means the use of small flippid.
So Smallf is sort of the in between of soybean based oil, intralipid and fish oil based omegaven, it's made-up of soybean oil, medium chain triglycerides, olive oil and fish oil.
It has Omega 6 and phytosterols in it.
More than what Omegaven has in it, but less than what soybean based intralipid has

in it.
Though again, there aren't really any true prevention studies, but the FDA approval.
And I'm showing you the package insert for smooth is not necessarily explicit against the use of prevention for efld in this case.
But there are several treatment studies that show smooth can be efficacious.
I'm showing you first the data from Olivier Goulet's group that took 28 children with short bowel syndrome, all of whom had required PM for at least four weeks and had an elevated total Billy at baseline.
And those patients were randomized to receive either SMOF or INTRALIPID for 2129 days.
Excuse me.
At which point a repeat Billy Reuben was drawn.
And as you can see, the repeat bilirubin was lower in the smooth group at the later timepoint as compared to the soybean oil and motion group.
So the group at sick Kids subsequently completed an efficacy study, though they were looking to see if they could specifically prevent the progression of what they called early eifed. They define this to be a patients having a conjugated Billy between 1:00 and 3:00.
And enrolled patients either were randomized to either get smoth or intralipid for 12 weeks.
At the end of the trial, the smooth patients had a lower conjugated bilirubin than at start, but the interleukin group had a higher Billy at the study completion so.
Those Moff or the use of Moff has also been quite impactful in the way we manage TPN. I would say there's still questions that have not been answered, such as is smooth, better than low dose intralipid, or is lower dose smof also really needed to see the he.
Effect, and if that's the case.
What's the risk of EFA deficiency, or at which point does the EFA deficiency become a concern?
So pretty significant advancements, but still with questions that remain.
And then to finish up, we'll talk about some potential medication options.
I'm showing you a German paper that specifically looked at ersodioxy colic acid or ursodiol, and they conducted a randomized placebo-controlled, double blinded study to test the efficacy and prevention of Cholestasis.
They had 29 infants enrolled who were all on PM.

They were given either ursodiol or a placebo on day starting on day of life 3.
And as you can see.
The black line indicates the Ursodiol group and the White line indicates the placebo group.
There was an overall downtrend in GGT that was clinically significant.
They also saw a similar downtrend in AST and Alt.
But I will say though that their stated purpose was to look at whether whether or not Cholestasis could be prevented.
You'll see actually in this chart that both groups at baseline had an elevated GGT.
So I would say this really supported previous studies that have shown improvement in bile flow when Cholestasis has already developed.
And I will caution that before you start Ursa dial in a patient, you really have to make sure that your patient's anatomy is suitable. Meaning we know that distal small bowel or terminal ileum is really responsible for the absorption of bile acids. If your patient does not.
Have that giving Ursodiol which is a soluble bile acid.
Can actually lead to bile acid diarrhea.
So you wanna make sure that you're you're choosing to do this in the right patient population?
And then other proposed but not really recommended interventions include phenobarbital and CCK to promote bile flow. But studies haven't really shown efficacy, and there's actually concern for neurotoxicity with long term phenobarbital use.
So we don't really use this in practice. And as we've discussed before, while the treatment of SIBO is is recommended, the use of antibiotic therapy to prevent or its empiric initiation really isn't.
Supported by the literature.
And then finally, I'll briefly mention a potential newer pharmacological medication being studied.
So here I'll show you the results from a Chinese study that looked at the effect of trope effectsor, which is an FXR agonist in neonatal in a neonatal piglet model for the treatment of eiffeled.
Just to recall, some of the Physiology. You'll remember that FXR stimulation leads to the release of FGF 19 by enterocytes.
That then leads to suppression of SIP 7A1 expression that subsequently suppresses

bile acid synthesis.
So overall, an FXR agonist will suppress bile acid synthesis.
They had four study groups here, piglets that were entirely fed only as indicated by en.
And truly fed piglets that were also given tropifexor, which I'm indicating by en plus TROPN piglets only, and PN plus trope effects were and APN plus trope effects or group.
So in first showing you that in either the EN or the P or PN only groups.
When you're looking at stimulation of FXR, you have much more stimulation of FXR.
As evidenced by FGF nineteen production in the EN group as compared to the PN group only.
And then I'm showing you, when you look at liver markers, Alt, AST, bilirubin that the PN group PN only group has elevated liver panel in comparison to the en groups.
And that when you add trofexor 2:00 PM there is an improvement in all liver markers.
So in summary, intestinal failure associated liver disease or I felt is really a multifactorial disease, an infection, lack of enteral feeding, bowel discontinuity, and prematurity all play a role in addition to PN. And in addition to the four lipid emulsion that we give. And as such we have.
Certain tools that we can use to prevent the development of eifid.
Such as the treatment of SIBO clabsee prevention and feeding.
I've cautiously put ursodiol on the prevention side.
Umm, though I'm sure that studies really uh pan out in this respect. Umm, and I'm throwing in some.
Indirect management strategies to help us from a feeding perspective, though we didn't talk about these in detail.
Umm. By stating that in some patients we do use bowel lengthening procedures and newer medications like TODUGLATIDE or Gattex to help us achieve enteral feeding.
And in the case where Eiffel has developed, we can certainly use alternate lipid emulsions ursodiol as I mentioned.
But I would say that the management side of things is certainly the space that requires continued work if we're really to completely prevent the need for intestinal transplant in pediatric patients with intestinal failure.
So that's all I have.
I am happy to open it up to questions if there are any.

Kamat, Deepak M 37:04

Into Doctor Patel for that fascinating presentation on intentional failure, associated liver disease.

There is question by Doctor Branco.

Any thoughts about kinolipid? It got FDA approved for use in children in May 2024?

There are studies reporting high EPA levels in premature infants with the use of SMO and concerns of vitamin E toxicity in smallest preterm babies.

Patel, Shreena 37:33

Yeah, that's a great question.

So I'm trying to go back to the table.

So the clinical is in this table.

And there is actually a smoth shortage, maybe a year or two ago, and one of the options that we had was use of clinolipid.

I will say that and we did.

Our center did actually use it because the alternative was using replacing smoth with intra lipid.

But I will say that the CLINOLIPID has a higher Omega 6 to omega-3 ratio. Actually the highest of the group and even more so than in the intralipid group.

I think in the patients we used it we there were not a very large number but an end of maybe two who actually developed worsened Cholestasis.

I think that was likely multifactorial.

Again, probably not directly related to Clinolipid.

But I have been somewhat hesitant because they this group does have actually a higher Omega 6 to omega-3 ratio, which can be more pro inflammatory.

So I think there are certainly patients, you know, where there is some enthal feeding where the intestine is in continuity where the their family is reliable and they're not getting recurrent cloud seas where clinolipid could be used.

But in the patients with higher risk or more risk factors for eifld, I would be a little bit more cautious.

Kamat, Deepak M 39:11

Thank you, Doctor Patel.

Any other questions, comments.

The pasaden please.
Go, go ahead and ask question.

patherndon 39:28
Yeah. Can you hear me?

Patel, Shreena 39:30
Yes.

Kamat, Deepak M 39:30
This weekend.

patherndon 39:31
I'm curious.
About how this would inform adult disease.
Can any of this has any of this data been transferred to adult disease?
We just had this pandemic.
There are a lot of people that have come out of that pandemic with inflammatory bowel disease of one sort or another, plus or minus an infectious agent, and I'm wondering.
If if preparations with olive oil or coconut oil or other things.
Are have any value in this?

Patel, Shreena 40:06
Yeah, so also a great question.
The use of smooth was approved in adults before it was approved in in pediatric use, so the adults had actually been using it for a much longer period of time.
I'd have to look at the data of use of omegaven in adult the adult patient population.
I'm not as familiar, but that is a great question.
You know, all of all of the studies, though, for smooth were.
1st in adults, so I'm I'm sure that the adult patient population is using it.

patherndon 40:44
OK.

Kamat, Deepak M 40:47

The Barton, go ahead and ask your question.

Barton, Theresa 40:50

Hi I was.

I was pleased and simultaneously pleased and frustrated to hear that in one of your before, before getting it really into the omegaven that for SIBO.

P

patherndon 41:03

Play.

Barton, Theresa 41:04

That the literature doesn't really support the use of like ongoing alternating antibiotics.

And and so, because of course that remains a very common widespread practice.

And so I guess my question, which is sort of.

Piggybacking on to our last week's grand rounds is does the this omegaven or this other these other strategies?

Are there studies that show its impact on the microbiome of the remaining gut?

PS

Patel, Shreena 41:35

So I'll clarify 1.

It is our practice, once a patient has developed symptoms of SIBO, we do use alternating antibiotics indefinitely.

When I'm saying empirically starting I'm I'm talking about just for example, maybe a gastrosis kid with poor bowel motility that has dilated proximal bowel.

They don't really have symptoms of SIBO.

We are advancing enteral feeds in that kid.

We probably wouldn't start alternating antibiotics.

But generally, at some point in their life, they do develop some symptom of SIBO, and once they do, we do put them on alternating antibiotics.

P

patherndon 42:20

Play.

Patel, Shreena 42:21
I think the science of CBO or the management of CBO is not.
Amazing. We I think we use certain antibiotics and the Aga has proposed which antibiotics to start with.
But at some point for the kids who have been on it long term, eventually it stops working.
And you have to kind of change the regimen or you have to revisit pre?
Ones that they've done before, so I will make that clarification, I'm not.
Sure. To be honest with you about the impact of lipid emulsions on the microbiome, I think that's a great question. I would imagine that the more we rely on four nutrition that in and of itself and the lack of enteral feeding is what impacts the microbiome.
But talking about a direct effect I that I am not sure about, that's a great question.


Kamat, Deepak M 43:22
Any other questions, comments for Doctor Patel?

patherndon 43:31
No.


Kamat, Deepak M 43:33
To hunt down, do you have question? I'm not sure.

patherndon 43:37
No, I I I thought.
I thought.
I put my hand down.


Kamat, Deepak M 43:43
Go ahead if you have questions, go ahead and ask it.

patherndon 43:47
I don't have AI.
Don't have another question.

Kamat, Deepak M 43:49
No, you don't. OK. OK.

patherndon 43:50
One second.

Kamat, Deepak M 43:51
Thank you.
Thank you.
Any other questions, comments for Doctor Patel?

patherndon 44:01
I can make a comment.
There is a folk cure for a lot of these problems with coconut.
And apparently on some people it works.

Patel, Shreena 44:13
Mentally.

patherndon 44:15
No, they just bought.
Sources, cookies, macaroons, things like that made out of coconut and it actually, for some some magical, even the most skeptics were actually their problems were improved dramatically.

Patel, Shreena 44:33
Do you mean call their liver labs are better or?

patherndon 44:38
Means that the the the the fact of their inflammatory bowel disease that you know the diarrhea and all of that, yes.

Patel, Shreena 44:47
OK.

Interesting, we sometimes you will use entreal like sunflower oil or safflower oil in patients where we get worried about essential fatty acid deficiency if they're being actually fed.
To supplement the Omega 6.
But we have not used it necessarily for.
The malabsorption that occurs with shore bowel syndrome.

patherndon 45:17
OK.

Kamat, Deepak M 45:19
I don't see any other questions or comments for Doctor Patel, so I'm gonna conclude this morning's grand round.
Thank you, Doctor Patel.
I know this is very early in the morning for you, so thank you for presenting a fascinating grand rounds on intestinal failure, associated liver disease.

Patel, Shreena 45:28
OK.
Thank you so much for.
Calling.

Kamat, Deepak M 45:35
Thank you all for attending this morning's round.
Please fill out the evaluations, which delay will be sending after after we conclude and we'll see you next week.
At same time. Thank you. Bye bye.
Thank you Doctor Patel again.

Patel, Shreena 45:48
Thank you.

Patel, Shreena 45:49
Thank you.

◉ **Kamat, Deepak M** stopped transcription