



Long-term Increase in Intrathecal Baclofen Dosage in Severely Disabled Cerebral Palsy Patients

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Introduction

Cerebral palsy (CP) is caused by non progressive lesion in central nervous system motor centers, that happens during their development - either during fetal period, delivery or up until 3 years of age (1). CP has an incidence of 2-3 per 1000 live births in industrialized countries (2). Surveillance of Cerebral Palsy in Europe (SCPE) classification includes five groups of patients, according to their neurological signs: unilateral spastic CP, bilateral spastic CP, choreo-athetotic CP, dystonic CP and ataxic CP (3). Spastic CP, either bilateral or unilateral, is the most common form of this condition, corresponding to about 80% of patients (4). Spasticity can cause pain and interfere with daily life activities causing a negative impact on the patient's and the caregiver's quality of life. Intrathecal baclofen therapy (ITB) has proved to be effective in this disease, however there's been concern about the long term drug tolerance. Our goal was to study the dosage evolution in ITB in severely disabled patients with spastic CP.

Methods

The authors conducted a retrospective analysis of all patients with severe spastic CP (Gross motor function IV and V) that were implanted with baclofen pump, in our Center, between 2000 and 2013. Exclusion criteria were pathology other than spastic CP or follow-up inferior to 12 months. Data concerning patient demography, follow-up time and dosage, in micrograms/day at each consultation after pump placement was collected from clinical records. The baclofen dilution used in all patients was 2000 µg/ml. Statistical analysis was performed with Microsoft Excel 2011 and Graphpad Prism 6 software - the former was used for mean, median, standard deviation and long-term evolution graph construction and the later was used to build the correlation graphs.

Results

16 patient met the inclusion criteria, of 20 patients operated during this period. The mean age was 16.72 years (range: 9 to 42). The minimum follow up was 1 year, the maximum 13 years - average of 3.7 years. The mean daily dosage at implantation was 257 ± 105 micrograms/day. The dosage increased by 125% during the first year - mean daily dosage at one year 580 ± 205 micrograms/day. There was an increase in mean daily dose until the 3rd year after implantation, with a 12 to 18% yearly increase - [Table 1](#) and [Graph 1](#).

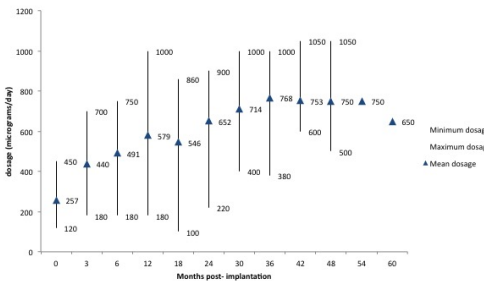
Table 1

Years post-implantation / Dosage	Initial dosage (n = 15)	1 st year (n = 16)	2 nd year (n = 15)	3 rd year (n = 13)	4 th year (n = 5)	5 th year (n = 2)
Average dosage $\pm$ standard deviation (µg/dia)	257 $\pm$ 105	580 $\pm$ 205	651 $\pm$ 226	768 $\pm$ 168	750 $\pm$ 200	650 $\pm$ 0
% of yearly increase		125%	12%	18%	- 2.3%	- 13%

Yearly evolution of baclofen dosage and percentage of annual variance

After the third year there seems to be stabilization in dosage, although there were only seven patients with follow-up longer than 3 years - [Graph 1](#).

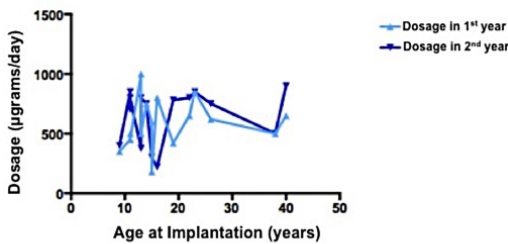
Graph 1



Mean, minimum and maximum intrathecal baclofen doses after implantation – dosage in micrograms/day, baclofen concentration 2000 micrograms/ml

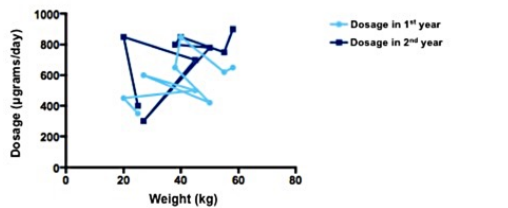
We found no correlation between dosage and age or weight at implantation - [Graphs 2](#) and [3](#).

Graph 2



Correlation between baclofen dosage and age at implantation

Graph 3



Correlation between baclofen dosage and weight at implantation

Discussion

The large dosage increase found in this study was similar to a previous study (5) and is probably related to individual dosage tailoring. We also found an yearly increase of dosage between 12 and 18%, which was also reported before (5). This long-term increase can be related to drug tolerance. The possible development of baclofen tolerance is worrying because the major benefit from ITB is usually obtained in younger patients, which are also the ones with the higher risk for drug tolerance. Further studies are needed in order to confirm our observations and to find ways to diminish possible drug tolerance.

Conclusions

In our study there was a large baclofen dosage increase in the first year that is probably related to individual dosage tailoring. It was also observed an annual dosage increase afterwards that can be related to long-term tolerance. This aspect must be taken into account especially in the treatment of younger patients.

Learning Objectives

Describe the dosage evolution in intrathecal baclofen therapy in severally disabled CP patients and point different explanations for the long-increase observed.

References

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