The added value of Vagal Nerve Stimulator (VNS) implantation following Corpus Callosotomy (CC) in children with Lennox-Gastaut Syndrome (LGS)

A multicenter, multinational study

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Background

Lennox-Gastaut syndrome (LGS) is a severe form of epileptic encephalopathy, presenting during the first years of life, and being very refractory to anti-seizure medications. LGS may cause various generalized seizure phenotypes, and has a major destructive impact on neurodevelopmental achievements, behavior, and quality of life. Thus, seizure reduction is of uttermost importance especially amongst children. Moreover, the drop seizure which are one of the major characteristics of the syndrome are a significant socurce of morbidity, causing severe injuries. Therefore, many of the patients require close and constant supervision, including continuous head protection with special helmets, which are not well tolerated by many of these patients.

Once conventional anti-seizure medications have failed, palliative surgeries such as VNS implantation, or corpus callosotomy (CC) should be considered. Comparison of the efficacy and safety of CC and VNS, which are the most common palliative surgical methods, suggests the superiority of CC in terms of efficacy: between 74-85% reduction in tonic and atonic seizures following CC compared to about 55% following VNS[1,2].

However, CC is associated with a higher rate of adverse events, both major and minor, when compared to VNS, with a similar or higher of QOL improvement. For this reason, in many cases either the physician or the family, favor VNS over CC as the primary surgical palliative treatment. In cases of VNS failure, CC may have an added value, improving seizure control despite the VNS failure. Hong et al. described that half of patients who underwent CC following VNS, reported

>50% seizure reduction, with 7/9 patients experiencing total elimination of drop seizures[3]. Guillamón et al.[4] reported a small case series of 3 patients whom were treated with CC following VNS in the setting of severe drug resistant epilepsy (DRE). They reported up to 98% decrease in total seizure frequency following the CC. In another small series of 7 cases, Arya et al.[5] reported all patients were free of drop attacks, with a 34.7% decrease in total daily seizure frequency at a mean follow-up of 2.6 years. The largest series to date focusing on this group – a multicenter multinational retrospective study by Roth et al., has shown a significant value of CC following VNS, with at least a 50% reduction in drop attacks and other seizures in 83% and 60%, respectively[6].

In a reverse order, Katagiri[7] et al. evaluated 10 patients with LGS who underwent CC followed by VNS implantation due to residual seizures. Six of ten (60%) patients had ≥50% seizure reduction for all residual seizure types after VNS, while 77.8% showed total resolution of drop seizures, like the reported efficacy after CC only. Another series on 13 patients by Hatano et al. has shown that the addition of a VNS will improve seizure control (>50% reduction) in about 54%[8].

Mirroring the results of a prior multicenter study showing the added value of CC following prior implantation of VNS, we hypothesize that VNS will have a significant value for failed CC.

Hypothesis

We hypothesize that for children with LGS that continue to suffer from drop attacks (tonic or atonic seizures) following a corpus callosotomy, adding a VNS has a significant value.

Goals of study

The primary goal is to assess the efficacy of VNS following CC for children with LGS for drop attacks, as well as other seizure type reduction.

Methods

Multicenter, multinational retrospective study.

Following direct contact with pediatric neurosurgeons from around the world and using data basis of neurosurgeons with an interest in epilepsy surgery (via the PESIG under the ISPN, and through the IESS), and based on agreement to collaborate, we will send an excel database sheet with the relevant variables of interest, as well as a copy of this IRB template. There is no specific period for inclusion (years in which the procedures were performed).

Data acquisition

Data will be retrospectively collected from various origins, including: patient files located on the departments server (PNS-SERVER), patient files. Included cases are from the years 1.1.2010-1.12.2023.

Collected data will include:

- Demographics
- Data relating to the epilepsy syndrome
- Surgical (CC) treatment – technique, complications, and outcome
- Data relating to VNS surgery and outcome
- Short and long-term outcomes

Anonymization procedure

The identified data separation will be done by the principal investigator /co- investigators. All data handling and the separation of the identified data will be done by the PI and the sub-investigator.

Anonymized patient clinical data from other participating centers will be sent to the PI (Jonathan Roth) at the central office (Dana Children's Hospital, Tel Aviv Medical Center) for analysis and publication. Material transfer agreement (MTA) from other centers will be sent to the PI, and our local legal office will finalize the MTA.

The data file will not be sent outside the hospital.

Primary outcome

Rate of drop attack reduction following VNS

Secondary outcome

“other seizure” type reduction following VNS

Inclusion criteria

Age at VNS surgery up to 18 years old

Prior CC of any extent

LGS of all etiologies

Need of at least 1y of neurological follow up after the VNS (unless patient died earlier)

Exclusion criteria

No exclusion criteria

Expulsion from study

As this is a retrospective study, no patients (which fulfil the inclusion criteria) will be expelled from the database.

Gender

M+F

Special populations

Children (<18 years old) and adults (operated as children) will be included in the study.

Pregnant women included too (if operated as children)

Impact on participating patients

As this is a retrospective study, the study will have no impact on the participating patients

Duration of the study

2 years

References

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