ABOBOTULINUM TOXIN-A PROSPECTIVE RANDOMIZED DOUBLE-BLIND MULTICENTER STUDY FOR DEGENERATIVE COXARTHROSIS

Roberto Eleopra[a,*], Sara Rinaldo[a], Grazia Devigili[a], Christian Lettieri[a], and the BOLD Italian Study Group[b]

[a]*Neurological Unit, Neurosciences Department, S. Maria Misericordia University Hospital, Udine, Italy;* [b]*BOLD Italian Study Group, Udine, Foggia, Pergine-TN, Savona, Italy*

INTRODUCTION AND OBJECTIVES

Hip osteoarthritis (HOA) arises from degeneration of articular cartilage with subsequent changes in joint bone causing deformation and blockage of the hip joint. Before the development of total hip arthroplasty (THA), HOA was commonly treated by Voss operation (1952), a surgical procedure that included osteotomy of the femur and/or the contracted pelvis. Our preliminary, open-label study[1] reported that a focal treatment with BoNT/A in the adductor muscles of subjects with HOA decreased the pain and improved hip mobility.

The **aim of this study** was to confirm these data in a multicenter, randomized, phase III, double-blind, placebo-controlled study.
The first objective was to evaluate the efficacy of abobotulinumtoxinA (500 international units [IU]) in improving the Harris Hip Score (HHS) in patients with HOA.
A second objective of study was to evaluate the temporal profile of the clinical outcomes with respect to reducing pain and improving joint mobility and quality of life.

METHODS

Study Population

The inclusion criteria were: subjects with HOA as defined by the Kellgren-Lawrence (KL) coxarthrosis radiological classification; age 18-80 years; voluntary signed written consent; no previous surgical treatment; HHS score > 20; Visual Analogue Scale (VAS) rating >4 (minimal value defined as "significant pain").

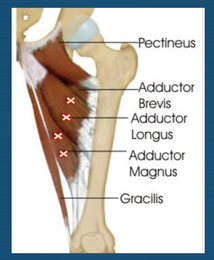
The exclusion criteria were: history of allergy; pregnancy; previous treatment with BoNT/A; physiotherapy or articular injections in the previous 60 days; relevant central or peripheral neurological diseases; apparent remission of coxarthrosis within 3 months; changes in analgesic oral therapy in the previous 4 weeks.

Study design

The duration of the study was 9 months (mo): 6 mo to enrolment and 3 mo for follow-up. The clinical assessment was done at time 0, 2, 4, and 12 weeks (w) after treatment using the HHS, VAS, Short Form 36 (SF-36), and Medical Research Council (MRC) Scales. Safety was assessed through the collection of adverse events (AEs), clinical and biochemical evaluations, and changes in vital signs.
Patients enrolled were randomized into two treatment groups: a drug-treated (DG) group and a placebo-treated group (PG).
The primary efficacy variable of the study was HHS score at week 4 post-treatment. The secondary variables were VAS score, MRC value, and SF-36 score at weeks 2, 4, and 12 post-treatment; and HHS score at weeks 2 and 12 post-treatment. Concomitant analgesic treatments were authorised if they had been used at a stable dose for at least 4 weeks before enrolment and were used throughout the study.

METHODS

Treatment procedures

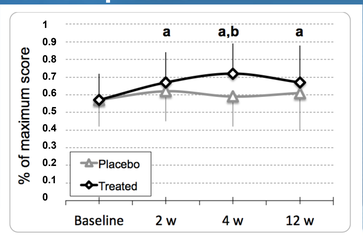


The DG group received 400IU of AbobotulinumtoxinA (500IU diluted in 2 ml of saline solution 0.9%, concentration of 250U/ml): 250 IU slowly injected in the adductor longus muscle in two different points under electromyographic guide; 150 IU injected slowly in the adductor magnus muscle in two different points under EMG guide. The PG group received injections of saline solution 0.9% using the same volume, sites and injections procedure of DG group.

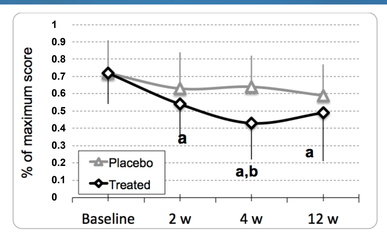
RESULTS

We included 46 participants: 31 in the DG group (16 women and 15 men) and 15 in the placebo group (11 women and 4 men).
The HHS and VAS findings were significant improved at 4 weeks to the treatment in the DG group compared with the PG group ($p<0.05$; Fig 1 and 2, Table). No AEs has been reported. Values for weight, height, age, and KL, MRC, and SF-36 scores (both physical and mental components) were similar between the groups at baseline with no significant differences (Table 1).

Harris Hip Score



VAS values



Data are calculated as percentage of maximum score (100) and presented as mean ±standard deviation. Placebo group, n =15 and Treated group, n =31. **a**, statistically significant difference with the corresponding baseline value (**a**) or with the corresponding Placebo group value (**b**).

Scales	Group	Time point				
		Baseline	2 w	4 w	12 w	Diff.
HHS	Placebo	60 (45;66)	65 (46;69)	66 (46;67)	62 (48;66)	**NS**
	Treated	56 (44;67)	62 (56;78)*	74 (60;86)*	66 (53;87)*	**p=0.000**
	Diff.	**NS**	**NS**	**p=0.026**	**NS**	
VAS	Placebo	7.2 ±1.9	6.3 ±2.1	6.4 ±1.8	5.9 ±1.8	**NS**
	Treated	7.2 ±1.8	5.4 ±2.3*	4.3 ±2.1*	4.9 ±2.8*	**p=0.000**
	Diff.	**NS**	**NS**	**p=0.001**	**NS**	
MRC	Placebo	5 (4;5)	5 (4;5)	5 (5;5)	5 (5;5)	**NS**
	Treated	5 (5;5)	5 (5;5)	5 (5;5)	5 (5;5)	**NS**
	Diff.	**NS**	**NS**	**NS**	**NS**	
SF-36 (PC)	Placebo	34.0 (31.1;38.7)	34.3 (28;42.3)	33.6 (29.0;42.3)	34.4 (25.3;42.7)	**NS**
	Treated	30.3 (22.2;38.1)	32.4 (28;40.0)	35.0 (26.9;47.2)	36.8 (30.4;43.0)*	**p=0.05**
	Diff.	**NS**	**NS**	**NS**	**NS**	
SF-36 (MC)	Placebo	40.2 (36.8;48.1)	43.4 (37.7;49.0)	39.0 (35.0;49.3)	47.0 (36.7;54.0)	**NS**
	Treated	45.2 (36.0;55.9)	47.1 (34.7;54.1)	46.2 (33.8;54)	49.3 (38.0;55.5)	**NS**
	Diff.	**NS**	**NS**	**NS**	**NS**	

Data are presented as median (25^{th};75^{th} percentiles) or mean ±standard deviation.
Placebo group, n =15 and Treated group, n =31. **Diff. :** significance of the difference between the groups within each time point, or over time within either group.
* : statistically significant difference with the corresponding baseline value ($p<0.05$, at least).
NS, difference not statistically significant.
SF-36(PC) = Physical component Index; **SF-36 MC SF-36 (MC)** Mental component Index

Conclusions

In HOA, abobotulinumtoxinA injection in muscles involved in hip movements enables a substantial and immediate restoration of the best functional activity of the hip with remarkable benefits in the mobility of the joint and a reduction of pain. Therefore, this therapy is useful in delaying THA or improving mobility and pain for patients awaiting surgery.

References
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