

Cutting Edge therapies for Autism

Dr. Shahanaz

Ahamed.M

Pediatric Neurologist

SATH

A case study

- M a 3rd child born to an upper middle class urban family of non consanguinous parents
- He was alright except for persistent allergic symptoms- allergic rhinitis , Otitis media, ET tube catarrh etc . He was administered 3 or 4 courses of antibiotics
- He faced intense sibling rivalry from his sister who wanted attention so that he was mostly kept in front of Television with poopy ,manjady etc
- At 9 months he began to call Umma clearly.
- His father being a paediatrician gave him MMR instead of the usual measles at 9 m.
- In that month he developed HFMD which got aggravated with amoxyclav.
- Within 2 weeks he developed diarrhoea which was prolonged with slight foul smel which subsided only with folic acid
- After this he gradually regressed to moderate to severe autism .

Course

His father diagnosed him as autism by 1.5 yrs. By that time 2nd dose of MMR was also taken

He had no sensitivity to milk products in particular. He was given lactogen , Anchor etc

Gradually problems came with irritability, Sleepless nights , crying without reason, abdominal colic etc

By Gods grace his mother detected an expert homeo specialising only on autism in mumbai who was consulted & medicines began

With the starting of homeo med Sleep became normal, allergies subsided, irritability decreased

With the starting of probiotics along with homeo & sending to nearby playschool eye contact improved considerably & socialization improved

But the main problem was lack of adequate therapist in trivandrum. Hence had to be shifted to ernakulam where a combined speech+behavioural + Occupational therapy was began.

Now he is improving .GRADUALLY, COMPREHENSION HAS COME . Vocalizing single words. Beginning interactive play. He is being administered Vit D & sunshine as addl treatment.

Effective treatment modalities

- Allopathy
- Homeopathy – Classic & Houston Method
- Ayurvedic-Naturopathic treatment
- Intense Prayer & Charity

- “ WE TREAT ,GOD HEALS ”

Allopathic & Related therapy



- Megavitamin Therapy
- Probiotic therapy
- Mitochondrial boosters
- Ca-Mg therapy
- DMG-Glutathione
- Neutraceuticals-
- Biofilm Protocol
- Vancomycin- IVIG therapy
- Antifungal therapy
- Psychoactive drugs
- VitaminD based therapies

Related Therapies

- Speech therapy
- Behavioural therapy
- Occupational Therapy
- Sensory integration therapy
- Music Therapy
- Berhard Auditory integration training
- Chelation Therapy
- Aquatic therapy

Alternative therapy

- Allergy desensitization
- Pet therapy
- Art therapy
- Lovaas Method-ABA
- Anthroposophical Camphill T
- Drama therapy
- Dance / Movement therapy
- Specific carbohydrate diet
- Helminthic therapy
- Floortime Therapy

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- Relationship development intervention
 - Kaufman speech to language protocol
 - Transcranial magnetic stimulation
 - HANDLE-
 - Homotoxicology
 - Enzyme based therapy
 - Integrated Play groups model
 - Technology based interventions

Principles

- A multipronged approach is definitely needed
- One single therapy is not superior to other. Each has its advantages & disadvantages
- Moreover all children do not respond similarly to the same therapy or drug.
- Allopathic practitioners should let go of their Ego when treating children as there is no known definite cure for autism till now
- There are recently 3 potential cures which are in preclinical & clinical trials.
- No miracle cure but Hard work & persistence yields results
- While allowing alternative or complementary medicine we should also protect our patients from potentially harmful therapies like chelation therapy, unnecessary use of risperidone etc

COMBOs

- Ideal is a combination of
- Allopathy + Homeopathy + Therapies
- Allopathy+ Ayurveda+ Therapies
- Therapies mean either Applied behavioural analysis done for 6 hours a day by therapist + mother
- OR
- Speech therapy+Behavioural +Occupational therapy

Pharmacotherapy

- Megavitamin Therapy

- Vitamin C 500mg once daily for 1 month followed by thrice weekly for 1 year
- Folinic acid trial – calcium folinate(Leukovorin) daily for 1 month- If there is dramatic response continue, otherwise switch to plain folic acid & continue
- Pyridoxine 25-40mg daily for 6 months . Give a break of 1 month & continue another 6 months
- Change over from polished rice to Chamba rice to get adequate thiamine. Bitter
- Methyl cobalamin 500-2000 microgram daily for 1 year
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Probiotics

- The bacterial strains most useful are Lactobacillus & Bifidobacterium species which bring balance to the microbiome of intestine
- They produce an acidic environment unfavourable to the growth of clostridia which produce several neurotoxins
- The worsening of autistic symptoms when given antibiotics is due to the clostridial & candidal overgrowth
- Certain toxins elaborated by candida have structure similar to LSD
- The ideal combination would be a combination of 4 bacteria which is given by Darolac+Prowell daily

GFCF diet

- **Gluten free Casein free diet**
- That is avoidance of all milk & related products & also all wheat & maida related products
- This is because there is Leaky inflamed gut in Autism colonized by pathologic bacteria due to antibiotic use
- These will degrade milk protein casein into toxic peptides which cause neurotoxicity
- Regarding gluten everyone knows the intestinal & neural damage it causes in coeliac disease. Leaky gut leads to high chance of anti gliadin & antineuronal antibody formation

Mitochondrial Boosters

- In many cases of autism it is seen that there is a mitochondrial dysfunction to varying degrees

- This is shown by the elevated Lactate & Ammonia levels

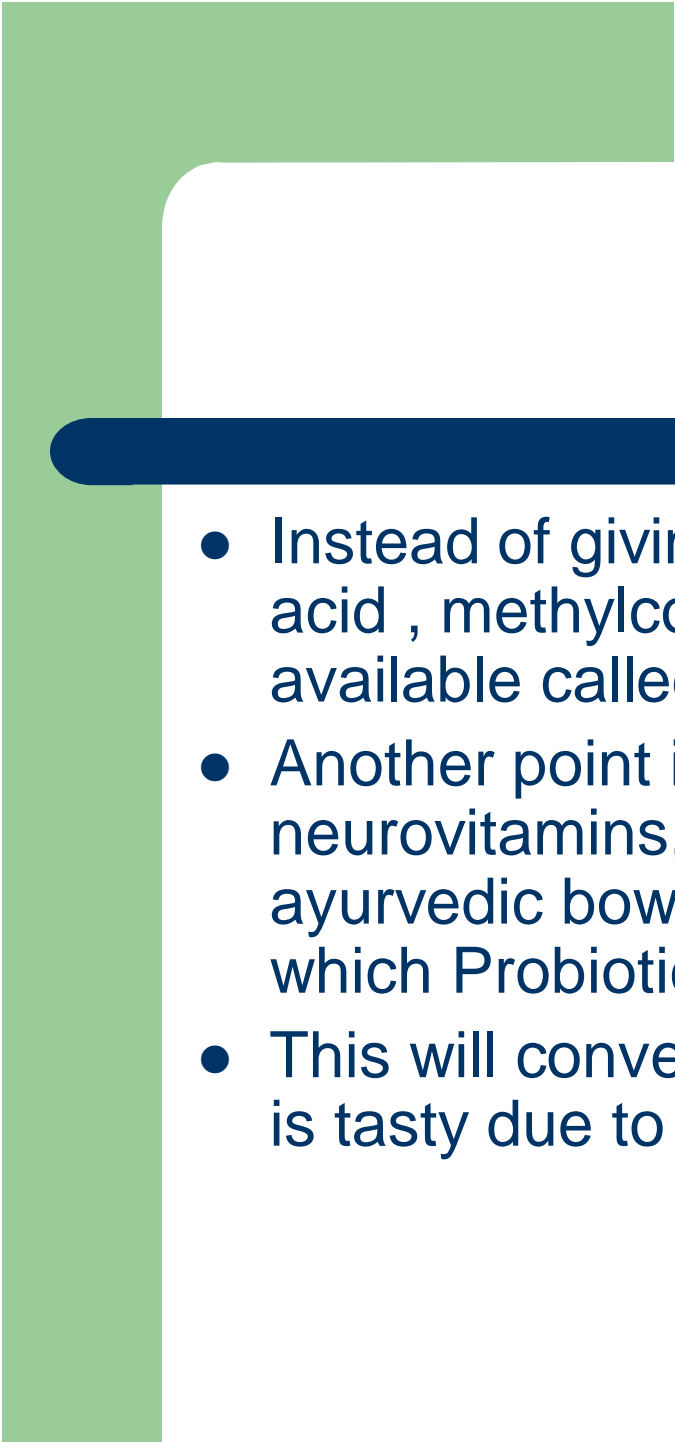

Mitochondrial dysfunction can contribute to intellectual, Behavioural, speech disturbances

Moreover many autistic & epileptic children may harbour IEMs like urea cycle disorders

The cocktail that is useful is a combo of

Thiamine+ Carnitine+ Coenzyme Q10+ Riboflavin which is available individually & in combinations.

Palatability is a problem with certain preparations. Hence alternate day treatment is best eg HiQ plus, Calco Q,etc

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- Instead of giving separately a combination of folic acid , methylcobalamin, & pyridoxal phosphate is available called tetrafol plus ,or folvite MP etc
 - Another point is you can powder 3 neurovitamins, VitaminC & biotin together in ayurvedic bowl & dissolve it in half glass water to which Probiotic mixture can be added.
 - This will convert 5 drugs to a single decoction which is tasty due to orange flavour of vitaminC

Ca –Mg therapy

- High dose magnesium has been useful in certain children with Autism
- This can be given using a calcium magnesium syrup containing higher magnesium concentration or preparation like magvion 600
- Similar Mag-C is a drug used by homeopaths in improving core symptoms of autism.
- Magnesium has roles in brain energy metabolism , formation & regulation of neurotransmitters , antiepileptic effect & also synaptogenesis.

DMG, Super neu thera, Neuroprotek, L-Glutathione

- These are nutraceutical preparations used world over for the relief of core features of autism
- DMG- dimethyl glycine a normal metabolite in high doses has been found useful by many mothers in reversing certain features
- Neuroprotek is a Quercetin containing preparation usseful in neuroprotection & relief
- L glutathione acts in reducing oxidative damage to brain caused by free radicals & brain inflammation in autism
- Glutathione also inactivates heavy metals in brain . So has almost the same effect of chelation
- VitaminD deficiency leads to reduced glutathione in brain by genetic mechanisms
- Many of these are imported from outside via Kirkman labs, ebay or Akhil health solutions bombay.

Biofilm protocol

- This concept is that neurotoxic or pathogenic bacteria in gut form Biofilms in gut which are self reliant apartment complexes of bacteria with channels for circulation of nutrients
- These biofilms are unapproachable to antibiotics & hence these bacteria freely produce neurotoxins which pass to the brain via the leaky gut producing sustained brain inflammation
- Biofilm protocol aims at using Kaolin, Activated charcoal &, purgatives & locally acting antibiotics to destroy these biofilms so that the child recovers from autism.

Vancomycin & IVIG

- Vancomycin when administered orally is not absorbed & selectively decimates the clostridial bacteria thus freeing gut – Brain system from neuro toxins
- Studies have shown that a 4-6 week oral course was capable of producing much improvement in all parameters but many cases regressed back within next 3 months
- The same situation holds good for IVIG with difference that it is given as 400mg/kg every month over 6 months
- It was especially found useful in OCD & tics of PANDAS

Antifungal treatment

- The mechanism is that in autistic children there is a higher incidence of candida infections of skin & gut due to 2 reasons
- Reduced local gut immunity, reduced macrophage function & use of antibiotics
- Hence it is advised that Fluconazole given for 2 weeks to 3 months is able to eliminate candida & produce remarkable improvement
- Because of risk of hepatotoxicity I give a 14 day course of 5mg/kg once daily every 2 months .

Vitamin D & Autism

- A growing body of literature suggests that higher serum 25-hydroxyvitamin D [25(OH)D] concentrations, either in utero or in early life, may reduce the risk of autism.
- **Vitamin D Deficiency & inadequate sunlight exposure in the mothers are risk factors for Autism & speech delay in children**
- The critical periods are after 6 months of pregnancy & the period of rapid brain growth & synaptogenesis ie 1st 2 yrs
- In a recent study, children with autism had lower serum 25(OH)D concentrations than did control subjects (19 vs. 33 ng/ml), despite parents of each group reporting the same amount of sun exposure.
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- The same study found highly significant inverse correlations between 25(OH)D and autism rating scales and between 25(OH)D and levels of an antineuronal antibody.
- **This finding indicates that higher serum 25(OH)D concentrations may reduce the symptoms of established autism.**

Mechanism

- Calcitriol acts as a molecular switch activating many target genes via the vitamin D receptor (VDR)
- Most organs in the body show evidence of end organ responsiveness to calcitriol including multiple brain areas
- Because activated vitamin D, a secosteroid, upregulates DNA-repair genes, vitamin D deficiency during development may inhibit the repair of de novo DNA mutations in fetuses and infants and thus contribute to risk of autism.
- Vitamin D might also reduce the risk or severity of autism through its Anti-inflammatory actions, Antioxidant, Antiautoimmune effects, increasing seizure threshold, increasing T-regulatory cells, protecting the mitochondria, etc
- It is seen that in Autism the normal Immunity ie both cellular , humoral & macrophage mediated immunity is reduced while abnormal immunity ie Atopy ,autoimmune antibodies etc are increased

Vitamin D & Autism

- Quantitative genetic variations (not qualitative mutations) in some facets of VitaminD metabolism such as VDR or the enzyme activating VitD may explain the heritability of autism
- The mechanism is similar to the schnatz study which found a strong negative association between the number of VDR in coronaries & Atherosclerosis
- Suppose a child who inherits a smaller number of VDR in brain, if his mother avoids sunlight & does not take fish & the child also does not get adequate VitD from weaning foods.(200ml cow milk provides only 100 iu of D).

Genetic aspect

- The low VitD level will interact with the low number of VDR to produce or allow brain injury → Autism susceptibility by DNA damage, mitochondrial damage & oxidative damage
- Remember that > 95% of indian population are deficient in VitaminD ie famine in the midst of plenty
- In USA the incidence has risen 10 fold over last 7 yrs after women were directed by AMA to avoid sunlight & outdoor activity to avoid skin cancer.

De novo mutations – cause/effect?

- You may well have a genetic disease that you did not inherit
- One may develop de novo genetic mutation such as those seen in Autism & schizophrenia while you were living
- The MC finding in Autism is multiple small genetic de novo mutations
- **Correlate this** with the fact that there are at least 5 Vitamin D dependant genes which code for **DNA repair proteins whose only job is to fix mutated DNA**
- Thus the widespread point mutations seen in Autism **could be the effect rather than the cause** ie VitD (d) is the FATHER of both Autism susceptibility & these denovo mutations

DNA Repair –Genomic Guard

- Calcitriol protects cells by upregulating DNA repair genes which even repair double stranded breaks
- In a recent RCT in humans a small dose of 800iu VitD reduced the level of 8-OHdG a marker of Oxidative DNA damage by 25%
- In another RCT VitD significantly increased levels of Bax which helps stop mutations by promoting apoptosis
- VitD also regulates the activity of PARP another fast acting DNA repair enzyme

Prevention of DNA damage

- Chatterjee et al reports that VitD protects cell membranes, cell proteins & DNA against oxidative damage
- It stabilizes the chromosome structure & prevents double stranded breaks-
- Hence VitD def is associated with DNA damage due to various cellular stresses & obtaining adequate VitD is imp in preventing DNA damage
- Adequate VITD is that found in hunter gatherers in the equatorial regions (50ng/ml) rather than that found in Polar region indoor workers (20ng/ml)

Antioxidants

- It also upregulates gamma glutamyl transpeptidase which is the rate limiting step in glutathione synthesis
- Glutathione scavenges oxidative by-products and chelates (captures and excretes) heavy metals like Iron ,Zinc & mercury.
- Glutathione thus protects nerve cells & nerve conduction
- VitD also upregulates Superoxide dismutase & Thioredoxin reductase which protects mitochondria from oxidative damage.

Allergy

- Vitamin D deficiency during pregnancy and childhood is a widespread and growing epidemic.
- Maternal & childhood vitamin D deficiency is an important risk factor for Allergic diathesis & Asthma.
- It is seen that most of the autistic children have Allergy which causes rec infn → Antibiotic use → worsens autism
- So here also Vit D def is the father of both allergy & brain dysfunction in autistic children
- Hence in Asthma & atopies it is best to correct Vit D deficiency & keep levels above 40

Antinflammatory action



- Overall effect of VitD is to serve as an Immunomodulator or regulator which reduces inflammation while enhancing protective immune responses
- Calcitriol modulates various immune cells including Monocytes, macrophages, dendritic cells T & B lymphocytes
- Proinflammatory chemokines such as MCP-1 & TNF-Alpha are consistently elevated in autism
- Supplementation with VitD consistently & markedly reduced both
- Calcitriol inhibits the synthesis & actions of proinflam PGs which are elevated in autism
- It inhibits NF-Kb activity which causes inflammation & aberrant signalling in autistic brains.

Serotonin metabolism

- Recent research shows that VitD upregulates the genetic expression of Tryptophan Hydroxylase-2 in brain & downregulates Tryptophan hydroxylase-1 in peripheral tissues like Resp tract, GIT etc
- This leads to increased serotonin in brain leading to positive effects on behaviour ,mood,sleep, Emotions etc
- Remember that in autism there is very low serotonin in CNS while blood levels of serotonin are high(paradox)
- VitD suppresses peripheral serotonin levels leading to reduced inflammation , Resp Allergy ,reduced GI Inflammation & leaky gut
- Just remember carcinoid syndrome where there is inflammation & allergy in the GI & resp tracts

Auto immunity in Autism

- Autism is one of the 160 autoimmune diseases in that Antibodies to brain are seen & their levels correlate with autism severity
- Most AUTO ID so far studied are somehow involved with VitD def & large body of multi subject evidence indicates that the VitaminD ssteroid system helps to establish & manintain immunological tolerance
- In animal models of these diseases Vit D supplementation produces therapeutic effects
- A recent human study inversely correlated Anti Myelin asociated glycoprotein antibody levels with 25OH D levels

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- Researchers in China administered 1.5 lakh vitamin D per month for 2 months along with daily supplements of 400 iu to an severe autistic child who dramatically improved in all core features.
 - This report appeared in AAP-pediatrics, Dec 2014. Further long term trials are needed in this direction.
 - Autism speaks is closely supporting research in this direction
 - Vitamin D also upregulates synthesis of Vasopressin & oxytocin which are imp in behaviour & emotions.

GcMAF

- A sharjah boy of 4 yrs recovered completely from autistic features & integrated with normal children over a period of 6 months in 2013 on being given GcMAF injection once weekly for 24 weeks. Dr.Bariah Dardaari is treating doctor.
- Gc protein is the carrier protein of vitamin D in blood
- Activated macrophages are important both in brain organisation & anticancer surveillance
- GcMAF is used in preclinical trial of autism & clinical trials of Anticancer treatment & has yielded beneficial effects.
- VitaminD receptors are seen in Brain, macrophages, lymphocytes, Spermatogonia among others.

Seizures & VitaminD

- In a recent open study 8 out of 13 seizure patients were extremely vitamin D deficient & all 13 were given 40000-2 lakh units stat dose foll by 2000 units per day for 3 months .
- This reduced seizures by 40% . One pt no of seizures dropped from 450 to 30.
- So VitaminD def in all seizure patients should be corrected incl autism withseizures

T reg cells & neurotrophins

- Treg are suppressor T cells which calm the immune system & maintain tolerance to self & arecent study demonstrated their def in 74% of Autism patients.
- VitaminD increased Treg from 4.8% to 5.9 over 1 months when administered a total 3 lakhs vit d in 2 portions 4 weeks apart
- Neurotrophins like NGF, GDNF induce the devpt, function & survival of brain & nerve cells & Vit D upregulates them by 5 fold
- So could this repair the damaged brain in autism?

Diabetes ,obesity & vitaminD

- Diabetes is more common in autistic children
- In a study of 85 autistic children Insulin resistance was 7 fold higher in those with Vitd level below 10 when compared with levels above 30
- Another famous prospective study showed that VitaminD suppl in 1st year reduced the risk of Type 1 diabetes significantly
- In adults it is well proven that Vit D increases insulin sensitivity by 40%
- Also Vit D increases adiponectin levels which inversely asssd with obesity

Psychoactive drugs in Autism

- FDA approved drug is **Risperidone** which is used for various autistic features like hyperactivity, self injury, irritability, poor sleep, stereotypies etc
- **Naltrexone** has been used in very low dose 3mg for stereotypies & aggression in autism
- **Atomoxetine** has been effective in some but not all patients with ADHD co with autism
- **Melatonin** is a safe Hypnotic for insomnia & normalisation of circadian rhythm in autism.
- **Piracetam** has 2 uses in autism. It reduces irritability & also has stimulant action on language circuitry. Action not always consistent.

AAP- PAEDIATRICS

- In their report, autism specialists at China's First Hospital of Jilin University describe a toddler they diagnosed at 32 months with autism spectrum disorder (ASD).
- They describe how the boy did not respond to his name or instructions and spoke only a few isolated words. He didn't play with toys, but instead compulsively smelled objects and shredded paper. He ran in circles "endlessly" and suffered from tantrums that involved head banging.
- Blood tests showed that the boy had borderline low blood levels of vitamin D (12.5 ng/mL). The doctors administered a monthly injection of vitamin D3 (150,000 IU) and prescribed a daily oral supplement (400 IU).

Improvement

- After two months, the boy's vitamin D blood levels had risen to 81.2 ng/mL, and his parents were reporting clear improvements.
- The boy had stopped running in circles and banging his head. He was responding to his name, playing with toys and asking his parents to hold him in their arms. Re-evaluation with a diagnostic checklist likewise showed significant improvements in all areas of core autism symptoms.
- “It is important to note that this single case observation cannot be generalized to all patients with ASD,” the doctors write. “It is hoped that this case report will encourage researchers to conduct further long-term controlled clinical trials.”

Autism with epilepsy

- Always be on the look out for underlying IEM in this situation as a significant proportion has IEM
- Iems commonly seen are Urea cycle D, Mitochondrial D, Cerebral folate d
- Biotin pyridoxine & carnitine metabolism Defects
- Epilepsy may be refractory to AEDs if these are not treated.
- Mitochondrial dysfunction in autism is seen in both nervous system & immune system.
- The development of CNS & immune system occur in parallel & Vit D is imp to both
- An increased vulnerability to oxidative stress is responsible for the mitochondrial dysfunction in autism.
- Vitamin D upregulates expression of antioxidants like glutathione & also DNA repair genes.

Egyptian study

- **Objective:** The aim of this study was to investigate the potential role of vitamin D in autism through serum level assessment.

- **Design:** This was a case-controlled cross-sectional study.

Results: Children with autism had significantly lower 25(OH)D ($p < 0.00001$) and 1,25(OH)₂D ($p < 0.005$) as well as lower calcium ($p < 0.0001$) serum values than the controls.

A significant positive correlation was obtained between 25(OH)D and calcium (correlation coefficient $r = 0.309$, $p < 0.01$) within the children with autism. No significant difference was found on comparison of birth month and season of birth between children with autism and healthy controls.

Furthermore, associations linking parental consanguinity or convulsions with vitamin D could not be established.

- **Conclusions:** Serum values of 25(OH)D in the children with autism of this study could classify them as being
- “vitamin D inadequate,” which lends support to the hypothesis that autism is a vitamin D deficiency disorder.

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- THANK YOU & God bless all of us in our fight against Autism & Cancer