NUTRITIONAL SUPPLEMENTATION WITH SALICORNIA EXTRACTS AS A PREVENTION STRATEGY IN PATIENTS AT HIGH CEREBROVASCULAR RISK

Ana Mª Nájar[1], Marina Romero[1], Soledad Perez[1], Reyes de Torres[1], Cristina López[1], Carmen Domínguez[1], Rosa Acevedo[1], Carmen del Río[1], Joan Montaner[1]

1 Neurovascular Research Laboratory. Institute of Biomedicine of Seville (IBiS), Hospital Universitario Virgen del Rocío, CSIC, Universidad de Sevilla, Sevilla, Spain; Department of Neurology, Hospital Universitario Virgen Macarena, Seville, Spain.

INTRODUCTION

Stroke is an acute cerebrovascular event that occurs when a blood vessel that carries oxygen and nutrients to the brain bleeds or is blocked by a clot or bleeds resulting in tissue damage due to ischemia. Despite scientific evidence shows the importance of dietary polyphenols in the prevention of several diseases, only 1 in 10 people meets the daily intake of fruit and vegetables that would provide the necessary amount of polyphenols. *Salicornia ramsissima* is a halophyte plant that manages to live in salinity conditions thanks to adaptive responses, such as the production of polyphenols. This plant has been traditionally used in food preparation in our region, which makes it safe for human consumption. Recent studies in our laboratory have shown that supplementation with an ethanolic extract of Salicornia in experimental models of stroke in flies and mice has a clear neuroprotective effect. For these reasons, we have started the process of translating our findings to humans by administering oral supplements of the ethanolic extract of Salicornia from different regions (Huelva and Portugal). We will target healthy subjects and patients with mild strokes or those with slight neurological involvement to assess the safety and to study its correlation with the clinical evolution of the disease; we will also explore the effect on vascular risk biomarkers.

METHODS

Characteristics of Clinical Trial: Multicenter, randomized, triple-blind, parallel-group, placebo-controlled pilot trial aimed at evaluating the efficacy and safety of the administration of a food supplement based on ethanolic *Salicornia ramosissima extracts* (from Huelva and Portugal) versus placebo in four substudies (details in Table 1).

Treatments of Clinical Trial / Frequency of administration / Dose / Pharmaceutical form: *Salicornia ramosissima* extracts from Huelva or *Salicornia ramosissima* extracts from Portugal or placebo / once daily / 1 g / 2 capsules.

Study Arm	Study population	Study subjects (n)	Randomization	Treatment period
A	Healthy volunteers	90	Huelva extract, Portugal extract or placebo (1:1:1)	3 months
B	Patients with transient ischemic attack (TIA) or minor stroke	80	Portugal extract or placebo (1:1)	11 months
C	Patients with small vessel brain disease (lacunar stroke)	80	Huelva extract or placebo (1:1)	12 months
D	Patients who have suffered a non-disabling stroke and are going to receive carotid angioplasty and stenting (CAS)	100	Huelva extract or placebo (1:1)	7-30 days (pre-CAS)

Table 1. Summary of trial design.

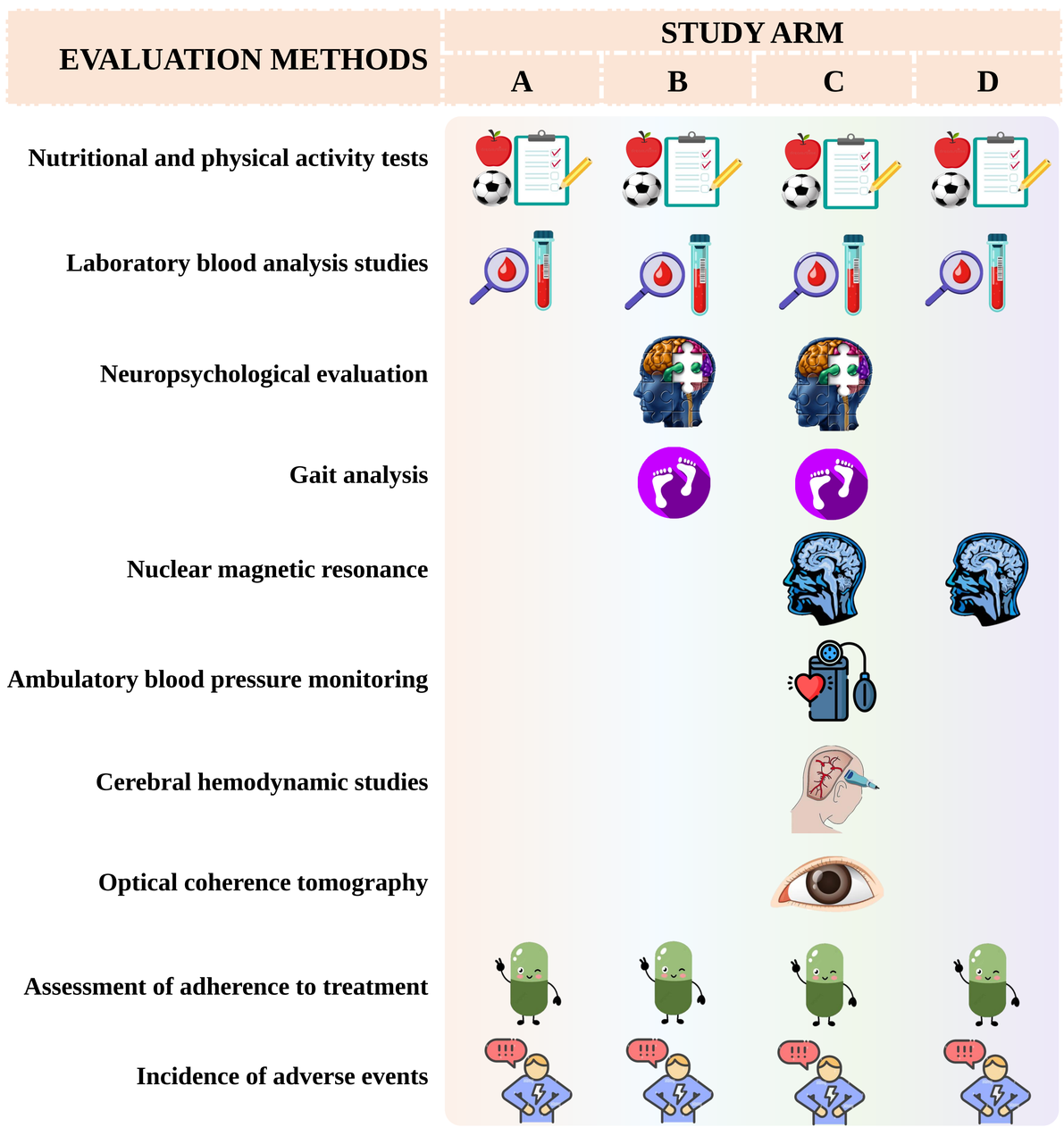

Figure 1. Evaluation methods in each study arm to assess the safety and efficacy of the experimental treatment.

RESULTS

The study began in September 2022. Study arm A ended in February 2023 and participants for arms B, C and D are currently being recruited (Figure 2).

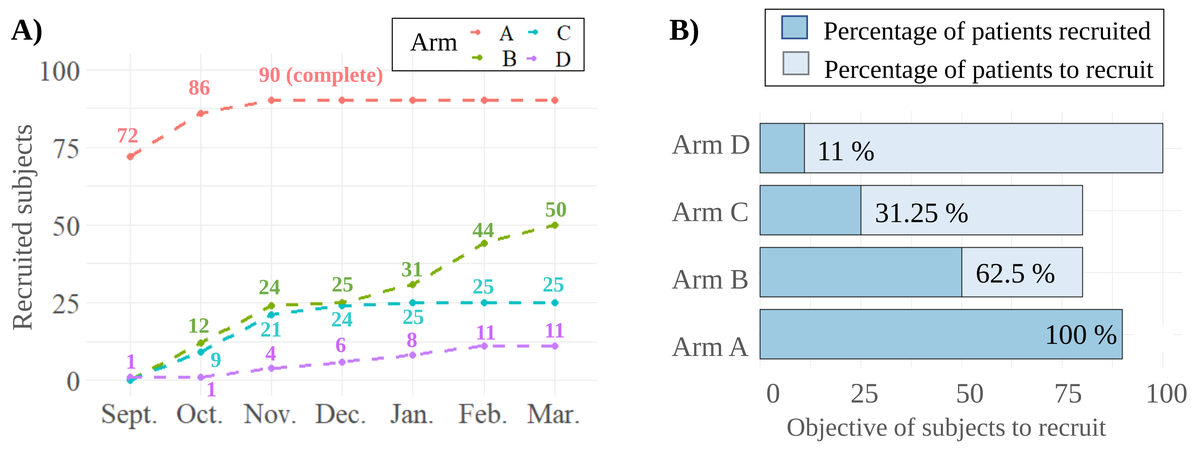

Figure 2. A) Recruitment of patients since the start of the study. B) Subjects recruitment as percentage of the objective.

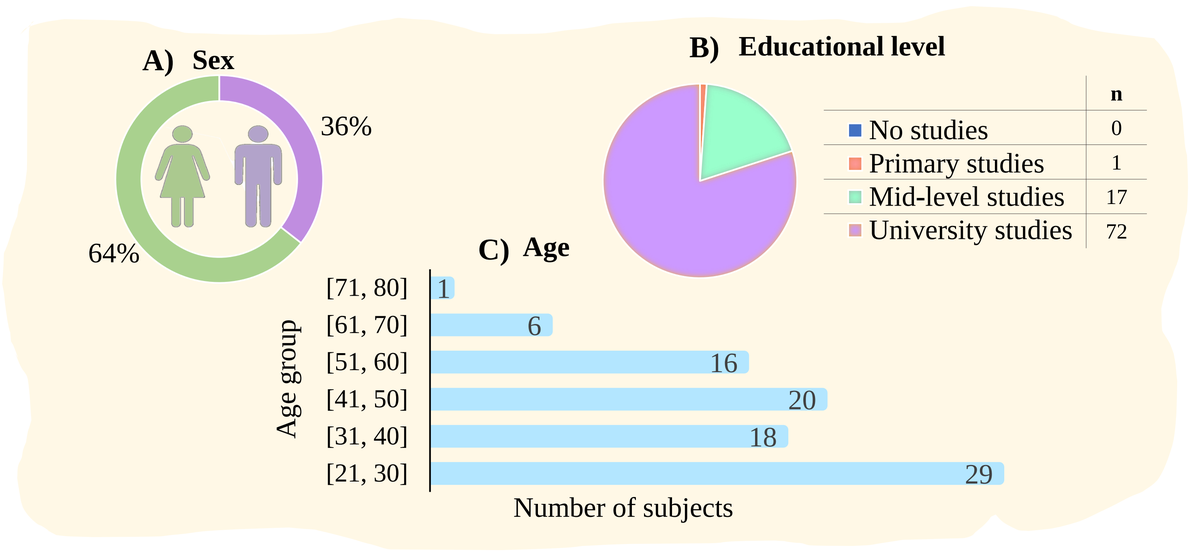

Figure 3. Demographic data of study arm A.

The results of the study arm A are being analyzed blindly. There is no significant difference in the incidence of adverse events between the three treatments (table 2) and no participant in arm A has suffered any serious adverse event.

Adverse effects and side-effects	Treatment 1	Treatment 2	Treatment 3
Gastrointestinal disturbance	5	6	2
Neurological alteration	0	1	1
Excretory system disorder	4	0	1
Circulatory system disturbance	0	2	0
Menstrual disturbances	0	3	0

Table 2. Adverse events described in arm A for each treatment group in order of frequency.

In addition to routine blood tests (which include general biochemistry with lipid profile and liver proteins, complete blood count and specific proteins), other laboratory parameters such as total blood polyphenols, oxidative stress markers (such as 8-hydroxy-2'- deoxyguanosine) and cardiovascular damage (using the Olink target 96 cardiovascular panel) will be determined.

CONCLUSIONS AND FUTURE PERSPECTIVES

The study is progressing as expected. After three months of treatment, no participant in arm study A reported any serious adverse event. Also, currently, no patient included in the other arms, some of whom have already completed five months of treatment, has reported any serious adverse event.

The available data from our clinical study will determine the safety of the extract and may help to understand the mechanism of action of this type of compounds.

This study could be the first step in the development of a nutritional strategy for long-term prevention of neurovascular disease in population at high vascular risk.

More info here: SEARCH http://proyectosalicornia.com/ SCAN

REFERENCES AND AKNOWLEDGEMENT

García-Rodríguez P. et al. Diet Supplementation with Polyphenol-Rich *Salicornia ramosissima* Extracts Protects against Tissue Damage in Experimental Models of Cerebral Ischemia. *Nutrients* **2022**, *14*, 5077.

Nájar, A.M. et al. A Review on Polyphenols in *Salicornia ramosissima* with Special Emphasis on Their Beneficial Effects on Brain Ischemia. *Nutrients* **2023**, *15*, 793.

The authors received financial support from “CSF-Proyectos estratégicos de I+D+i. Proyectos cofinanciados en un 80% por fondos del Programa Operativo FEDER de Andalucía 2014–2020”, grant number PE-0527-2019. This research was partially funded by “Consejería de Transformación Económica, Industria, Conocimiento y Universidades (CTEICU) y 80% cofinanciados por la UE, PO FEDER Andalucía 2014–2020”, grant number [PY20_01351]. C.R. received financial support from the Sara Borrell program funded by ISCIII, grant number CD21/00148. M.R. received financial support from the PFIS program funded by ISCIII grant number FI22/00202.