POSSIBLE EFFECTS OF NUTRACEUTICALS IN THE MANAGEMENT OF SOME NEURODEVELOPMENTAL DISORDERS IN NIGERIAN CHILDREN

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ABSTRACT

Introduction: A nutraceutical is a pharmaceutical grade nutrient or nutrient complex that may be used for medicinal purposes. Most nutraceuticals are derived from plants and have been shown to be generally safe when used as food supplements. There is growing interest in the use of these natural products in delaying, ameliorating, and treating acute and chronic diseases. Ong W.Y and co-editors in 2016 edited a special collection of reports on beneficial effects of nutraceuticals in the management of neurodegenerative diseases and aging. However, there is paucity of reports of their use in sub-Saharan Africa.

Case Reports: Here we describe a case series of some of the children managed at our center using nutraceuticals and other supportive care. Details of the observed effects are described in this report.

Discussion: Globally, there is rising evidence of improved treatment outcomes with use of nutraceuticals. Our experience in the management of Nigerian children with neurodevelopmental disorders suggests that they may be beneficial and are deserving of well-controlled studies. We hope that this case series will raise interest of researchers in Nigeria in designing observational studies and clinical trials aimed at generating evidence for or against their use.

Keywords: Autism, Autism spectrum disorders, Neurodevelopmental disorders, Nutraceuticals, Nigeria

INTRODUCTION

Neurodevelopmental disorders

Autism spectrum disorders (ASD) are neurodevelopmental disorders that are characterized by varying degrees of impairments in psychosocial development. They are caused by disruptions in early stages of central nervous system development and are usually diagnosed in the first few years of life.1 These disorders may result from genetic mutations (or "misreadings") during pregnancy, maternal exposure to infections, and other harmful elements during critical stages of brain development. Mishaps before, at, or shortly after delivery, and neonatal period to three years of age (as in the case of autism) are other risk factors.¹ Poor maternal health or inadequate access to health care, disempowering socio-cultural and religious beliefs, poverty, ignorance, complacency, among other reasons, are other risk factors that may result in children being born with defects or suffering trauma during the birth process. These may result in irreversible brain damage (or dysfunction) requiring a lifetime of visits to neurologists. Conventional therapies and interventions can be challenging and expensive with little or no improvements in many cases. Neurologists and pediatricians at hospitals in the Federal Capital Territory (FCT) and all over Nigeria routinely see and manage

cases of ranging from mild to severe brain disorders, but unfortunately see very little by way of resolution.

Patterns of Presentation in Nigerian Children: Our Experience at the Brain Centre (at No. 39 Suez Crescent, Abacha Estate, Zone 4, Abuja, FCT)

Our experience (unpublished) in the management of children with autism related conditions suggests the following:

- 1. Infections, whether *in-utero*, or in the early stages of life, seem to occur much more commonly among Nigerian children than among Caucasian children.
- 2. Speech seems to be much more severely affected among Nigerian children.
- 3. Regardless of the cause of the neurodevelopmental condition, poor digestive system function is a common denominator, with patients presenting with constipation in at least 90% of cases.
- 4. Nigerian parents are more apt to report that their children display greater physical strength and have a higher pain threshold than their peers or their siblings at that age.

- 5. Hyperactivity is more pronounced among Nigerian children.
- 6. There appears to be a much later average age of presentation in Nigerian children as opposed to children in the western world which may be attributable to ignorance, cultural beliefs, denial, financial constraints, etc.

Use of Nutraceuticals

A nutraceutical is a pharmaceutical grade nutrient or nutrient complex that may be used for medicinal purposes. Nutraceuticals have been shown to have health as well as nutritional benefits.^{2,3} The term "nutraceutical" combines two words – "nutrient" (a nourishing food component) and "pharmaceutical" (a medical drug). The name was coined in 1989 by Stephen DeFelice, founder and chairperson of the Foundation for Innovation in Medicine, an American organization located in Cranford, New Jersey.

Most nutraceuticals are derived from plants and have been shown to be generally safe when used as food supplements. There is growing interest in the use of these natural products in delaying, ameliorating, and treating acute and chronic diseases. Ong W.Y and coeditors in 2016 edited a special collection of reports on beneficial effects of nutraceuticals in the management of neurodegenerative diseases and aging.⁴ However, there is paucity of reports of their use in sub-Saharan Africa.

Our approach, which focuses on providing the brain with the nutrients it requires for healing, suggests improvement in some of the children we managed for neurodevelopmental diseases. This paper describes cases of children with neurodevelopmental disorders in whom the use of nutraceuticals appear to be of benefit. However, there remains a need for controlled observational studies and clinical trials to verify these preliminary observations. The objective of this case series is to raise interest in the use of nutraceuticals in the treatment of children with similar neurodevelopmental disorders. There is also a need for controlled clinical trials to generate evidence for the effects described here.

CASE REPORTS

The cases presented in this paper are divided into two segments: Autism spectrum and non-autism neurodevelopmental disorders. The nutraceuticals used are shown in the tables included in the descriptions.

A. Autism Spectrum Disorders

1. M.A., a 13 year old girl from Kogi State with a severe form of Autism

M.A. is a 13 year old girl who was referred to the Centre with features suggestive of severe autism – inability to speak, limited coordination, and anti-social tendencies. In addition to being impaired behaviourally, she presented with these other problems: Aggression towards siblings, she has two younger sisters, aversion towards affection and physical contact, faecal smearing, poor fine motor control (she could not brush her teeth or wear clothes herself), chewing on plastic containers, repeated bed-wetting and occasional defecating on herself. She also displayed hyperactivity, especially in Church (mother had to tie a rope around her to keep

Table1: Nutraceuticals used for M.A.

Nutraceutical	Dose	Frequency of usage
Pure Body Drops	4 drops	Three times daily
(Zeolites)		
OmegaRX	2 gel capsules	Twice daily
	(2 grams)	
Stem Kine	One capsule	Twice daily
NeuroBright	2 capsules	Twice daily
Probiotics	One capsule	Once daily

her from running onto the podium and disrupting proceedings).

She was placed on a nutraceutical regimen which included zeolites. Within two weeks, she stopped bedwetting, became more aware of her surroundings and was more submissive to her parents. Most telling was the fact that her parents no longer needed to have restraints put on her in Church to keep her from running around and causing commotion. Presently, she is more sociable, sings songs on her own, responds well to instructions, and initiates chores rather than waits to be told to do them. She has spoken her first word: "Hello," and is trying to communicate more. She however still chews on plastic containers. Recently we were able to secure more supplements for a period of three months for her.

2. Miss S.A., a four-year-old girl with severe autism

S.A. is a four-year-old girl whose parents complained of hyperactivity, lack of eye contact, speech regression, hypersensitivities and allergies, lack of coordination, behavioral issues and difficulty in swallowing and constipation, among others. She was initially given nutraceuticals that work by passively removing toxins, including heavy metals from the blood. Parents noticed a reduction in hyperactivity, along with more concentration, and increased attempts at speaking. At their next visit, we expanded the treatment to include nutraceuticals targeted at promoting apoptosis in the brain, gut, immune and endocrine systems. There was significant improvement within two weeks. Even her teachers began to notice that she was more "settled," paid attention in class, was more cooperative and submissive to parents, and seemed more interested in the world around. Her eye contact had also improved, and she was more apt to tell her parents whenever she wanted to use the rest room. Constipation had also reduced. Parents are elated, but table. After a few weeks on therapy, her mother noted that she could take several steps without falling over, her vocabulary and speech had improved - she was able to pronounce new words clearer and makes simple sentences.

According to her parents:

"H.A. now responds well to correction if she has done something wrong and is scolded. She notices when her father is angry and she says 'sorry."

Nutraceutical	Dose	Frequency of usage
Pure Body Drops (containing zeolites)	Four drops	Three times a day
Aroga Immune	One capsule	Twice daily
Aroga Endocrine	One capsule	Twice daily
Aroga Gut	One capsule	Twice daily
Aroga Brain and Nerve	One capsule	Twice daily

 Table 2: Nutraceuticls used for Miss S.A.

finances/cost remains a factor. Parents are struggling to keep up with treatments.

3. Miss H.A. a three-year-old girl with autism and cerebella ataxia

H.A. was referred to our center by a pediatric neurologist in within the city of Abuja. She presented with an unsteady, staggering gait made worse by febrile illnesses, causing her to fall over and hit her head repeatedly, and a history of frequent seizures. She also had a history of "allergies" to certain foods (while showing unusual preferences for others), poor communication and socialization skills, a very limited vocabulary, hyperactivity, "unusual strength," a high pain threshold, and unusual "stubbornness" along with frequent temper tantrums. She had been diagnosed with autism and cerebellar ataxia (a condition in the brain responsible for the unsteady gait) by the pediatric neurologist who referred her to us. Whenever she attempted to walk, she would stumble and fall over and hit her head on the ground. As a result, she had

"We have also introduced her to some kindergarten exercises such as coloring and she is showing some interest in it."

After another five months of taking supplements, parents reported that:

'H.A. has been taking the supplements for almost 5 months now and she has shown remarkable improvement. Her speech is getting better; her balance improving every day. She falls down less often. She doesn't wear diapers, except when she goes to sleep at night. She tells me when she wants to go to the toilet.

"She has started schooling also. It has been 2 months now, and she is doing good. I am told by her teacher that she is socializing very well with her classmates. She likes sporting activities. But she has challenges when it comes to writing, but with time she will be better. In sha Allah."

It is now over three years since she first started therapy. Parents (as well as neighbors and relatives) report steady improvement. She is now on a single supplement for

Table3: Nutraceuticals used for Miss H.A. a three-year-old girl with autism and cerebella ataxia

Nutraceutical	Dose	Frequency of usage
Supergreens +D (mixture of probiotics and enzymes	One capsule	Thrice daily
for digestive health)	_	
Protandim (nrf2 synergizer)	One caplet	Once daily
Vitaloe (mannose polysaccharide complex)	One scoop	Once daily
	(powder)	-

multiple bumps and bruises on her forehead, which her mother attempted to cover using a scarf.

After taking a detailed history and examination, she was placed on nutraceuticals to heal her gut. This included concentrates from the *aloe vera* plant (supergreens) and other components as shown in the maintenance, as parents were unable to sustain the high monthly cost of treatment.

4. Master S.D, a six-year old boy with autism

Master S.D. is a six year old boy who was referred from the American International School (AIS), with a diagnosis of autism - along with inability to speak, hypersensitivity to sugars and gluten. He also had a history of communication and socialization problems, as well as hyperactivity. Following assessment, he was placed on nutraceuticals to aid gut health (probiotics, digestive enzymes and fermented foods) and reduce "Another improvement is that when he is called, he answers me Ma' and his dad 'Sir.""

"Other noticed improvements are: he welcomes us when we get home and does not stool on himself anymore which he occasionally used to do."

Table 4: Nutraceuticals used for Master S.D, a six-year old boy with autism

Nutraceutical	Dose	Frequency of usage
Gastrex (nutrient complex for intestinal health)	One capsule	Thrice daily
Omega 3 fatty acid gel capsules	2 grams	Twice daily
Pure body zeolite drops	Four drops	Three times a day

hyperactivity and aggression, and parents were counseled on dietary restrictions.

Within two weeks, mother reported he was calmer and paying more attention at home. Sean's assessment reports written by his teachers showed significant improvement. At school, comments from his teachers included the following (all taken from his daily reports): *"He is becoming more cooperative,"*

"Started getting used to the morning routines," "Very cooperative, greets all the teachers, calling them by names,"

"I am very proud to say that Sean has started to follow some of the classes" daily routines."

"Becoming quieter during lessons, becoming friendlier with classmates, hugging his classmates now."

"Has started hugging teachers and classmates, is less hyperactive."

5. Master JWS, a 9-year-old boy from Plateau State with a severe form of autism

JWS's mother contracted an untreated yeast infection while pregnant with him. While delivery and first two years of life were uneventful, his parents soon noticed that he was not making any attempt to speak, displayed hyperactivity, and would not allow others to hug or carry him. He was later diagnosed with autism and his mother brought him to the clinic when he was about seven years old. We started with a series of nutraceuticals promoting glutathione synthesis in the body, detoxification and gut health (digestive enzymes, probiotics, aloe vera extracts/concentrates, and fermented foods). This was continued for about three months. The parents observed the following improvements: JWS became a little calmer, there was an increase in babbling, and he was able to understand and respond to instructions a little more.

After three months, we modified the regimen and gave nutraceuticals for another two months. Parents noted "a little improvement in his speech." In their own words:

"JWS now greets us (parents) in the morning without asking and he now goes on errands which before he didn't understand.

Table 5: Nutraceuticals used for Master J.W.S.

Nutraceutical	Dose	Frequency of usage
Gastrex	One capsule	Three times daily
Protandim	One caplet	Once daily
Aroga Immune	One capsule	Twice daily
Melatonin	One capsule	Once daily
Pure Body Zeolite drops	Four drops	Thrice daily

His parents have reported steady improvement since the commencement of the Nutraceuticals. He now attempts to brush his teeth and wear his clothes himself. These were both activities he was unable to perform in the past. His treatment over the last three years has been paid for by the Brain and Body Foundation (BBF).

B. Non-Autism related Neurodevelopmental disorders

1. Miss D. A. - A 1 year old girl with Agenesis of the Corpus Callosum

D.A. was referred from the National Hospital physiotherapy centre with a history of limb spasms and spasticity (including tightly clenched fists), poor neck control, continual drooling of saliva, inability to achieve certain physical developmental milestones (neck control, crawling, grasping of objects), and constipation. Examination revealed a small for age girl, with bulging eyeballs and a "sun set" appearance, tightly clenched fists, and spastic upper and lower limbs.

Table 6: Nutraceuticals used for Miss D. A.

Nutraceutical	Dose	Frequency of
		usage
Stem Kine	One capsule	Twice daily
NeuroBright	Two capsules	Twice daily
Vitaloe (powder)	One scoop	Once daily
OmegaRx	Five mls	Thrice daily
Probiotics	Once capsule	Once at night

Magnetic resonance imaging (MRI) scan showed complete agenesis of the corpus callosum with gross dilatation of the ventricles. She was placed on a series of nutraceuticals targeted at restoring gut health, addressing inflammation, and improving brain function. Within a month on these nutraceuticals, the drooling had stopped, she started attempting to stand, had better neck control and coordination, she showed more liveliness and she had begun to use her left arm more. She is now on the ninth month of therapy and has continued to improve on the nutraceuticals.

2. Miss BAT, a ten year old girl born with severe neurodevelopmental deficits secondary to chromosomal deletion(46XX deletion (21) g 22.2) Miss BAT was born at 36 weeks of gestation with a rare deletion in a portion of a set of her chromosomes, specifically, the 22.2 band of the 21st set of chromosomes (46XX deletion (21) q 22.2). Some of the features observed at birth included microcephally (small head circumference), low-set ears and nipples, "rocker-bottom feet," and spasticity in the upper and lower limbs. Diagnosis neurodevelopmental disorder with chromosomal abnormality was made based on the genetic test findings carried out at a laboratory in Chicago, USA. The exact nature and prognosis of the disorder was unknown. She also had a slight heart murmur that was expected to resolve as she grew up. Parents were told that she would have possible developmental delays.

Nutraceutical	Dose	Frequency of
		usage
Gastrex	One capsule	Three times daily
Aroga brain and nerve	One capsule	Twice daily
Aroga Gut	One capsule	Twice daily
Aroga Immune	One capsule	Twice daily
Aroga Endocrine	One capsule	Twice daily

Magnetic Resonance Imaging (MRI) done at the time of diagnosis showed cystic lesions at lateral and inferior aspects of the left cerebellar hemisphere. Computerized Tomography (CT) and ultrasound scans showed widespread abnormalities in the kidneys (mild abnormality of renal cortices), heart (biventricular hypertrophy),

Therapy after birth: In the first year of her life, Miss BAT had about three sets of surgeries and remained on admission for a total of four weeks after birth. By her eighth year, she had had occupation therapy, physical therapy and speech therapy, all on multiple occasions. Her speech was limited to a few words. Socially, she was withdrawn, usually preferring to be on her own, playing with herself, and she was severely constipated.

Our first approach at management was to administer a nutrient formulation for improving gut health, especially that of the mucosal lining. Within two weeks, her parents noted that she had improved in the number of words she used; she danced more, seemed happier and more relaxed, and played more often with her two younger siblings. Socially, it seemed, she had "opened up". Her parents noted that she had developed an interest in the cartoon show *Tom and Jerry*, and she would "laugh so hard while watching it." Before then her parents said they "never really could pinpoint a particular thing on television, for instance, that she liked," but now, "she shows more interest in different things, which we are more than happy to see."

We then expanded her nutritional intake to include those targeted at brain, digestive, immune and endocrine systems repair and regulation. Within a month, her parents saw even further improvements: she could count from one to twenty, she added more words to her vocabulary, could move more freely (her movements were not as stiff), and danced more easily. She also started to sing songs from her favorite TV shows.

On a few occasions, her mother caught (and videotaped) her washing her clothes, and later her dishes, unprompted and unaided. She had never attempted to do these before, according to her mother. "She now tries to make sentences, though not very audible at the moment."

3. Miss Z.M., a five year old girl with flaccid cerebral palsy secondary to birth trauma

Miss ZM was born on January the 10th, 2012 after a fifteen hour labor period. She did not cry at birth, "looked lifeless" and had to be resuscitated. Her parents brought her to the Centre just before her second birthday. Unfortunately, no records were available from the previous hospital where she was initially managed.

Table 8: Nutraceuticals used for Miss ZM
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Nutraceutical	Dose	Frequency of
		usage
Stem Kine	One capsule	Twice daily
NeuroBright	Two capsules	Twice daily
Vitaloe (powder)	One scoop	Once daily
OmegaRx	Five mls	Thrice daily
Probiotics	One capsule	Once at night

We promptly placed her on a series of nutraceuticals – omega 3 fatty acids, a glyconutrient complex containing the dissacharide mannose, the composite *superfood*

spirulina and antioxidants – when she was about two years. Parents noted a marked improvement after three months of therapy, but this could not be maintained, as the funds were inconsistent. Presently, her parents are in dire financial needs and progress has not been sustained. We were able to secure nutraceuticals recently and have since placed her on them. Within a month, her parents noticed some significant improvement, including increased limb activity (she now makes an effort to move her limbs and reach for objects), and display of positive affect and emotion. She now looks up and smiles any time her father comes into the room, and her neck control has improved.

4.Miss H.A., a ten year old girl with severe neurological defects and developmental delays

According to her mother, HA's pregnancy, delivery and neonatal period were uneventful. On the night she received her vaccination at nine months (measles and Hepatitis B), her mother reports that she had a generalized convulsion. She started drooling shortly afterwards and stopped crawling. She did not progress any further for a while. She experienced delayed developmental milestones – stood at 14 months and walked two months later (18 months).

Speech: She has been able to say only a few words – "Tata" for water, and "Kelvin" for her brother. Later, she has been able to say "daddy" and "Nana," her grandmother. She refers to every other person as "Vee," including her mother. She still has not been able to call her mother "Mummy."

Hyperactivity: mother notes that she became increasingly hyperactive and agitated since the vaccination at nine months. She has had generalized seizures since then a total of eight times – thrice at nine months, once at 11 months and 12 months, and at 13 years. She has had two at 14 years.

She was introduced to the Foundation in 2014, and was promptly commenced on nutraceuticals. Report written by mother was as follows:

Table 9: Nutraceutical used for Miss H.A.

Nutraceutical	Dose	Frequency of
		usage
Pure Body Zeolite drops	Four drops	Thrice daily

"My daughter H.A. was placed on zeolite drops for a period of two months. She took four drops of zeolites three times daily. During this period, I observed the following; she stopped drooling, she began to sleep better and for longer periods, and there was remarkable improvement in her speech. Her communication level greatly improved and her pronunciation of words became clearer." In addition to the observations made by the mother above, she has become much less hyperactive, her teacher at school reports greater attention and concentration. At home her mother says she now does many chores on her own and without assistance, is much more playful and cheerful, and sings a lot more often now.

DISCUSSION

The uses of nutraceuticals in the cases described here appear to have resulted in some beneficial effects. However, well controlled studies are required to clearly reveal the effects of nutraceuticals in these chronic, debilitating, neurological diseases in children. Autism spectrum disorders are multi-factorial conditions that affect proper brain development, specifically in the areas of social connections, speech and behavior. Because of their complexity, autism spectrum disorders can be an extremely difficult (and expensive) to treat. A lot remains to be understood about the condition.

Treatment Challenges:

Treatment still presents a particular challenge in developed and developing countries. One reason for this is that, despite the huge advantages in brain research and diagnostic technologies, little is still understood about the condition. Unfortunately, the tools available to clinicians for managing autism are generally limited to drugs for controlling hyperactivity, aggression and seizures, while symptoms such as social withdrawal and speech deficits, those most distressing to parents, are largely left unaddressed.

Behavioral and speech therapy are gaining greater and greater popularity.⁵ They have been shown to improve behavior (and even speech) among these children, but therapists are in short supply in developing countries. They tend to be drawn more to the larger, more developed urban areas than the smaller towns and villages, where the majority of cases are found. Further compounding the situation are allergies, including food and environmental allergies, increased sensitivity to heavy metals and chemical toxins present in many of these children.^{5,6} It is for these reasons that our Foundation has decided to explore safe approaches to alleviating the suffering of these children and develop protocols that can be adopted by physicians and other health care providers in the developing world.

Our Experience

Autism is not only a brain disorder; it is literally a systemic one, affecting many cells and organs, and systems, most especially the immune, digestive and endocrine systems.⁷ Most autism-like conditions start long before birth, during the early stages of brain formation in the womb (first and second trimesters).

Conditions such as maternal infections, poor diet, exposure to heavy metals and other toxic chemicals, and even substance (and alcohol) abuse in the mother can all predispose to the development of autism-like symptoms in the growing child.

Focusing on helping or strengthening the body's ability to do what it naturally does – repair, regulation, detoxification – is one of the ways we have found of dealing with complex brain disorders like autism. This is shown in the case series described in this report. Our experience over the years has shown that no single agent works on its own. It takes a combination of different nutraceuticals acting on different pathways, organs and tissues to achieve the most benefits. One of the keys to improvement may be the restoration of gut health, and nutraceuticals have been shown to support gut health.^{8,9}

Controversies still surround the use of nutraceuticals in the treatment of chronic illnesses. However, evidence seems to be mounting in support of their use. In a systematic review by Nabavi and colleagues in 2017, the authors concluded that growing evidence suggests that the consumption of these compounds (nutraceuticals) may represent an alternative strategy to delay the onset and progression of depression, and depressivelike symptoms.¹⁰ However, they stated, further randomized and placebo-controlled trials are necessary to confirm the potential of these compounds as a possible remedy for this debilitating disorder. In a special edition on Neuronutraceuticals edited by William RF, Moharakumar KP, and Beart PM in 2017, contributions from experts in nutraceutical research provided a contemporary overview of how selected chemically identified molecules from natural products can beneficially affect brain function at the molecular level.¹¹ Contributions addressed key emergent issues such as bioavailability, neuronal health, inflammation and the holistic benefit of multi-targeted actions that impact upon how nutraceuticals ultimately improve brain function.

The evidence suggests that naturally occurring molecules can be advantageous to both the young and aged brain, and that they have actions that ultimately can be directed to aid either in the improvement of cognition or in the management of debilitating neurodegenerative and neuropsychiatric conditions.¹¹ Globally, literature on use of nutraceuticals as additives or sole agents in the management of chronic illnesses is rising; our report provides some preliminary observations from work done in Nigeria. *Study limitations*: this report is based on clinical observation of the cases described. A systematic clinical trial was not conducted. It is hoped that the case series will raise interest for the conduction of controlled clinical trials that will generate stronger evidence for or against the use of nutraceuticals in Nigerian children with neurodevelopmental disorders.

CONCLUSION

In all the cases managed at the Brain Foundation described in this report, we added nutraceutical agents to the therapy of the children. These cases suggest beneficial effects in these children and we believe the use of nutraceuticals described deserves further evaluation nationwide. The cases point to the probable efficacy of nutraceuticals in the management of the described neurodevelopmental disorders in children. In conclusion, more research needs to be carried out to explore the use of nutraceuticals in larger populations and proceed to developing effective protocols supporting children for with neurodevelopmental conditions.

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A major limitation faced at the center remains the high cost of the nutritional agents used in the management of the children. As a result, the Brain and Body Foundation provided the nutraceuticals used in most of the cases described above at no cost to the patients' parents. There is hope that with increasing evidence of the benefits (and safety) of this approach (the use of nutraceuticals), demand will increase and lead to a reduction in cost.

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