

History of Targeted Migraine Treatments - Pediatric Grand Rounds-12-6-24-Meeting Recording

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56m 14s

● **Calderon, Delia** started transcription



Ranch, Daniel 0:07

Alright, it's 7:30. So we're going to get started.

Good morning, everybody, and thank you for attending pediatric grand rounds at UT Health, San Antonio. Our speaker today is Doctor Azra Akbar.

So it was my pleasure to introduce doctor introduce Doctor Akbar.

She is an associate professor in the Department of Pediatrics.

She's our pediatric neurologist, epileptologist and headache management specialist.

Doctor Akbar received her medical degree from Dow Medical College in Karachi, Pakistan.

And then after moving to the United States, she did her residency at Cardinal Glen and Children's Medical Center in St.

Louis, Missouri after that, she did her child Neurology fellowship and neurophysiology fellowship at UT Southwestern, followed by her Headache Fellowship and Allison Headache Management and Baylor Dallas.

It's a lot of fellowships. And then Doctor Akbar's faculty at UIC in Peoria before coming to UT Health San Antonio in February 2024.

So please.

As a reminder, mute your devices as you're logging in the CME Gran Rounds code we placed in the.

Cat box periodically, so please don't bug Delia and doctor Doctor Akbar.

The floor is yours.



Akbar, Asra 1:18

Thank you so much.

Thank you for the introduction, Dr. Ajay. Appreciate it.

OK. Can you I can see my slides.

Should I just start?



Ranch, Daniel 1:27

Yes.



Akbar, Asra 1:28

OK, sounds good.

All right. Thank you again.

So the objectives for this talk are to talk about common headache disorders in the pediatric population and the most common would be migraine.

Migraine without aura could also be migraine with aura.

I'd also talk about other headache disorders that we commonly see, including chronic daily headache, chronic migraines and most importantly, medication overuse headaches because that is preventable.

And quite difficult to treat if it comes on and is not treated appropriately at the at the right time.

Other factors contributing to migraine and recent advances in management, including neuromodulation and injections, other than just Botox, the CGRP.

There is quite a lot to talk about and it is rather exciting because I think oral medications can be quite tedious and there is a risk of medication, non compliance in our pediatric population with that.

So the pediatric migraine.

So migraine prevalence in children can be about three to 1015% and out of all the cases of headache encounters that we see in our clinic, about 80% or more of them, 50 to 80% of them are actually migraine related.

There are other headaches we see, like cluster tension, sunk headache, sooner headache, medication overuse, chronic daily headaches, new daily persistent headache, which is not as common.

Certainly some of them are actually more.

Older population anyway.

So migraine in our pediatric neurology clinic would be the most commonly diagnosed headache disorder and the ratio as we know is before puberty is equal.

But after puberty, there is a female preponderance and the theory with that we'll talk about that more is also because CGRP apparently is.

Higher it is elevated at the time of migraine, but it's also elevated in the female gender.

Most patients will continue from their childhood to their adult to continue to have migraines and.

25% will transition into other headache disorders, but 50% will continue to have migraines.

I'm just disclosure, I am a migraine and I've I think the first migraine that I've had was when I was 5 and I've had migraines with or I had migraine with migraine and I've tried several of these medications on myself and we can talk about that. It's an.

NL One, but still as a patient, there'll be some a patient talking as well.

OK, so migraine in history, so 1550 BC.

Apparently that's the first time it was described by.

Pepperis and bloodletting was a treatment that was used so bloodletting was an Asian treatment.

OK, Hippocrates mentioned it as also described it. Then in 460 BC as a bright light in the eye and in 17th century Thomas Willis founded this vascular theory, which honestly we are still to date this vascular theory about the decrease in blood flow or cortical spreading DEP.

Is the other term we use is still used?

And then Mobius, I think this is the doctor from Mobius Syndrome 1898 who described it as parenchyma is the master and circulation is a servant.

Took me a little bit to understand, but I think what they mean is parenchyma is stagnant and circulation is what makes the migrant dependent on it.

So when the circulation changes, the parenchyma suffers the pain.

These are very interesting theories from centuries ago, but we are still kind of working around those theories.

The first medication for management of migraine was around 1918. The 1920 in which you know is the DHE and then in the 1980s, CGRP research had started.

Cgrp was discovered as the calcitonin gene related peptide which is involved in the neurogenic inflammation.

These are the theories of migraines that started coming out.

The International Headache Society and that has been quoted in this in this presentation many times.

And we'll talk about that.

Their classification started coming out in the nineteen 1980s, and CGRP research continued.

Interestingly, it started in 1980s, but anti CGRP has been approved like literally four

years ago.

So that's interesting, but it is also exciting.

So again, we'll talk about what exactly is a migraine.

How does it differ?

How does it differ so migraine is a complex.

Debilitating recurrent multi system disorder.

That is multifactorial also, and has a genetic component. I think one important thing to take home from this presentation would be that migraine can respond to a single pill like you can use Eli Topamax taperupadine, which are the most commonly used ones. But if it is a Chr.

Migraine and it is multifactorial, which it could very well be. That is patients significant number of patients will have a history of depression, anxiety, some other mood disorder, you know.

Psychosocial issues.

Family history, obesity, low self esteem, all of that.

They usually will not respond to a single bill.

It has to be a multidisciplinary disciplinary approach, so a multi center like a headache center with where there's involvement of.

And perhaps psychologist, psychiatrist, you know, and headache neurologist. All of that is usually very helpful.

Also, weight loss, lifestyle modification and using natural substances should also be advised. Other than hydration and adequate sleep, we'll talk about that more, but I just wanted to say this that it is multifactorial and migraine is chronic and debilitating and migraine can be pretty stressful to the patient.

Life. OK, so migraine without aura. And this is the classification that I just mentioned.

According to the International Headache Society, this is the most recent classification and it's published in the Headache Journal of CEPHALGIA 2018.

So migraine without aura. So a migraine differs from your other headaches like tension headaches or whatever will describe the five attacks.

Usually, unilateral usually patients have said behind the eye pulsating, moderate to severe intensity, aggravated by routine physical activity.

And during the headache, the patient will have one of the two, like either nausea or vomiting or photophobia phonophobia. Usually there's a family history and it's not better explained by other diagnostic criteria. Then the migraine with aura is obviously a similar presentation, except it comes with an A.

Which is gradual, starts with a source activity of 5 minutes or more and then will go on from 5 to 60 minutes and within 60 minutes you'll see the headache.

And it could be a positive or a negative or an aura.

Visual sensory speech motor brain stem.

I didn't go into all of the types of other migraine with aura, but hemiplegic migraine only because I have seen it more here at the center in the past nine months that I've been here. And also it could be quite stressful because people could think it's a T.

Or is it not?

Or OK.

So this is again filling the for criteria that we talked about earlier and in aura, which would consist of both.

Fully reversible motor symptoms and fully reversible either visual sensory or speech motor language.

This is like I said in 1996 is when the first gene was identified and there are three genes that are identified with it and it's the cacna ATP 1A SCN 1A.

And it's interesting because cacna ATP 1A, as you know, are associated with other neurological disorders.

Scn 1A with other epilepsy syndrome disorders as well, but not necessarily like, doesn't mean it has to. OK chronic migraine is, I think what we see mostly in our clinic. Patients are usually very appropriately managed by the paediatricians here and then they come to us usually we.

Don't see the episodic ones, of course. We see the chronic ones, which is.

Patients having more than 15 days of headaches for the past three months.

My name.

With aura migraine without not better explained by and of course, the patient will tell you that they have other symptoms and they respond to the medication which is used typically for migraine.

This I made two slides on it because I think this is if there's one thing we need to understand from this lecture, well 2-3 things. But one of the things that you need to understand would be medication overuse headaches because it's very it becomes very difficult to.

Treat but it is preventable.

So prevention is better than cure.

So preventing it and how do we prevent it?

Preventing medication overuse headache is more than 15 days of headaches a

month over the past three months because the patient is overusing the medications for the past three months.

Some are worse than the others.

So if they're using 15 days of, you know the over at the counter and set it all, that's 15 days, OK, but ten days a month of these Ergon strip 10s. That's why whenever we prescribe the triptans on the script, we write not more than ten a month.

So we don't prescribe that much anyways, right?

Or other, you know, opioids.

We we do not like to use that risk of medication over users much, much higher and of course some of these other medications and this is preventable.

So how do we prevent it?

Entered by initiating lifestyle modifications sooner and initiating a daily preventative medication if needed. If they meet criteria. If they have chronic migraines, sooner rather than just giving PRN medications and they get into the habit of it.

So the neurons in the brain called the microglia will start to appreciate pain more, and it's called central sensitization.

So it becomes harder and harder and harder.

And when the patients come to us and we tell them, don't take your Tylenol, that you're taking every day, that kind of really upsets. It can be quite upsetting because it helps them, at least for the first first few hours.

So it's intimidating for them to just stop the medication.

This slide explains the pathophysiology of migraine as well as the other two slides.

The pathophysiology of migraine is thought to be initiated by the hypothalamus, which is the early phase hypothalamus apparently.

Because the premonitory phase and then activation of the trigeminal vascular system, which is the trigeminal nerve which is the big, you know the nerve that take usates into the brainstem and then projects to the calibers which is involved in the propagation of migraine and the term they use.

Is cortical spreading depression, CST stages of migraine.

Not necessarily, but a lot of people will have that Pro Dome and aura.

A lot of people will actually have yawning also as.

Before their migraine starts.

So this is kind of what we had talked about in our second slide.

That mentioned, even in the 17th and the 18th century when they said the parent kaima is the master and the worker is the.

I think this is what they meant by the vasculature, because the blood flow is decreasing. Is the thought the term the uses cortical spreading depression, which is depolarization and decrease of blood flow followed by a period of hyperpolarization and it is 2 to 6mm per minute?

Another.

OK.

This is another slide that explains this better. That is the brain stem pathway that modulates the sensory input. As you can see over here, these are the trigeminal, these are the meningeal vessels and these meningeal vessels pass through the trigeminal, the trigeminal.

Go through the trigeminal nerve and as they pass through the trigeminal ganglion, these synapse over here in the mid ring or the pawns.

And the deck you sit over here 2nd order neuron.

And then third order neuron goes to the thalamus, but over here they also decussate and they project into the superior Salivatore nucleus, which is involved with lacrimation etcetera.

So people who have a stronger arc between the trigeminal ganglion and superior Salivatore nucleus will be the ones that have the trigeminal autonomic selves, which includes trigeminal neuralgia. If you've seen it or sunked, or sooner headach.

Even cluster headaches in which they will have tearing from the eye and injection from the eye, and other signs like that.

As pediatric neurologist or a headache?

Pediatric neurologist who also manage headaches.

In our clinic template, usually we also include this in our template actually and we like to talk to patients about this, families about this a lot of times, a smaller child, a younger child will maybe have migraines, but they can't speak.

So colic, infantile, infantile colic. Certainly abdominal migraines, and they can evolve into cephalic migraines later.

Cyclic vomiting etc.

Benign proxies for Vertigo, actually.

Bed wetting, nose bleed. Teeth grinding is also included, which is not mentioned here.

I talked to my other my senior colleagues, especially doctor Gross and all, and they've been managing patients with headaches for quite a long time pretty well.

And they also mentioned a cyclic vomiting and abdominal migraines, etc.

So working hand in hand with other.

Subspecialists for example BI would be very helpful.

At this center, we do a pretty good job. All of us at that.

PEDs Midas, this is.

Reported in a lot of studies, whenever we are doing objective data classification, comparing Topamax or amitriptyline or Botox and you want to see did it work? Did it not. Headache diary is great but this is a very objective method and this is quick. We give them to the.

We give it to the families and clinic and they fill it out.

The higher the score obviously is not good.

Small better score is, you know, it just asks you how many days in the past three months you've had an improvement or worse.

Times. Did you miss the time or school or other activities?

Pronomal symptoms are actually quite common in our children and children with headaches like we've talked about before.

That's why we keep talking about lifestyle modification and not just a single medication approach. A single L level or single topamax approach will probably not be effective if it's pretty intense chronic migraines.

So looking at other risk factors and why they are there and if they can be addressed and how they can be addressed.

That's why I'm multidisciplinary.

Multifactorial approach would be good, so screening them for anxiety and depression is very helpful.

We work well here, hand in hand with the pediatricians.

Also, the Phq Depression assessment and there are of course several other tools that the Pcps here use and pretty manage very well managed.

Otherwise, this is a good slide because a lot of times patients will come and they will ask why?

My Mri's normal.

But why am I having this?

So it's it's great that the MRI is normal and usually in a migraine, the MRI would be normal.

So because it's a diagnosis of exclusion exclusion, remember. So the things that are associated with it could be genetic as we know quite a few genes have been identified. The first one was in 1996 for the Amygdic migraines, which was a long

time ago, 1990.

Six environment stress.

You know, elevation, height, diet, exercise. Keep talking about that diet and exercise very important and menstration pregnancy after menopause they can get better because.

Estrogen can cause more migraines.

Estrogen is a broken bilson and also can cause migraines. So estrogen.

So menstrual migraines are the term fancy term is called catamenial migraines, and there are some triptans which are long acting, so they work very well for that. And we'll talk about that for catimina, 'cause if they don't have migraines any time else, they only have it during the.

Period. Then we just give that to them and again, this explains the theory that I just went over hypothalamic activation, cortical spreading depression and release of these cgrps cgrps are important because it's new. It's recently come out. It's exciting. So we'll talk about that.

So the first medication that ever came out was in 1920.

Sumatriptan was approved in 1991.

Sumatriptan's very well tolerated, but I'm sorry, it's very effective.

But not as well tolerated as others like maxalt. So that's usually my preference.

And then Botox was approved in 2018.

There was a study called the Preempt trial that included about 1300 adults and it was over a period of 52 weeks and that after that.

And that's called the preempt trial. And I'll show you slides about the 31 site injections.

And also Botox actually was first used and approved for wrinkles and it was first approved in April 2005. In those time period, people noted that their migraines have significantly improved after that. This pre health trial was done and Botox was given and then in 20.

18 which is actually much later, so the advances have been between 2018. I mean, after 2010 there wasn't much after Botox.

So this is when the Cgrps started coming out and the CGRP inhib.

Have been approved 2019 this lampseed item which is I'll talk about it briefly.

This is also new, but it's approved for 18 years and older.

Overall, well tolerated, but can cause a lot of sedation. And then of course, we'll talk about more anti cgrps which are called G pans.

So the other cgrps in 2018 that were approved.

They are injections in 2019 is oral, so we'll talk about that in a minute.

We'll start by talking about treatment that includes like triptans, which most of us have treated headaches are quite familiar with.

There are seven of these. The first one that I'll be talking about, the one that's most commonly used as Sumatriptan.

It's fine, it's good. But usually side effects are a little bit more, especially nausea, vomiting.

And about 2015, I believe they came out with a patch, but the patch caused significant side effects, including burning.

So they withdrew that.

So now the one that's used Treximet is very commonly used.

It comes with an end set in it.

The one I use commonly most commonly is this Reza triptan maxalt.

It also comes in oral, dissolvable, it is approved.

For children six years and older, the other ones are for 12 years and older, so resatripten really works good in my experience and six years and older.

So the other ones Solitryptan is fine.

It comes in a spray, but then again then we talked about Sumatriptan.

There are other devices that are approved and we will talk about that, which is actually quite exciting because medication needs medication compliance and if the patient is not medically compliant then that's a little problem.

So if we have.

Cgrp injections?

They're once a month.

Botox is once in three months, so it's much, much easier to do. And these neuromodulation devices that we'll talk about, you know, you don't have to eat it.

So hopefully this is and I've had it done on myself.

I'll talk about that a little bit.

So again, just talks about how it, how these strip tans are supplied.

These are usually easily covered by insurance. Most even patients who come to us and clinic have already been tried, have already been prescribed at least.

By their PCP.

So that's that's good.

How do they act?

5HT_{1D} and 1B receptor 1D is involved with the release of neurotransmitters again substance P, which is the pain, and the CGRP, again tryptans on.

Act also on the VISOCONSTRICTOR to the 1B and because vasoconstriction, because again theory is cortical.

Sparing depression, decreased amount of blood flow, so constriction will increase the blood.

But of course it can be associated if the patient is older, which is usually not a problem.

We encounter.

But if they have risk factors and there's a risk of TIA, but that's in the much, much older population, several risk factors.

The newest medication that has come out acts on the five HT_{1F}, which is the Lamsee Titan, and we'll talk about that again.

They're all approved for 18 years and older.

This is a good slide because I think our pediatricians who send patients to us use strip tans quite frequently just to know that the half life of naratriptan 10 and robotyp 10 is very good.

Foratriptan is something that we use for catamenial migraines.

So if there's catamenial migraines, it's only.

I you I started one day before the period and I say take it for the next 5 days and you just give them six or so.

And it works out fairly well, but other than that, Sumatriptan that you already know about, but Reza Triptan is my go to.

This is a picture I took from my phone and you can see the sunset and this is actually the Illinois River and this is from my condo and this is UI comp, Peoria. This is kind of behind this, this is Caterpillar.

Yeah. So that's a view from our from the winter there in Peoria.

OK so.

Of the other than the neuro modulation devices and the PRN medications, this is the daily preventative medication that's approved for children 12 years and older.

And we I usually started one to two milligrams per kilo and then you can go up of course with an older child, you can start at 25, usually American headache society or A and even 75 milligrams total.

But that's for an adult. Usually side effects, as you know, are word finding difficulty.

Weight loss, tingling, numbness, teretogenic side effects are also.

Can be reported.

Right here.

Loss actually.

Some patients have also told me about that.

Then the propane and all I, we don't use it so much in the periodic population for risk of, of course, bradycardia, hypertension, elevable, amitriptyline is quite often used and of course, all the dry mouth, dry eyes, all those symptoms can occur.

Depakote works well also for mood and I start we we can start at 15 or so. But of course you have to look for any kind of mitochondrial disorder if they have any of that.

Big gain, hair loss, et cetera. And of course Teratogenicity which is important.

Most of my colleagues.

At our center, we use a lot of topamax and our epilepsy colleagues like Doctor Linda Leary, who are more experienced in epilepsy.

They use that and this is great because if the patient also has a history of absence, epilepsy, depakote is a very good choice.

If she's not a female, though, if it's a boy. So Depakote is like, my go to.

For that case, so ciproheptidine I've used it a lot, especially for abdominal migraines and L level.

There are more studies on that.

Lyrica is really not something I use too much because of sedation, too much sedation and weight gain don't really use that Botox. We'll talk about that more in a minute.

This class one evidence in the pediatric population though it is off label and the 75 units to.

155 the pre empt trial that we talked about used 155 international units, but they also use.

Protocol, which is excellent.

Follow the brain protocol basically meant that if the patient feels that on this side on this side, they have more pain, you can use more Botox, which is leftover cause a lot will be leftover oxybile occipital nerve blocks. I've done that for occipital neurons.

Yeah, it's very uncomfortable.

Patients didn't.

I didn't really have the best of experience, but so now actually we have neuro modulation devices that will address occipital nerve as well as the other branches of the trigeminal nerve.

So this is great if we can use.

Devices. So this is Botox.

Yes, definitely.

I would highly recommend that again we talk about lifestyle modification, weight loss, regular exercise, hydration, sleep hygiene, identifying triggers, eating regular healthy meals, avoiding foods which are processed, and a processed aged meat eat cheeses.

Aged cheeses are not recommended then.

Highly encourage all of our physicians and respectationers who are managed headaches at our center, encourage the use of.

Lifestyle modification and the vitamin supplementation, coenzyme Q10 and riboflavin.

Both of them support the mitochondria. The concept I think behind this is that migrainers also have some form of undisclosed mitochondrial dysfunctioning and they respond well to coincide with and there are enough studies, even on riboflavin, that it is comparable to a preventative other preventative medication 200.

To one a very easily tolerated side effects are discolors. Your urine is also.

In food like in almonds, you can in the, but supplementation is fine.

Coenzyme Q10.

Same thing, 100 milligrams magnesium. Magnesium actually is an NMDA receptor antagonist.

So what it does is that it stabilizes the neuronal membranes, so it decreases the excitability, the hyperexcitability.

So magnesium is great. Side effect is diarrhea. As we know melatonin there are.

There has been some studies on it. Most of them will show that 3 milligram is right.

The appropriate toes in Pediatrics, but in adults.

So this works very well for something called.

Hypnic headaches, which is not seen in the pediatric population.

So that's why there's no slide on it.

But Hypnic headache is actually a side effect of medication overuse headaches, after which the patient is so primed that they wake up in the middle of the night with a headache. And the MRI's normal.

And these are older people.

They respond very well to melatonin, melatonin. It will not hurt, but in adults, of course, you will use a higher dose.

We can use 6 or 9 milligrams, but in children this is what we would use.

Mike, I do recommend using something called Mic Relief.

It's over the counter. You can get all of this individually, or you could get mic relief or microwent and they're over the counter.

I get mine from Amazon.

It's like I think \$39.00 or \$29.00 for more than a month supply and it's one pill and it has these. It has coenzyme Q10, riboflavin, magnesium already in it.

So instead of taking so you know just something to think about.

This is a slide of Allison Wonderland syndrome depiction, which was actually.

Seen a long time ago, but it was also reported after Second World War when patients were subjected to trauma, traumatic brain injuries.

OK.

So again, we talk about Botox. I just told you about the preempt trial a little bit earlier.

The pre EMPT trial was in 2010, where 1300 individuals adults were studied and they showed a good response. So every three months is kind of these injections.

There are 31 site injections, 155 international units.

How does Botox like?

How does this add?

It acts on the sign up to be even VM or the snap protein and it cleaves it and this protein is associated with the release of SA Ticone and SC Ticoi will not be released and when it is not released, STI choline is associated with pain transmission MUS.

Contraction and also actually CGRP release.

So it keeps coming to the CGRP.

So once we get rid of that, this doesn't happen.

So this process doesn't happen.

So this is the thought behind it.

These are the injection site reaction.

The the sites that we do.

I have had Botox done for headaches and this area is very easy to do.

I've done it on myself because this is a fleshy beefy muscle, so this really does not hurt when I do Botox or when we we all should be doing Botox.

We I would advise to start at in this area in the back because it's very easy to tolerate for the patients.

So now the patient starts off.

Better followed by this the temporalis muscle, and then the most painful is actually in this region, because this is a tight muscle, right?

So the headache.

The forehead. It does hurt. So you can use other techniques like using ice, et cetera.

But honestly very well tolerated. Usually when patients hear 31 injections, they're like, Oh my God, 31 injections.

But really the they're the like an acupuncture needle. Very easy to tolerate. And like I said, it's really worth it. 'cause, if it works for you, you know it's every three months.

And if you can get rid of the daily medicine that that would be great. This is.

The protocol.

This is what they used, how they described it.

And the preempt protocol. However, the good thing is that.

They used follow the brain protocol, which means the leftover Botox, but whichever is leftover 'cause 155 units, 45 is leftover 'cause it's 290 days. You can give it, you know, spread it out to whatever the patient prefers.

For management of their headaches.

So they are about between 2020 to one to now. There are 18 studies on children. We published this at my old center.

We studied this on about 34 patients and they had an excellent response.

Oh, I'm sorry.

To Botox and most of them.

But they were my older kids.

They were 15 and older, and by the time this was completed they were already 18, but it and so and there are, of course, other studies too.

So now there are about 18 studies on Botox for adolescents.

I I it's it's hard to get insurance approval, but as long as we document that the patient has been tried on two classes of adequately tried doses of medications, including a beta blocker or a tricyclic antidepressant and.

They have been tried for the past three months.

They continue to suffer.

They have more than 15 days of headache a month for the past three months.

Hopefully we can work on it.

It takes about two months to get that approved.

This is my niece.

I have 3 nieces, but this is one of my nieces.

We talk about anti CGRP.

So again, we've even in the other slides we've talked about, CJ, because it's one of the more newer, more exciting other than neuromodulation.

So CGRP is the protein that is released from the nerve terminals.

For propagation of pain, it is a vasodilator, and it's also pro inflammatory. The drugs and it's been studied since 1980s as I spoke to you about it in the earlier slides, the medications have come out in 2018 and 2019.

The research has been ongoing, so there are some which are called G pans.

And which is the Uber LV and the Rima G pant that we are commonly more easy to use. So those will directly block the signal.

They'll directly block the receptor and their oral.

They're a small molecular oral, so you can give that the other ones which are the other anti cgrps, for example aimovig, ajovy et cetera.

Mg gality.

They are injections and they are just once a month injection, usually with some you give a loading dose with not others.

Yeah. So I just talked about it, right.

Hov and these are the the ones at the bottom.

These are the injections and the ones at the top are the oral ones.

And the ejections are just once a month. So the EMO week was approved in 2018, Ajovy was approved. Also IN2018MG galatine 2018.

And then there's a newer 1, which I actually have not used in 2020, but I have used aimovig and M galatimol and the G pads, which are the oral ones.

Which are the direct receptor blockers?

They are and you have the the three kinds, right?

The Rima G pent. And the Uber.

The Uber G pent. And the G pent is a nasal spray.

I haven't used it.

There are.

Studies no published data on children yet? OK, but there is a consensus statement that we can use it if everything else is failing and I have used it and not only I have doctor Brian Fox has used it quite frequently. I think Doctor Gross has to.

And I've had a very good response to this.

I just talked to you about it.

This is the oral right.

The G Bed 2019.

So this more recent and their tech 2020.

Alright. The other ones I haven't really used so much the most recent is this nasal spray. The Zabzi Pratt clinical trials are underway, but there are expert consensus guidelines, OK. And you can we can use it just like Botox even though it's for 18 and above we have.

Used it and we've had some good studies to prove our results.

Then we talk about something even more newer, something less invasive, and something you don't have to take every day.

That definitely not by mouth.

So no systemic side effects.

So remote electrical, neuromodulation, there are several types we'll talk to you about it, but this is the most commonly used one I know at our headache center, Dr. Gross and Doctor Fox, they have used it.

I have used it.

We've had a good response.

This is pretty simple.

You don't even like literally. You just sign it off with formal prescription.

Doesn't even need to be done, and it's \$49.00 for this.

In June of this year, at the American Health Society Conference, I had it done on myself.

As a migrator, I feel like it was pretty effective.

You can use it as needed, but also as a preventative for about, you know, 3045 minutes or so. It's to your phone and it's an app.

The It's for \$49.00, but you can only use it I think 12 times and then you need to buy another one.

It's like \$89.00, which you get a discount if you have three of them.

This is rather better tolerated and easier to do, so this is using.

Neuro modulation, electrical, neuromodulation.

This is also FD approved, but this is.

This is a magnetic stimulator. Transcriptional magnetic stimulator, and it's a proof of prevention as well as migraine with aura, which is good because migraine with aura doesn't really, you know, there's a lot of concern about using triptan with that even though the statement for migraine with Aura is.

That triptan can be used unless the patient has other risk factors predisposing them

to ATIA, like oral contraceptive pills or other risk factors like cardiac problems.

But anyways, so this is something.

And I've had it done on myself.

It has.

It was pretty good.

Transcutaneous vaginal stimulator. As you already know, vagus nerve is the largest nerve goes from the brain all the way down to the gut.

Vaginal nerve stimulator has been used for epilepsy for quite some time.

This is just kind of stimulating the vagal nerve. You use a group and then you do this.

In my reading and listening to several lectures, apparently the VA uses this a lot for episodic cluster headaches.

And this is great because in the past what was used for cluster headaches, right?

So many people coming in oxygen, so that was hard.

So apparently this is working very well for our older male population.

Or even our middle age population for cluster headaches. For in children I have not used it yet.

I these are not as easy to obtain and we really need to do a lot of lobbying to work with insurance companies, but it is approved for age 12 and 17.

Cephali these are.

Non invasive external trigeminal nerve stimulator I have as a patient and I speak not as a doctor.

I speak as a patient.

I've had coughly used on myself, but that was a long time ago and it was quite uncomfortable.

Because you could feel the buzzing sensation when it was trying to hyper stimulate the the drop layer.

Add this superb turnover.

So it was quite irritating and that is what in the following years most patients have said Socephaly is very easy.

It is \$400.

You don't even need a script for it. You just go online.

You get it and you use it as needed.

And but it really does need a lot of getting used to.

Yeah. So most patients, I I feel were not very compliant, even though it was so easy to do.

Then there's a new one, rellivion.

Relieveion apparently is much less uncomfortable.

And this can, but it's harder to obtain.

And is a little bit more expensive.

I think it goes in the thousands of 1000 something and The thing is that not only does it stimulate the front, it also stimulates the occipital area so the occipital nerve most patients. What I've heard will say it is much easier to tolerate.

Again, these are the neuromodulation devices that we talked about and this also tells you the price.

C cephales 430.

And.

The review is \$49.00 for the first device and then onwards so.

So this is not bad.

These are just some things to think out of the of the box when the patient is medically refractory.

They've tried amitriptyline topamax. Then you gave zonosomide.

They're still having, and then they're also taking Tylenol every day, and now they have medication over use headaches, and it's just not working out. Instead of giving another pill.

Think about Botox.

Thinks about.

Think about cgrps and of course these other devices as well.

So the International Headache Societies statement is that.

The new modulation devices modulate the brain activities.

Spinal cord paraphil nerves by means of different methods, including electrical current, magnetic field and other device.

We did it modalities.

Oops. Oh, I missed a slide.

This is a very important slide.

Thanks to Doctor Fox.

So Champ trial, which was in 2017, this is a very important thing because it this was a big study that was being done on children comparing the two most prescribed medications for headache amitriptyline and topamax and comparing them to placebo. And it was found.

This this had to be aborted because they found that these medicines were no better

effective than placebo.

And patients actually had a high placebo response rate, which again comes to the point about how effective will a single medication be for a patient who has migraines.

But he doesn't just have migraines, it is multifactorial.

He also has depression, anxiety, school stress, family history of migraines.

He has a poor diet.

He doesn't sleep well and he does not eat well and he does not exercise at all and he's depressed, so usually just this one pill will not work very well. So placebo.

Working with other modalities, including massage, acupuncture, etcetera.

Diet, exercise. So those were the outcomes.

Exercise is important.

I mean, the old theory is yes, it releases beta endorphins, which are your happy hormones, natural hormones, but also what kind of exercise?

Weight training, weightlifting, increasing lean muscle body mass because there's a direct association with improvement of headaches with increase in lean muscle body mass as well as with weight loss.

Lean muscle body mass.

Yeah. So a lot of patients will say that when we exercise our headaches get worse, which is possible certainly.

Because migraines get worse with routine physical activity, so don't really exercise during a migraine, but it's also protective mechanism.

And the theory is that because of the production of lactate also this can happen.

But regular exercise during periods of relatively low frequency of migraines or a dull headache not, not an acute status migraines, is highly encouraged and regular exercise, as well as increasing lean body muscle mass is highly recommended.

Interestingly, Aans guidelines is the first line treatment is ibuprofen, which is my mentioned that because that is how most of RB decisions here treat the patients and when they come to clinic. To us this is kind of what they've been on.

Just wanted to include this slide.

This is approved for 18 years and older.

There was an earlier slide on triptans that mentioned how triptans act.

So the Titans also act like the triptans, except they don't cause visa frustrations.

They act on five HT1F not 1B, because 1B is where it causes vasal constriction.

So they do not, which is great, but there's a lot of sedation associated with it.

It's usually in AI, seen it being used in the older population, but so they can become very sedated and driving. It's something I'm not so far used.

For a pediatric patient yet.

Because I have so many other interesting toys right now to play with.

So it's like, you know, that personal choices now.

So triptans, you already know about Titans?

We talked about this just a slide going over.

You know, G pans are the oral cgrps and the monoclonal antibodies which you know about are your injections and of course, Botox. I am a big proponent of that side effects.

Of course, anybody can have side effects. I've had side effects. Botox.

Can cause like muscle twitching, but it can cause injection site reaction. But the most common side effect of CGRP is injections. Side effect with Botox really.

Process. Sometimes you know asymmetric maybe, but other than that, Botox is well tolerated.

Otherwise, propane and all, I don't use too much and topamax are the most commonly used, followed by maybe Depakote.

A lot of people will ask, like when do we image do we image?

So do we get brain imaging?

So the AM guidelines are, you know, the chances that you actually pick up on something that surgically needs correction is less than 2% or so.

And there's a choosing wisely campaign. That said, that neuroimaging is only needed. Of course, if there are focal neurological findings.

Not anybody and everybody needs head imaging and not. And most people with headaches don't really need an EEG unless you're suspecting something like Penetopolis syndrome or one of those other secret disorders like gastroint or, you know, in which there's prolonged retching and dysautonomia. But other than that not.

Everybody needs it.

So this is from the ANS guidelines.

I would like to thank.

Our wonderful team.

For their help with patient management, their excellent care and actually helping with this.

Doctor Fox, Doctor Sheldon Gross.

Doctor Linda Leary. Doctor Natasha Varghese, doctor Daniel Lapid, Dr. Nicole Levin. Doctor Daniel Lanigan misses Sandra and our admin support clinic nurses, and most importantly, our patients, without whom there would be no presentations and really nothing to talk about.

So thank you very much.

I think I'm on time or maybe even faster.

So any questions?



Ranch, Daniel 43:19

Doctor Akbar, thank you for that wonderful presentation from the audience.

If you have questions, you're free to place them in the chat, or you can raise your hand unmute yourself.

Guess while we're waiting for question, I have one that is half related.

Maybe so I get asked a lot 'cause I see a lot of kids with hypertension, right?

And so the question always is, does hypertension cause headaches? And, you know, always get mixed answers and opinions when you ask around.



Akbar, Asra 43:50

Play.

Yes.



Ranch, Daniel 43:57

But Kirsten oh, your thoughts on that question.



Akbar, Asra 44:01

So I would say yes to that, because PFOS, for example PFOS, are directly related. So shunting they say if you have a PFO, the patient will have an increased risk of migraine, especially with aura.

But PFO management surgically doesn't really do that.

So yes, basically to answer your question, if there's decrease in blood flow, certainly people with hypertension, if you've talked to them they and I'm sure you have, they will have a lot more migraines. If it's disturbing your vasculature like in the slides.

It is decreasing the OR causing any form of decreased blood flow, cortical spreading depression.

I I think it certainly can.

Hence Propinolo will work and the theory behind how these medications how does propenolo long work is because they decrease the excitability of the the neurons. So. So I I I think it's it's certainly certainly a good question. But yes people with hypertension we don't see a lot of.

Children with hypertension, except if they're coming from the nephrology clinic, but yes.

They are at risk for having more migraines and they're easier to treat candisarten. I think I share a patient with you already, right?

Yes, yes, the candidate certain patient.

Yeah, can disarton so yeah.

So I would say yes to that.



Ranch, Daniel 45:17

Thank you.

We've got a question from Doctor Matalik.

You can go ahead and unmute yourself.



Mandlik, Nandini 45:25

Hi, thank you for the wonderful presentation.

I'm an outpatient pediatrician in the John Peats group, so I have kind of more lifestyle related questions.



Akbar, Asra 45:29

Yes.



Mandlik, Nandini 45:37

I've seen kids where I wonder about the effect of screen time on their like as a headache trigger, but also.

Making kids who wouldn't otherwise be prone to headaches or migraines be at risk because of the amount of screen time that they get, even if it's not sleep related, right? And then.

The other related thing I've wondered about is head pain.

Like sometimes, patients will come in usually like school age or teenage, where they are complaining of headaches. But on palpation they actually have tenderness.

And maybe it's because I'm ad O, but I think about the muscular strain because of

positioning. Maybe because they're holding their screens in front of them and they're, you know, hunched over.

So I I wondered if there's any data or or evaluation on those things.

Thank you.



Akbar, Asra 46:28

I asked.

They are absolutely.

I'll start with your second question, which is very interesting because, yes.

This what you're talking about? This tenderness that is called the term they use for it is called allodynia.

Allodynea and Elodynea is a term, and there's there are actually case reports on it, so if you.

Being a migrant of myself, I I also have.

I can never tie my hair 'cause when I tie them.

I can't it, it just pulls on the scalp and there will be a migraine, a lot of patients with migraines say so we are very sensitive.

Migrainers are sensitive because they are sensitive to noise, light, sound and there's a term they use for it called central sensitization, in which they are just hyper vigilant, that they are OK so there. So to answer that the palpitation when you do that that, that allodynia so if.

I don't know how frequent their headaches are.

How and do they need to be?

On a daily preventative medication, I'm guessing yes. So, but that that was central sensitization or first question, yes, screen time I think AP guidelines are like 2 hours a day maximum. And if you actually listen to the people.

Who are apple? And if you listen to them, I've listened to their talk. They say we don't let our children near these devices.

So these devices are addictive.

They activate your limbic system.

It's this reward. Quick reward, quick reward.

You know I want it.

I get it right now and this is how I'm going to be now for the rest of my life because I need it right now.

There's no this.

So it's it's messing.
It's messing with the children. I I'm extremely against it.
So screen time shouldn't be more than an hour.
For two hours a day.
I mean, it's easy for me to say because I don't have any kids, but still.
But reward this reward system even when we see these reels on Facebook.
I think it's this quick reward system.
It's it's very bad for us.



Ranch, Daniel 48:15

There are a few questions in the chat.
The first one is for the general pediatrician.
Do you have a preferred sequence or order of medications you would like to see them use, including over the counter medications?
Vitamins lifestyle recommendations before they're referred to your clinic.



Akbar, Asra 48:33

A good question.
Usually I give them two months because this data has shown that it takes two months for daily preventative medications to work.
So when I start with vitamin supplementation, like I said, the one that I like to use is mic relief.
And then there's another one microvent I don't use so much all over the counter.
I usually like to give them at least two months off that, but I like to do everything together. 'cause I will say OK.
Let's give you a vitamin supplement for two months. Then you start losing weight the next two months.
So you know, doing everything together.
And I speak more so also personally, as a patient myself, because I think acupuncture and these vitamin supplementations lifestyle modification at least should be tried for two months or so.
You can do it all together.
It wouldn't hurt.
You know, and then if it's still not working or if they have any focal neurological sign or if they are in medication overuse, then that's that.

We just don't want to go there.

We just do not want to go there.

Uh review the order of medications you would like to see.

Vitamin lifestyle modification I think I would do this all like I wouldn't wait weeks between them.

I would probably do them together. You know what I mean?

The next question is how often is doctor Gross?

How often is?



Ranch, Daniel 49:49

Yes.



Akbar, Asra 49:51

Seen in migraine patients, doctor gross, we see a lot of patients with migraines and we see a lot of patients with epilepsy also and you know syncope and I I won't be able to tell you exactly the percentage, but I can tell you that a lot of M.

Are prone to syncope. Vertigo now could that be a part of your aura?

Could it be a brain stem?

Aura, difficult to say. Of course. We have to look at the literature very closely and their slides that I have on it.

Are you meeting the criteria for migraine with aura?

Yes or no.

Your slides on it if they're not. If it's just simply it's it's I. I have not seen it very frequently.

However, there's a term called dysautonomia and or pots.

Right. So in those cases, the patients are prone to having headaches and they can have Sykes quite frequently.

We again the work up for syncope is like you already know would include like the cardiac workup and you know the tilt test, et cetera.

But there's no medication I would give for SIM could be other than, again, lifestyle modification, adequate hydration, etcetera.

Why are we still perspective Max and Amy tripling if they're not better than placebo?

That was one study that showed that, but there are other studies, so the chance study was supposed to be, you know, I think I was.

I was still a fellow.

I was a headache fellow at that time.

No, I had just graduated in 2017.

Yeah, two years out.

So I remember it was like the big study that was coming out.

Everybody was excited about it, but it's it's sad.

There it could be several other factors too, but there are several other studies that have shown amitriptyline to be effective dopamax quite effective.

We had a poster recently, actually Doctor Fox and I and my other colleagues at University of Illinois and that showed.

No significant change.

We compared Amy tripling to dopamax, but again, having been treating migraine since 20, I think 15 in children. I think Topamax is overall very well tolerated.

The other thing is it can cause a lot of weight loss too and weight loss and headache is directly it will be great.

So if it can cause weight loss in a healthy you know way, that's also effective.

But amitriptyline overall can also help with mood and depression and sleep.

So if it's also helping with sleep.

Weight loss, but there are several other studies that have looked at these medications.

So unfortunately, yes, the Champ study was quite a disappointment, but it really.

It we brought it up, I talked to Doctor Fox about it too, because it's important because it highlights the importance of placebo and also multidisciplinary multifactorial approach.

Medication over youth headaches.

Chronic daily headaches. Ndph.

Ndph is very hard to manage and success rate is not going to be high unless and until we have a multi factorial approach.

Which includes everything we talked about, not just one pill, not just dopamax.

That's where we fail.



Ranch, Daniel 52:43

We have a question hand raised from Doctor Herndon.

You wanna unmute yourself, Sir?



patherndon 52:48

Yeah. So.

In the.

In the process of discovering a new cancer drugs, we have a bunch of plant biologists who've been involved.

With that kind of discovery work, and it turns out.

Well, I I have a sister-in-law who has horrible migraines and they seem to be aggravated or related to exposure to molespores when the cows get really have their allergic related.

And somebody in the community knew about a plant.

That's called something like horse Clover or something like that.

And they made a tea out of it and gave it to her in her and her headaches, which might last for days.

Just disappeared.

All of a sudden, and as the most dramatic thing I've ever seen in a long time. So I went to the plant biologist.

And and it turns out that we had samples of that, and some people were looking at it, but not for that as a as a chemotherapy agent.

And it had been.

In in folklore, times had been used for a menstrual cramps, so that led to the discussion.

Well, it's a prostaglandulant.

And I mean this is kind of a convoluted story, but.

There are people, there are plant biology.

In the pharmacy department here in San Antonio.

Who had these catalogs of all kinds of things? And I don't know.

You know what these things are, but it seems like it an area of discovery to me.



Akbar, Asra 54:38

Sounds sounds amazing.

I am personally I'm a big believer in herbal medicine.

I use it on myself. Of course I can tell.

I mean, yeah, but I've used it on myself.

It's it's it's. I can talk about it for a long time using turmeric and other stuff.

I use it.

Can you tell me the name of the plant again?

This is very interesting.

 **patherndon** 54:55

I think it's it's called.

I think it's called horse Clover or something like that.

It's a very unusual plant. It has.

It has a flower and the stock grows through the middle of the flower to the next level, and there's a series of flowers. And of course it gained its name because horses like to eat it.

 **Akbar, Asra** 55:05

Yes.

Very interesting. I think that's kind of the theory behind are Vedic medicine and that's not something we you know, but Ayurvedic medicine it's it's worked very, very, very well.

So I wonder if that's something I'll look it up for.

 **patherndon** 55:33

Human.

 **Ranch, Daniel** 55:38

Are there any additional questions from the audience?

I guess not.

As a reminder, the code for the CME credit is in the chat and Doctor Akbar, thanks very much again for your wonderful presentation discussion and have a great rest of the day.

 **Akbar, Asra** 56:03

Thank you.

So thank you very much.

Thank you so much.

Thank you. Bye.

I'm done, Sandra.

● **Sheila Reifle** stopped transcription