Infantile Epileptic Spasms Syndrome and Trisomy 21: Treatment response and outcomes

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Introduction:

CONTEXT: In France, the current treatment protocol for infantile epileptic spasms syndrome (IESS) in Down Syndrome (DS) consists of a first line monotherapy with vigabatrin (VGB) and if failed, the addition of oral corticosteroids or less frequently bitherapy (combination of vigabatrin and prednisone) from the start.

OBJECTIVE: Our aim is to describe IESS cases followed at Institut Jérôme Lejeune, in terms of therapeutic response, side effects and evolution following received treatment protocols.

Methods:

Retrospective study based on the electronic medical files of DS children with the diagnosis of IESS followed up in a trisomy 21 expert medical center, Institut Jerome Lejeune between 2012 and 2023.

Results:

Diagram 1: Breakdown of different therapies in our cohort

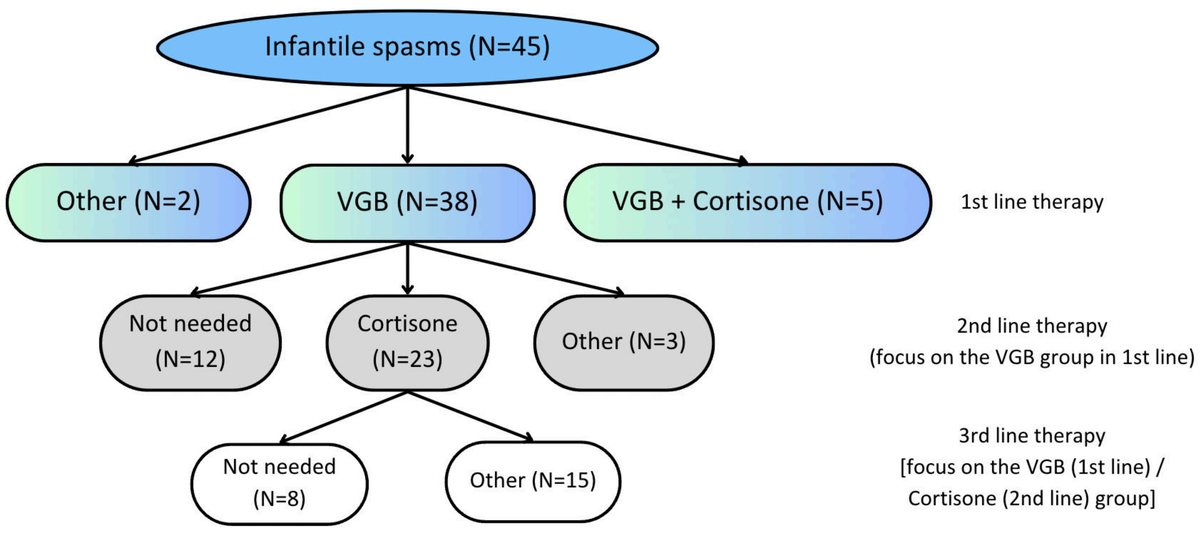

Table 1 : Patients' demographic and clinical characteristics

	T21 with West Syndrome (N = 45)	T21 without West Syndrome (N = 366)*
Female	12/45 (27)	167/366 (46)
Genetic diagnosis		
T21 free and homogenous	31/45 (69)	366/366 (100)
T21 clinical	9/45 (20)	0
Other : translocation, mosaique, unkown, …	5/45 (11)	0
Comorbidities		
Cardiac	20/45 (44)	215/338 (64)
Dysthyroidism	15/45 (33)	97/340 (29)
Gastro-intestinal	4/45 (8.9)	68/241 (28)
Prematurity	10/45 (22)	22/188 (12)
Regression at presentation	30/38 (79)	N/A

**Children between 6 and 8 years of age with T21 free and homogenous diagnosis without any history of spasms*
Statistics: n/N (%)

Table 2 : Description of spasm characteristics and long term outcomes in VGB monotherapy vs. VGB and cortisone (bitherapy) groups, as first medication.

	First line therapy	
	VGB (N = 38)	VGB + Cortisone (N = 5)
SF. after 1st line drug*	12/38 (32)	1/5 (20)
Time between diagnosis and SF. (months)	3 (1.0, 5.8)	3.5 (3.3, 3.8)
Missing data	11	3
Spasms characteristics (months)		
Age at onset	6.0 (5.5, 9.3)	6.0 (5.5, 8.5)
Missing data	6	2
Age at diagnosis	8.6 (7.0, 13.3)	7.7 (7.2, 9.0)
Time between onset and diagnosis	1.3 (0.6, 3.5)	1.2 (0.8, 1.2)
Missing data	6	2
Follow up period	80 (42, 121)	22 (17, 63)
Age at last follow-up	87 (49, 134)	29 (23, 74)
Number of drugs needed to achieve spasms cessation		
1	12/37 (32)	0
2	6/37 (16)	1/5 (20)
3	5/37 (14)	3/5 (60)
4	8/37 (22)	0
5	4/37 (11)	1/5 (20)
6	2/37 (5.4)	0
At last follow-up:		
Active epilepsy	8/38 (21)	0
Long term treatment**	32/36 (89)	3/4 (75)
ASD	10/37 (27)	1/5 (20)
Severe developement delay	11/28 (39)	1/3 (33)
Behavior concerns	11/37 (30)	0
Lennox-Gastaut	3/37 (8.1)	0

**SF = Seizure free*
***Anti-epileptic drugs for more than 12 months*
Statistics: n/N (%), for qualitative data
Median (Q1, Q3), for quantitative data

Table 3: Medication side effects in the two groups

	First line therapy	
	VGB (N = 38)	VGB + Cortisone (N = 5)
Side effects	16/37 (43)	2/5 (40)
Irritability	4/37 (11)	1/5 (20)
Sedation	9/37 (24)	1/5 (20)
Myoclonus	7/37 (19)	0
Encephalopathy	1/37 (2,7)	0
Hypertension	1/37 (2,7)	0
Weight gain	2/37 (5.4)	1/5 (20)
Severe infection	1/37 (2,7)	0
Death	1/37 (2,7)	0

Discussion:

On the 45 DS children included, 38 (84%) received a first line monotherapy and 5 (11%) a bitherapy. Spasms stopped in 44 of them (97.8%). Only 12/38 (32%) receiving monotherapy were seizure free after one medication (VGB). Whereas in the bitherapy group, 1/5 (20%) were seizure free after their first line therapy (VGB + cortisone). The two groups had a similar percentage of side effects. At their last follow-up, 10/37 (27%) receiving monotherapy were diagnosed with autism spectrum disorder, 8/38 (21%) had active epilepsy and 11/28 (39%) severe developmental concerns.

Conclusion:

The results show a poor response to the current French treatment protocol for IESS in DS with an unfavorable outcome and highlight the importance of studying the pathophysiology of this syndrome in DS to establish a more targeted treatment.

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