Title: Extension of a feasibility study to compare full-time and night-time brace treatment in AIS patients.

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Purpose

Adolescent idiopathic scoliosis (AIS) is a curvature of the spine in the adolescent paediatric patient whose cause is unknown. The goal of bracing treatment in moderate AIS in growing children is to limit progression of the deformity and, ideally, to avoid surgery[1, 2]. Curves of 20° or less before skeletal maturity are considered mild and are reevaluated at 6-month intervals. Curves that progress 5° or 10° or debut 30° curves are considered moderate and bracing is usually recommended because its early use prevents curve progression obviating the need for surgery in most cases [1]. Curves of less than 30° rarely progress after skeletal maturity, but larger curves, especially thoracolumbar or lumbar, may increase throughout the patient's life[1].

During the last decades, different types of braces have been designed. In general, these braces can be divided according to the number of hours of use into two main groups:

1. Full-time brace (Cheneau type), this brace should be worn day and night for a total of between 18h and 23h per day.

2. Night-time brace (Providence type), this brace should only be worn during sleeping hours, a total of about 8h-9h per day.

Although in recent years most studies have concluded that the daytime brace is the most accepted [6, 7] these results are based on retrospective studies. In addition, many studies suggest that the number of hours of use of the brace produces psychological and self-esteem problems in patients, so that adherence to treatment is low, which is detrimental

to the evolution of scoliosis [7]. However, there are no enough scientific evidence differences in effectiveness and adherence between these types of braces.

For this reason, we are performing a feasibility study comparing both treatment groups in an objective manner thanks to the funding of a National FIS grant from the *Instituto de Salud Carlos III* (Ref. PI20/0092). Since the nature of this study was exploratory in the sense that we have no previous data on which to base a formal sample size calculation, we estimated an n of 70 patients according to the recruitment possibilities of eligible patients attending our Spine Unit over a 12-month period.

After performing some initial statistical analyses with the data collected so far, we have seen that it will be necessary to increase the number of patients recruited, which is why we are requesting this extension. With 70 patients it is not enough to obtain conclusive results, so we are looking to extend the study to 120 patients by adding 50 patients in this extension.

If both cases have a similar effectiveness, the night-time brace may be better tolerated as it is worn for fewer hours and the patients are not exposed to psychological stigmas derived from the use of the brace during their time at school or daily activities.

If the results are conclusive, this study could provide important information for the non-surgical treatment of AIS, since bracing treatment is a challenge with adolescent patients, and their parents, who often refuse to use the brace because of the psychosocial problems it generates. Rejection of the treatment produce a worsening of the scoliosis that in many cases leads to surgical treatment.

In resume, and according with the purpose, these are the objectives of the study:

Primary: To compare the efficacy rate of Full-time bracing vs. night-time bracing for the non-surgical treatment of AIS.

Secondary objectives:

a) To compare the adherence in number of hours of both braces by means of thermal sensors in the brace.

b) To compare quality of life by means of SRS22 satisfaction questionnaires.

c) To compare the cost of the number of braces required during the treatment period.

d) To compare the rate of complications between both treatment groups.

Hypothesis

The treatment of adolescent idiopathic scoliosis with the night-time brace is more effective than the Full-time brace in slowing the progression of scoliosis, due to a higher adherence to the treatment.

Methodology

Design:

It is a non-blinded randomized feasibility study

Study subjects:

The initial sample size was 70 patients. Now, we want to recruit 50 more patients to achieve the objective of 120 patients. Taking into account the size and patient's flow of the Hospital Sant Joan de Déu (HSJD), we estimated that we could recruit 50 patients in 8 months.

We will split the 50 patients into two groups:

- **GROUP 1:** Full-time brace, Cheneau type (25 patients)
- **GROUP 2:** Night-time brace, Providence type (25 patients)

Inclusion criteria:

- Males and females < 18 and > 10 years old.
- Patients who attend outpatient consultations at the Spine Unit and present with AIS with curves above 25º and less than 45º with Risser 0-3.
- Patients that are willing to participate voluntarily in the study and can give their written consent

Exclusion criteria:

- Patients over 18 year old and under 10 years old.
- Patients who are in a treatment with another type of orthosis.
- Patients with non-idiopathic scoliosis.
- Patients whose scoliosis appeared before the age of 10.
- Patients with pathological findings in MRI such as syringomyelia or Arnold-Chiari.

- Patients with a history of spine or thorax surgery.
- Patients who have missed control appointments.
- Patients with curves greater than 45º or less than 25º.
- Patients with Risser > 3.
- Patients with congenital anomalies.
- Patients with MMII dysmetries.
- Patients with medical or surgical pathologies that, at the investigator's discretion, do not allow their participation in the study.
- Patients with inability to understand the nature and purpose of the study and/or to agree in writing to participate in the study.
- Patients who are unable to attend the pre-established clinical follow-up.
- Patients who do not wish to participate or give their written consent.

All patients who meet the inclusion criteria and none of the exclusion criteria will be asked to participate in the study, explaining to them what it consists of and the potential risks and benefits that may derive from it, and providing them with this written information on the Patient Information Sheet. Patients who agree to participate will sign in duplicate an informed consent form for the study, a copy of which will be given to them. After this, the patient will be randomized to one of the two study groups, the corresponding strategy will be applied, and he/she will be asked to complete the satisfaction questionnaires.

Variables and Data collection:

The primary analysis according to the main objective is the comparison of the Cobb angles of the main curve(s) before bracing treatment. This variable will be obtained from the radiographs of the patients taken before treatment, at 6 months and at one year after treatment.

The number of hours that the patients wear the brace will also be collected. For this purpose, thermal sensors will be installed in the brace to store this information, which will be exported every 3 months during the orthopaedic check-up visits.

Another of the main variables of this study is the result of the patient outcome questionnaires SRS-22 and visual analogue scale (VAS). Patients will complete these questionnaires before treatment, at 6 months and at one year of treatment, that is, every time they come to the hospital for the usual check-ups during this treatment. The results of these questionnaires will allow us to assess the psychological and self-esteem problems derived from this type of treatment.

	Day 1	3 months	6 months	9 months	1 year
Questionnaires	X		X		X
Radiographs	X		X		X
Reading of thermal sensors		X	X	X	X

Data analysis

First, a descriptive analysis of the variables collected in the study will be performed. Continuous variables will be expressed as a measure of central tendency: mean and/or median and a measure of dispersion: standard deviation and range. Qualitative variables will be expressed as counts and percentages. The sample will be checked to ensure that it follows a normal distribution using appropriate methods.

The primary analysis of this study will consist of comparing the radiological values of the magnitude of the curve between the two groups. This analysis will be performed with Student's t-test.

For the analysis of the secondary objectives, the relevant tests will be performed according to the type of variable: the statistical analysis of qualitative variables will be performed using the Chi^2 test, applying the Yates correction if appropriate. For qualitative variables, parametric (t-test) or non-parametric (Mann-Whitney U) tests will be used depending on their applicability.

In all analyses, the level of significance is set at $p < 0.05$.

Study development:

This study is divided in two work packages (WP):

WP_1: Recruitment and data collection

Duration: 20 months

Tasks:

- Recruitment and collection of variables in the database (months 1-8)
- Follow-up during 1 year for each patient and registration of variables in the database (months 3-20)

$\underline{WP_2}$: Statistical Analysis

Duration: 1 month

Task:

- Statistical analysis of data extracted from the database (month 21)

We estimate that the total duration of the study will be approximately 21 months.

	Months 1-20	Month 21
WP1: Recruitment and data registration		
WP2: Statistical Analysis		

Short literature review

Scientific studies with evidence indicate that bracing and surgery can alter the outcome of scoliosis compared to observation. The goal of bracing treatment in moderate AIS in growing children is to limit progression of the deformity and, ideally, to avoid surgery. Curves of less than 30° rarely progress after skeletal maturity, but larger curves, especially thoracolumbar or lumbar, may increase throughout the patient's life [1]. Fusion with instrumentation is indicated in growing patients with curves greater than 45° or for curves of 50° or greater after skeletal maturity and for those who continue to progress after bracing is stopped.

Brace correction of spinal curves is known to occur through the shaping of the spine, trunk and rib cage during growth, specifically by transverse forces to correct these curves with control. The application of transverse forces and curve correction have an additive effect in improving critical load and spinal stability [2].

The Milwaukee type brace was developed by Blount and Moe during the 1940's as a substitute for postoperative casting in scoliosis surgery and was subsequently adapted for non-surgical use in adapted for non-surgical use in patients with neuromuscular scoliosis and AIS. This CTLSO (cervical-thoracic-lumbar- sacral orthosis) consisted of a moulded pelvic support which was attached to a metal frame with lateral supports and on padded trapezes with axillary level braces (for curves with the apex above T7). An occipital and mandibular support was used to stabilise the head and create traction forces; however, the effectiveness of these components was later disproved[3].

In the 1970's, Boston Children's Hospital developed the Boston Brace, which consisted of six prefabricated pelvic and thoracolumbar modules prefabricated in polypropylene. The pelvic module is shaped based on the radiological findings and the radiological findings and pressure patches are added to the apex of the curve[4]. Nowadays, the Boston brace is the most widely used brace for the treatment of AIS around the world, with more than 16 prefabricated models available and marketed under different names (including the Cheneau as it is known in Spain). The advantages of the Boston type brace are rapid fabrication, 50% curve correction and a better acceptance than with the Milwaukee brace[5].

The Charleston and the Providence type braces were originally used as an alternative to the full-time brace for thoracolumbar or simple lumbar curves. During production, the orthopaedic surgeon maintains pressure on the patient's apex while applying a force contralateral to the curve above it. Correction of more than 75% of the curve is

considered adequate. These braces are considered to be for night use as their forces are applied with the patient in decubitus, their position being inadequate in standing position.

The only prospective controlled study of bracing treatment was presented in 1993 and published in 1995 by Nachemson and Peterson[6]. In this multicentre study supported by the SRS (scoliosis research society), 286 girls were divided into 3 groups consisting of: (1) no treatment of any kind; (2) bracing treatment of at least 20 hours/day until the end of growth; and (3) electrical stimulation. Although the results with electrical stimulation were not different from group (1), the investigators were able to show that bracing significantly altered the natural history of AIS ($P<0.0001$). Curve progression of 5 degrees or more was observed in 26% of patients treated with bracing, 67% in those treated with electrical stimulation and 66% in untreated patients, demonstrating a clear advantage of bracing. Because full-time bracing (23 hours/day) is difficult for adolescents to tolerate, many centres have modified the protocol to 16 hours/day[7], without finding an appreciable difference in the risk of progression between 23 and 16 hours/day. 23 and 16 hours/day.

The studies described show that bracing can be effective in the non-surgical management of AIS, especially for mild to moderate curves (20 to 35°) and alters the natural history of curve progression in immature patients.

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