

Stiripentol safety profile and efficacy in cases of SCN1A-related Dravet syndrome, multi-center experience, Saudi Arabia

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ABSTRACT

الأهداف: تقييم فعالية وسلامة عقار ستيريبيتول (STP) في المرضى الذين يعانون من متلازمة درافيت الناتجة عن طفرات في الجين SCN1A.

المنهجية: تم إجراء دراسة بأثر رجعي مع تركيز وصفي في عام 2023 شملت 44 مريضاً مشخصاً بمتلازمة درافيت. تم جمع البيانات عن طريق مراجعة الملفات مع إجراء مقابلات مع مقدمي الرعاية بناءً على ورقة استخلاص البيانات المعدة. تضمنت البيانات العمر في بداية النوبات، والتحول الجيني SCN1A، ومدة النوبات قبل بدء تناول STP، والعمر وقت بدء تناول STP، والتغير في تواتر النوبات أو مدتها بعد بدء تناول STP وبعد 6 أشهر من بدء تناول STP، والأدوية المصاحبة المضادة للنوبات.

النتائج: شهد 25 من المرضى انخفاضاً ملحوظاً في تواتر النوبات، في حين أظهر 12 من المرضى انخفاضاً طفيفاً إلى متوسط. شهد جميع المرضى تقريباً الذين تناولوا STP بالتزامن مع فالبروات وكلوبازام انخفاضاً ملحوظاً في النوبات. لوحظت أعراض جانبية لـ"STP" لدى 34 مريضاً، ولكن لم تكن أي منها خطيرة. وكان النعاس الأعلى في 20 مريضاً يتبع بالتغيرات السلوكية؛ الهياج وفرط النشاط في 18 مريضاً.

الخلاصة: أظهرت دراستنا أن مرضانا المصابين بمتلازمة درافيت الذين تناولوا STP انخفضت لديهم نسبة تكرار النوبات ومدتها بشكل ملحوظ. لم تكشف الدراسة عن أي أحداث ضائرة خطيرة. وشملت الأعراض الجانبية الطفيفة النعاس والتغيرات السلوكية.

Objectives: To evaluate the effectiveness and safety of Stiripentol (STP) in individuals with Dravet syndrome resulting from SCN1A gene mutation

Methods: A retrospective study with a descriptive focus was carried out in 2023, involving 44 patients diagnosed with Dravet Syndrome, with data collected by chart review and interviews of caregivers based on a pre-structured data extraction sheet. Data included age of seizure onset, SCN1A gene variant, duration of seizures before STP initiation, age at the time of starting STP administration, change in seizure frequency or duration after STP initiation, and at 6 months following initiation, and concomitant anti-seizure medication.

Results: 25 patients experienced a significant reduction in the frequency of their seizures, while 12 showed a mild to moderate reduction. Almost all patients taking Stiripentol concomitant with Valproate and Clobazam had marked seizure reduction. Adverse reactions to Stiripentol were observed in 34 patients, but none were serious. Somnolence was the highest reported (20 patients), followed by behavioral changes, agitation, irritability, and hyperactivity (18 patients)

Conclusion: Our study showed that over half of our patients with Dravet on Stiripentol had a marked reduction in seizure frequency and duration. The study revealed no serious adverse events. Minor adverse events included somnolence and behavioral changes.

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Dravet syndrome (DS), which was previously known as severe myoclonic epilepsy in infancy, is categorized as a developmental and epileptic encephalopathy. It typically manifests within the first year of life, between 3 and 9 months, in an otherwise healthy child as prolonged febrile focal clonic seizures (hemiclonic seizures), which frequently switch sides with each seizure, focal to bilateral tonic-clonic, or generalized clonic seizures at seizure onset. Other seizure types, including myoclonic and atypical absence seizures,

appeared between the ages of 1 and 4 years. These seizures are initially prolonged, and this condition is often triggered by fever and high environmental temperatures, or vaccination, and then become febrile and afebrile seizures. The seizures tend to be difficult to control and unresponsive to medication, and children show cognitive and behavioral challenges starting in their second year of life.¹ The clinical diagnosis is supported by identifying pathogenic variants of the sodium channel gene *SCN1A* (observed in over 80% of cases).² Other rare mutations are *SCN1B*, *GABRG2*, and *PCDH19*, which are categorized as DS- or DS-like syndromes.^{3,4} The incidence of DS is one in 15,700 live births.¹

Treatment is limited to DS being a drug-resistant developmental and epileptic encephalopathy, and no single effective treatment has been successfully used to manage these patients. Current treatment recommendations include preventing seizure-provoking factors, avoiding hyperthermia (hot baths, hot weather), and rigorously controlling fever in febrile illnesses. Neurologists should be cautious in choosing anti-seizure medications, mainly drugs that exacerbate myoclonic seizures, such as sodium channel blockers including lamotrigine. Treatment is usually initiated depending on the type of seizure, with limited efficacy, and includes Levetiracetam, Valproic acid, Topiramate, and Zonisamide.⁵

Stiripentol (STP) (4,4-dimethyl-1-[3,4-(methylenedioxy)-phenyl]-1-penten-3-ol) is an innovative antiseizure medication that has a distinct structure compared to other drugs currently on the market. It exerts its anti-seizure effects through multiple mechanisms of action, such as enhancement of central gamma-aminobutyric acid transmission, blocking both of T-type calcium channels & voltage-gated sodium, with reduction of neuronal excitability by inhibiting lactate dehydrogenase.^{6,7} It was approved for use in Europe in 2007 and in the United States of America in August 2018 in combination with an adjunct treatment (either Valproate or Clobazam), reducing seizure burden, particularly generalized tonic clinic, focal, and status epileptic attacks, by up to 50 percent.^{5,8}

The objective of this research was to evaluate the effectiveness of STP in reducing the frequency of seizures and the incidence of status epilepticus in individuals with DS.

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Methods. A descriptive retrospective cross-sectional study done in 2023, including all patients diagnosed with DS who received STP as treatment and were referred to an epilepsy clinic. In total, 44 eligible patients with complete medical records were identified. No patients with incomplete medical files were excluded. Data were collected by reviewing medical files and interviewing caregivers using a data extraction sheet (Table 1) with informed consent. Approval from the Institutional Review Board at King Fahad Medical City was obtained, numbered 23-141. Six tertiary centers participated in the study.

The diagnosis of DS in our study relied on the subsequent clinical signs: To begin with, seizures tend to manifest during the first year of life. Additionally, the first instance of “convulsive seizures” (prolonged hemiclonic seizures or generalized tonic-clonic seizures) is triggered by fever and evolves into status epilepticus. Third, the subsequent appearance of myoclonic seizures or atypical absence. Fourth, age-appropriate developmental milestones are required before the onset of seizures. Genetic analysis for *SCN1A* mutation confirmed this diagnosis.

Drug effectiveness was assessed by comparing the degree of seizure control among patients with epilepsy on STP based on caregiver seizure diaries, as well as on physicians’ notes in the electronic medical record. A marked decrease was characterized as a reduction exceeding 50% in both the frequency and duration of seizures, along with no instances of status epilepticus (defined as a seizure lasting more than 5 min), no cluster of seizures, and no need to use rescue medication (benzodiazepine). A mild-to-moderate reduction was defined as less than 25–50% seizure reduction or occurrence of status epilepticus or cluster of seizures.

Safety was assessed by documenting the reported adverse events that occurred after STP initiation. Adverse effects were considered serious if the event led to death, required hospitalization, caused significant disability, or required medical intervention; otherwise, such effects were considered non-serious adverse drug reactions.

Data analysis. The data was collected, examined, and analyzed using with Statistical Package for Social Sciences version 21 (An IBM Company). A descriptive analysis was performed by determining the frequency distribution and percentages for the variables under study, including patients’ personal data, family history, seizure-related data, STP frequency, doses, and initiation data, in addition to adverse events (safety measures) and changes in seizure frequency

Results. Forty-four patients with DS referred to an epilepsy clinic were included in our study. One patient was below the age of 2 years (2.3%), eight patients were 3–5 years old (18.2%), half between 6 and 11 years (54.5%, n=24), one-quarter between 12 and 18 years (22.7%, n=11).

Most patients with DS were male (70.5%, n=31). All patients harbored *SCN1A* mutations, as confirmed by genetic studies.

The age at the first seizure onset was 4–8 months in most patients (72.7%, n=31), and ten patients (22.7%) had their first seizure at 3 months. The type of seizure was generalized convulsive seizures in almost half of patients (45.5%, n=20), and generalized convulsive seizures as well as focal seizures in 25% of patients (n=11). In contrast, generalized convulsive seizures, focal seizures,

and atypical absence seizures were observed in 13.6% of patients (n=6), and generalized convulsive seizures with atypical absence seizures were observed in 15.9% of patients (n=7).

Global developmental delay was present in most patients (77.3%, n=34); (63.6%, n=28) in patients above the age > 5 years and 13.6%, n=6) in patients below the age < 5 years. Additionally, speech delay alone was observed in six patients (13.6%), and three patients (6.8%) had only cognitive delay.

Table 1 - Characteristics of included patients. N= 44 patients.

Characteristics	n (%)
<i>Age</i>	
<6 years old	9 (20.5)
6–11 years old	24 (54.5)
>11 years old	11 (25)
<i>Sex</i>	
Male	31 (70.5)
Female	13 (29.5)
<i>Age at first seizure onset</i>	
0–3 months	10 (22.7)
4–8 months	31 (70.5)
>1 year	3 (6.8)
<i>Type of seizure</i>	
Generalized convulsive seizure	20 (45.5)
Generalized convulsive seizure + focal seizures	11 (25)
Generalized convulsive seizure +Atypical absence seizure	7 (15.9)
Generalized convulsive seizure + focal seizures+Atypical absence seizure	6 (13.6)
<i>Current developmental status</i>	
Global developmental delay (patients below the age of 5 years)	28 (63.6)
Intellectual disability (patients above the age of 5 years)	6 (13.6)
Speech delay	3 (6.8)
Cognitive delay	1 (2.4)
<i>Family history of epilepsy</i>	
Yes	8 (18.2)
No	36 (81.8)
<i>Concomitant Anti-seizure medications</i>	
Valproic acid	29 (65.9)
Clobazam	33 (75)
Levetiracetam	10 (22.7)
Phenobarbitone	3 (6.8)
Topiramate	4 (9.1)
Cannabidiol	1 (2.4)
Rufinamide	1 (2.4)
Clonazepam	3 (6.8)
<i>List of failed Anti-seizure therapies</i>	
Levetiracetam	24 (54.5)
Lacosamide	2 (4.5)
Clobazam	5 (11.4)
Topiramate	22 (50)
Lamotrigine	7 (15.9)
Carbamazepine	10 (22.7)
Rufinamide	3 (6.8)
Phenytoin	2 (4.5)
Clonazepam	5 (11.4)
Ketogenic diet	3 (6.8)
Zonisamide	2 (4.5)
Cannabidol	1 (2.4)

Table 2 - Stiripentol efficacy among patients with epilepsy (n=44).

Patients	Duration of seizures before STP	Frequency of ER visit or use of Benzos before STP	Age at starting STP	Current dose of STP	Change in seizure frequency and duration after STP*
Patient 1	> 5 min	Weekly	10 years	500 mg BID	Marked reduction
Patient 2	> 5 min	Weekly	3 years	250 mg BID	Marked reduction
Patient 3	> 5 min	Monthly	6 years	500 mg BID	No change
Patient 4	> 5 min	Daily	6 years	250 mg BID	Marked reduction
Patient 5	> 5 min	Weekly	8 years	250 mg BID	Marked reduction
Patient 6	> 5 min	Monthly	9 years	1000 mg BID	Marked reduction
Patient 7	> 5 min	Weekly	2 years	Stopped	Marked reduction
Patient 8	< 5 min	Monthly	14 years	500 mg BID	Increase seizure frequency
Patient 9	> 5 min	Daily	5 years	250 mg Q8hours	Mild to moderate reduction
Patient 10	< 5 min	Weekly	9 years	Died	Marked reduction
Patient 11	< 5 min	Daily	8 years	500 mg BID	Marked reduction
Patient 12	> 5 min	Weekly	5 years	500 mg BID	Marked reduction
Patient 13	> 5 min	Monthly	3 years	250 mg TID	Mild to moderate reduction
Patient 14	> 5 min	Weekly	2 years	250 mg BID	Marked reduction
Patient 15	> 5 min	Weekly	6 years	500 mg BID	Marked reduction
Patient 16	> 5 min	Monthly	3 years	750 mg BID	Mild to moderate reduction
Patient 17	> 5 min	Weekly	9 years	Stopped	Increase seizure frequency
Patient 18	< 5 min	Monthly	7 years	500 mg BID	Marked reduction
Patient 19	< 5 min	Monthly	4 years	500 mg BID	Mild to moderate reduction
Patient 20	> 5 min	Daily	5 years	250 mg am, 500 mg pm	Marked reduction
Patient 21	< 5 min	Weekly	3 years	250 mg am, 500 mg pm	Marked reduction
Patient 22	< 5 min	Weekly	4 years	Stopped	No change
Patient 23	< 5 min	Monthly	3 years	250 mg BID	Marked reduction
Patient 24	> 5 min	Monthly	3 years	500 mg BID	Mild to moderate reduction
Patient 25	< 5 min	Weekly	2 years	500 mg BID	Marked reduction
Patient 26	< 5 min	Monthly	3 years	750 mg BID	Mild to moderate reduction
Patient 27	> 5 min	Weekly	4 years	750 mg BID	Marked reduction
Patient 28	> 5 min	Weekly	9 years	Died	Marked reduction
Patient 29	> 5 min	Monthly	10 years	1,000 mg BID	Mild to moderate reduction
Patient 30	> 5 min	Monthly	2 years	500 mg BID	Increase seizure frequency
Patient 31	> 5 min	Weekly	9 years	500 mg BID	Mild to moderate reduction
Patient 32	> 5 min	Monthly	2 years	500 mg BID	Mild to moderate reduction
Patient 33	< 5 min	Weekly	15 years	750 mg BID	Mild to moderate reduction
Patient 34	< 5 min	Monthly	5 years	500 mg BID	No change
Patient 35	< 5 min	Monthly	14 years	500 mg BID	Marked reduction
Patient 36	> 5 min	Weekly	4 years	250 mg BID	Marked reduction
Patient 37	> 5 min	Weekly	14 months	250 mg BID	Marked reduction
Patient 38	> 5 min	Monthly	6 years	500 mg BID	No change
Patient 39	> 5 min	Monthly	3 years	250 mg BID	Marked reduction
Patient 40	> 5 min	Monthly	8 years	750 mg BID	Mild to moderate reduction
Patient 41	> 5 min	Monthly	8 years	500 mg BID	Marked reduction
Patient 42	< 5 min	Monthly	4 years	500 mg BID	Marked reduction
Patient 43	> 5 min	Monthly	8 years	500 mg BID	Mild to moderate reduction
Patient 44	< 5 min	Monthly	9 years	500 mg BID	Marked reduction

*Definition of Seizure frequency / Duration as follows: -Marked reduction: more than 50% reduction in seizure frequency and duration, no occurrence of status epilepticus (defined as a seizure lasting more than 5 minutes), no cluster of seizures, and no need to use rescue medication (Benzodiazepine). -Mild-moderate reduction was defined as less than 25-50% seizure reduction or occurrence of status epilepticus/ cluster of seizures, BID - Given twice daily, ER - Emergency Department, STP - Stiripentol

Table 3 - Frequency of adverse events with Stiripentol.

Number of Adverse events	Number of patients
One Adverse event	7
Two Adverse events	6
Three Adverse events	10
More than three Adverse events	11

In most cases diagnosed with DS, there was no observed family history of epilepsy (81.8%, n=36). STP was the last medication added to control seizures in all patients. The most common concomitant anti-seizure medications with STP were Clobazam (75%, n=33) and Valproic acid (65.9%, n=29). The most commonly tried and discontinued antiseizure medications in patients with DS were Levetiracetam (54.5%, n=24) and Topiramate (50%, n=22) (Table 1).

The efficacy of STP was based on the duration and frequency of seizures before and after STP initiation. The duration of seizures before initiating STP was more than 5 min in 65.9% of patients with DS (n=29). The frequency of emergency visits or use of rescue medications such as benzodiazepines (diazepam, lorazepam) before initiating STP was weekly in 40.9% of patients (n=18) and monthly in half of patients (50%, n=22). The age at the time of starting STP treatment was 3–5 years in 34.1% of the patients (n=15) and 6–10 years in 40.9% (n=18) with DS. The starting dose of STP was 250 milligram (mg) either once daily or twice daily, which was then increased according to the response, not surpassing the maximum advised dosage of 3,000 mg total per day.

Seizure improvement after STP initiation was assessed at a minimum of 6 months after starting STP, with no change in the other ASM doses, about half of the patients showed a significant decrease in the frequency of seizures (56.8%, n=25). A mild to moderate reduction was observed in about a third of patients (27.3%, n=12). Seventeen percent of patients still needed to use rescue medications or visit the emergency room because of breakthrough seizures (Table 2). Only one patient became seizure-free after STP initiation.

The STP has greater efficacy in controlling seizures when combined with Valproic acid, Clobazam, or both. Twenty patients were taking a combination of STP, Valproic acid, and Clobazam, the majority (99%) displayed a marked reduction in seizure frequency (n = 19). Eight patients were taking STP with Valproic acid, which showed decreased seizure frequency in six (75%) patients. In contrast, out of 14 patients taking STP in addition to Clobazam, 12 patients showed a decrease in seizures (Figure 1).

After initiating STP, adverse events occurred in most patients with DS (77.2%, n=34). The most

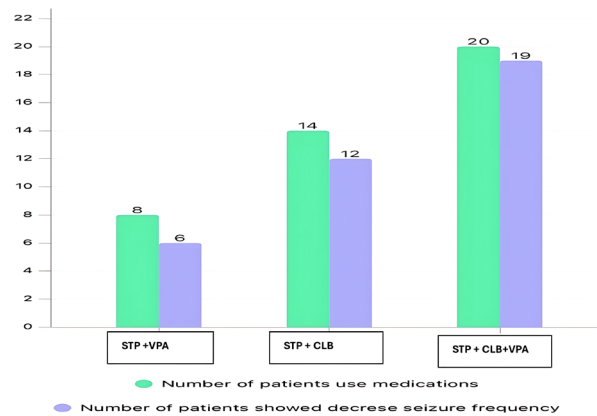


Figure 1 - Efficacy of Stiripentol on seizure frequency with either Valproic acid or Clobazam or combined.

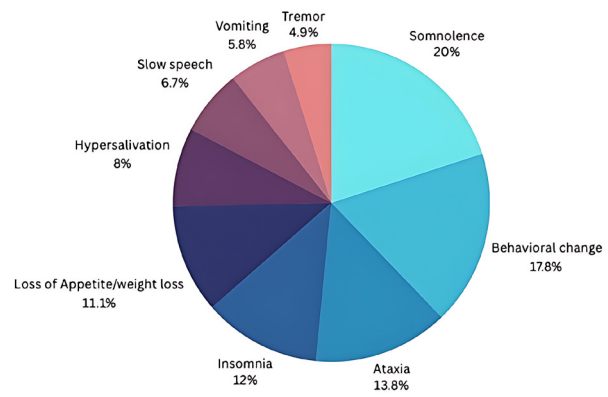


Figure 1 - Stiripentol-related adverse events.

frequent adverse events to STP in individuals with DS were somnolence (45.5%, n=20), behavioral changes (40.9%, n=18), such as agitation, irritability, or hyperactivity, followed by ataxia (31.8%, n=14). Insomnia was noted in 27%, (n=12) and loss of appetite and weight were reported in 25% (n=11). Additionally, eight patients (18%) developed hypersalivation after starting STP, whereas vomiting was reported in six patients (13.6%), and tremors developed in five patients (11.3%). One patient experienced an increased frequency of seizures after the initiation of STP. Three patients had to stop STP because of a lack of efficacy and adverse events, mainly somnolence. No clear predictors were observed, as each patient had a different STP starting age, different anti-seizure therapy combinations & failed medications. One patient stopped STP owing to the initiation of Fenfluramine. No serious adverse events were observed. Two patients died of severe pneumonia, which was most likely not related to STP (Figure 2, Table 3).

Discussion. Here, we studied the effects of STP on seizure frequency and duration. Results showed a positive change in seizure frequency after starting STP, with a marked reduction in seizure frequency in (56.8%) patients. Simultaneously, (27.3%) of our patients had a mild to moderate seizure reduction. This marked reduction of above 50% was similar to many other studies. In some studies, the response rate ranged from 70–80%.⁸ We believe that this is because all patients in these studies were also on both Clobazam and Valproic acid before the addition of STP, whereas only 65% of our patients were on valproic acid and 75% were on clobazam at the time of STP initiation, with STP initiated earliest at age 2 years (Table 2).

Perez et al⁹ evaluated the effectiveness and safety of STP in pediatric patients through a two-phase study. The initial trial was done as a placebo-controlled, single blind add-on for children experiencing various epilepsies, seizures intractable to drugs, followed by using STP open-label for long-term. In the randomized study segment, the responder rate (indicating a $\geq 50\%$ reduction in seizures) was 40% at one month, & 49% at 3 months after STP initiation. In the study's second phase, STP was given in an open trial to the patient group identified in the first study. It included twenty patients with DS, among whom 10 showed a response, and three achieved seizure freedom after 3 months.

In a trial by Chiron et al, specifically focused on DS. A randomized placebo-controlled method was employed. In the STP group, 21 patients exhibited a response rate of 71%, whereas only 5% was noted in those receiving a placebo. Within this group, nine patients (43%) were free of seizures during the double-blind phase of the trial, with five continuing throughout the open-label segment.⁸

The STP treatment group experienced a seizure rate that was 70% lower, as reported in a detailed review and meta-analysis by Chiron et al., which encompassed 23 uncontrolled studies alongside two randomized controlled trials comparing STP to a placebo.¹⁰

One study included 41 patients with DS who received STP. At 3 months of follow-up, Twenty-three patients experienced a reduction of 50% or more in generalized tonic-clonic seizures, 11 patients achieved a similar 50% or greater decrease in focal seizures, and 11 had a reduction of at least 50% in the frequency of status epilepticus.¹⁴

In a new post hoc data analysis published by Chiron et al group in 2024, the results reinforced the evidence of STP potency in DS. STP showed rapid action on seizure frequency from the fourth day of use; patients receiving a placebo were switched to STP in the third-month open-label extension, showing an 80.2% seizure frequency decrement from baseline.¹¹

STP combined with Clobazam and Valproic acid improved seizure control. Our findings are in line with those of Chiron et al, who found that 71% of patients saw a $>50\%$ decrease in seizure frequency when STP was added to Clobazam and Valproate.⁸

Our study revealed that a significant majority of DS patients, 77.2% (n=34), experienced adverse events following the initiation of Stiripentol. Notably, somnolence was reported by 45.5% of participants, a rate considerably higher than observed in prior studies.^{13,14} This increased frequency is likely attributable to the metabolic interaction with Clobazam, as there was no observed reduction in the dosage of concurrent anti-seizure medications upon the addition of Stiripentol in our study population.⁸ These findings underscore the importance of closely monitoring and adjusting medication regimens to mitigate adverse effects while optimizing therapeutic outcomes for DS patients.

Sedation and weight loss were the main side effects in the Chiron et al. study, necessitating a dosage decrease with concurrent clobazam administration. In 12 out of 21 individuals (57%), the side effects vanished with the Clobazam reduced.⁸

The second adverse event in our patients who visited the emergency room was vomiting, which was documented in 13.6% of cases. However, no patient developed a skin rash or other allergic reaction.

21 individuals in the STP therapy group experienced drug-related side events in the STICLO study. Nevertheless, no participant left the study's treatment group due to it, and 12 patients continued to receive STP through adulthood with good tolerability.^{8,11} Drowsiness and appetite loss were the most common side effects, and in 17 out of 21 patients in the treatment group, these side effects necessitated lowering the dosage of concurrent anti-seizure drugs. Adverse events were later resolved with lower dosages of co-medication, indicating that the adverse effects were most likely caused by suppression of the CYP450 enzyme.

Other studies have reported comparable rates of common side effects, such as sleepiness, lack of appetite, hyperactivity, and irritability or ataxia, that were reported during the dosage escalation phase, which did not result in study termination, less commonly required a decrease in STP dosage and improved with dose reduction of other anti-seizure drugs.^{12,13}

The most common events documented in 31 (38%) out of 82 children with DS treated with STP in a retrospective US research were drowsiness and decreased appetite. Two patients (2%) and four patients (5%) stopped taking STP due to ineffectiveness and side effects, respectively. More than 85% of the children treated with STP in this trial showed a notable enhancement in their quality of life despite the high proportion of early adverse events.¹³

All 41 DS patients who received STP in a study experienced adverse effects, including behavioral abnormalities in 22%, drowsiness in 34%, and anorexia and weight loss in 49% of cases.¹⁴

A comprehensive meta-analysis of the use of STP in DS showed that STP led to a more than half decrease in the frequency of seizures with increased rates of seizure freedom compared to placebo. Additionally, adverse events occurred less in the placebo group than in the STP group.¹⁵

The reasons for emergency room visits or rescue medication use in our study were generalized tonic-clonic seizures or prolonged hemiclonic or focal convulsions (status epilepticus). Before the initiation of STP, our study showed that 10% of patients required daily rescue medications or emergency room visits, 40% required weekly rescue medications or emergency room visits, and 50% required monthly rescue medications or emergency room visits. However, on STP treatment 2.8% required weekly rescue medications or emergency room visits, and 25% required monthly rescue medications or emergency room visits. None of the patients required daily rescue medication or emergency room visits.

This research has certain limitations. It is a retrospective analysis involving a limited patient population. A prospective study is needed to better understand STP's safety profile and effectiveness in controlling seizures. Another is that STP was used as an add-on therapy, not as monotherapy, which may reflect the combined effect of multiple antiseizure medications.

Conclusion and recommendations. The present research indicated that over 50% of the patients with DS taking STP experienced significant decreases in both the frequency and duration of their seizures. One-fourth showed a mild-to-moderate reduction, which indicates the high efficacy of the drug in controlling seizures. Regarding tolerability, no significant adverse events were seen, with the most frequently observed adverse effects being somnolence and behavioral changes. STP should be taken into consideration in medical therapy for *SCN1A* DS. Further prospective large-scale studies are recommended to assess how adverse events related to STP affect the quality of life and daily seizure burden of individuals with DS.

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