Teaching Subdirectorate
Research Coordination

RECEPTION DATE
PROVISIONAL REGISTRATION OPD
DO NOT FILL

REGISTRATION OF THE INVESTIGATION PROTOCOL

1. GENERAL DATA

1.1 TITLE OF THE PROJECT

"Effect of intravenous iron repletion on renal function in patients with iron deficiency and acute kidney injury, clinical trial"

1.2 START DATE FINISH DATE

Start August 2022, end December 2023

1.4 PRINCIPAL INVESTIGATOR

NAME : LAST NAME Chávez

PATERNAL:

MATERNAL: Iniguez

NAMES (S): Jonathan Samuel

SPECIALTY: Nephrology

SERVICE: Nephrology

1.5 THESIS DIRECTOR

NAME : LASTNAME Chávez
PATERNAL:

MATERNAL: Iniguez

NAMES (S): Jonathan Samuel

SPECIALTY: Nephrology

SERVICE: Nephrology

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1.6 CO-MANAGER

NAME : LAST NAME Ron

PATERNAL: Magaña

MATERNAL:

NAMES (S): Ana Lucia

SPECIALTY: Hematology

SERVICE: Hematology

1.7 ADVISOR

NAME : LAST NAME

PATERNAL:

MATERNAL:

NAMES (S):

SPECIALTY:

SERVICE:

1.8 PARTICIPATING INSTITUTIONS

INSTITUTION: Civil Hospital of Guadalajara Fray Antonio Alcalde

AGREEMENT: without agreement

INSTITUTION:

AGREEMENT:

INSTITUTION:

AGREEMENT:

2.1 PROJECT SUMMARY

The purpose of this clinical trial is to carry out research on the effect on hemoglobin and renal function of the intravenous administration of iron dextran as a repletion strategy in patients with iron deficiency anemia and acute kidney injury, in which the patient You may benefit from this medication since it is expected to correct anemia, iron deficiency and renal function parameters, when compared with a control group (placebo), the safety of the drug will also be evaluated by recording adverse effects. I will point out with the patient the risks and benefits of including her in this type of study and I will answer all the doubts that arise, and I will also immediately report any serious adverse effect to the research ethics committee.

2.2 INTRODUCTION

Acute kidney damage is a complication that occurs in up to 30% of hospitalized patients. Iron deficiency has a high incidence in the population of critically ill patients and has been associated with multiple complications such as the development of anemia and renal dysfunction. The presence of iron deficiency, anemia and acute kidney injury is a common combination in critically ill patients and iron deficiency has been shown to promote mitochondrial dysfunction and this can be improved with intravenous iron correction, as has happened in clinical trials of patients with failure exacerbated cardiac arrest, improving its clinical evolution.

The kidney is the second organ with the most mitochondria and mitochondrial dysfunction is a new therapeutic goal in acute kidney injury. It is possible that this combination is associated with an unfavorable clinical course in these patients.

2.3 JUSTIFICATION

There is insufficient evidence for the implementation of intravenous iron in order to improve the parameters of iron deficiency anemia in patients with acute kidney injury.
To our knowledge, there is no clinical trial that has explored our objectives.

2.4 SCIENTIFIC BACKGROUND

Acute kidney injury (ARD) is a serious complication that is independently associated with poor outcomes [1, 2]. Approximately one in five patients with non-severe sepsis develops AKI [3], which increases to two-thirds in critically ill patients. About 50% of ICU patients with AKI die (4-12), and those who survive an episode of AKI have a higher risk of progressing to chronic kidney disease (CKD). Currently, there are few pharmacological therapeutic options available to prevent or treat AKI, and management is limited to alleviating hemodynamic and toxic renal lesions. support measures, such as dialysis.

Iron deficiency occurs in up to 30% of hospitalized patients and has been linked to worse clinical evolution, even in the absence of anemia. This iron deficiency is worse even when anemia figures are reached. It has been documented that critically ill patients develop anemia as part of the process of their pathology. It has been seen that during processes of exacerbation of pathologies such as heart failure, the administration of intravenous iron avoids the probability of hospitalization and clinical evolution (13-16). It has been shown that in DRA there is mitochondrial dysfunction (17), specifically in the renal tubule where the greatest amount of mitochondria isconcentrated,

2.5 OBJECTIVES

Primary objective:

The endpoint of interest was the proportion of patients meeting one or more criteria for Major Adverse Kidney Events within 30 days (MAKE30): in-hospital mortality; receipt of new RRT; or persistent renal dysfunction.

In hospital mortality was defined as death from any cause prior to hospital discharge censored at 30 days after ICU admission. Receipt of new RRT was defined as receipt of any modality of RRT between ICU admission and the first of (1) hospital discharge or (2) 30 days in a patient not known to have received RRT prior to ICU admission. Persistent renal dysfunction was defined as a final serum creatinine value before hospital discharge (censored at 30 days after enrollment) that was ≥ 200 % of the baseline creatinine value.

And will be evaluated at 60 and 90 days.

Secondary objectives:all the following will be at hospital discharge and 28 days after hospital discharge between the intervention group (iron replacement) compared to the control group (placebo).

- ferritin value, (pg/dL)
- transferrin saturation (%)
- Hemoglobin (g/dL)
- serum creatinine (mg/dL)
- start of renal support therapy (any type of renal support such as: intermittent hemodialysis, peritoneal dialysis or continuous therapies)
- recovery of renal function, considered as a decrease in serum creatinine and approaching <0.3mg/dL of basal creatinine
- death

Exploratory objectives:

- safety of intravenous iron administration compared to placebo: assessed by the occurrence of adverse events such as allergic reaction, hypotension, dyspnea, rash, erythema. These will be evaluated during

drug administration and during hospitalization frequently every 24 hours by the nephrology staff, including the study investigators.

2.6 HYPOTHESIS

Our hypothesis is that intravenous iron dextran repletion during the treatment of acute kidney injury will improve renal function parameters, iron deficiency, anemia, and also that it will be safe compared to placebo.

2. DESIGN OF THE STUDY

Randomized placebo-controlled clinical trial, randomization method in blocks of 5 by frequency of occurrence. In patients with acute kidney injury, they will be randomized to receive the administration of intravenous iron dextran in a single exhibition according to the Mg provided by the Virizzi formula compared to placebo.

The sample size determined 55 patients per group, with a standard deviation of 1.5.

$n = [(Z_{\alpha/2}+z_{\beta})_2 \times \{2(or)_2\}]/ (\mu 1 - \mu 2)_2$

$n = [(1.96+ 0.84)_2 \times \{2(1.5)_2\}]/ (10.8 - 10)_2$

n=**55,125**

n = sample size required in each group μ1-μ2 =

clinically significant difference = 0.8 or = standard

deviation = 1.5

$z_{\alpha/2}$: 1.96

z_{β}: 0.84

The randomization process by random assignment was carried out with the tool NCI Clinical Trial Randomization Tool:

https://ctrandomization.cancer.gov/

Sequences have been generated for each arm and stratum of your trial using maximum asymptotic randomization.

group	Subject	Assignment	Assigned Arm Index
all	1	placebo	2
all	2	Dextran Iron	1
all	3	Dextran Iron	1
all	4	placebo	2
all	5	Dextran Iron	1
all	6	placebo	2
all	7	placebo	2
all	8	Dextran Iron	1
all	9	placebo	2
all	10	Dextran Iron	1
all	11	Dextran Iron	1
all	12	placebo	2
all	13	Dextran Iron	1
all	14	Dextran Iron	1
all	15	placebo	2
all	16	Dextran Iron	1
all	17	Dextran Iron	1
all	18	placebo	2
all	19	placebo	2
all	20	Dextran Iron	1
all	21	Dextran Iron	1
all	22	placebo	2

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all	23	Dextran Iron	1

all	24	placebo	2
all	25	placebo	2
all	26	placebo	2
all	27	Dextran Iron	1
all	28	placebo	2
all	29	placebo	2
all	30	Dextran Iron	1
all	31	placebo	2
all	32	Dextran Iron	1
all	33	placebo	2
all	34	placebo	2
all	35	placebo	2
all	36	Dextran Iron	1
all	37	Dextran Iron	1
all	38	Dextran Iron	1
all	39	Dextran Iron	1
all	40	Dextran Iron	1
all	41	placebo	2
all	42	placebo	2
all	43	Dextran Iron	1
all	44	placebo	2
all	45	placebo	2
all	46	Dextran Iron	1
all	47	Dextran Iron	1
all	48	placebo	2
all	49	Dextran Iron	1
all	50	placebo	2
all	51	placebo	2
all	52	Dextran Iron	1
all	53	placebo	2
all	54	placebo	2
all	55	Dextran Iron	1
all	56	placebo	2
all	57	Dextran Iron	1
all	58	Dextran Iron	1

all	59	Dextran Iron	1
all	60	Dextran Iron	1
all	61	placebo	2
all	62	placebo	2
all	63	Dextran Iron	1
all	64	placebo	2
all	65	Dextran Iron	1
all	66	Dextran Iron	1
all	67	placebo	2
all	68	placebo	2
all	69	placebo	2
all	70	placebo	2
all	71	placebo	2
all	72	Dextran Iron	1
all	73	Dextran Iron	1
all	74	Dextran Iron	1
all	75	Dextran Iron	1
all	76	placebo	2
all	77	placebo	2
all	78	placebo	2
all	79	Dextran Iron	1
all	80	Dextran Iron	1
all	81	placebo	2
all	82	Dextran Iron	1
all	83	Dextran Iron	1
all	84	placebo	2
all	85	Dextran Iron	1
all	86	placebo	2
all	87	Dextran Iron	1
all	88	placebo	2
all	89	Dextran Iron	1
all	90	Dextran Iron	1
all	91	placebo	2
all	92	Dextran Iron	1
all	93	placebo	2

Version 2.0, 29 June 2023

all	94	placebo	2
all	95	placebo	2
all	96	placebo	2
all	97	placebo	2
all	98	Dextran Iron	1
all	99	Dextran Iron	1
all	100	placebo	2
all	101	Dextran Iron	1
all	102	placebo	2
all	103	Dextran Iron	1
all	104	Dextran Iron	1
all	105	placebo	2
all	106	placebo	2
all	107	placebo	2
all	108	Dextran Iron	1
all	109	placebo	2
all	110	Dextran Iron	1
all	111	Dextran Iron	1
all	112	placebo	2
all	113	Dextran Iron	1
all	114	Dextran Iron	1
all	115	placebo	2
all	116	placebo	2
all	117	Dextran Iron	1
all	118	Dextran Iron	1
all	119	placebo	2
all	120	placebo	2

, and members of the nephrology staff, blinded to the allocation groups, administered the drugs to each patient every day.

All patients will have a detailed medical history and physical examination. Complete blood count, serum creatinine, serum urea, serum urea nitrogen, serum electrolytes, and blood test parameters were measured daily.

urine. The test will be presented in accordance with the CONSORT 2010 explanation and elaboration guide. Continuous variables will be presented as mean (SD) when they are normally distributed or as medians (interquartile range [IQR]) in the case of abnormal distribution, following the test Shapiro-Wilk. One way ANOVA was used to compare differences between groups. Categorical variables expressed as proportions will be compared with Fisher's x2 test or the exact test, as appropriate. For the rest of the tests, p values were two-tailed; p <0.05 will be considered statistically significant. Statistical analysis and graphics will be performed with the statistical software MedCalc (Ostend, Belgium, see 19.1.3).

4.1 INCLUSION AND EXCLUSION CRITERIA

criteria of **inclusion**:

Hospitalized patients with ARD, will be defined as the diagnosis using the KDIGO criteria of serum creatinine (Cr); Patients with AKI > 18 and <85 years, baseline creatinine <2 mg/dL and with written informed consent will be included.

Iron deficiency according to the criteria of the 2: serum iron <13 ng/dL, transferrin saturation <20%.

4.2 VARIABLES UNDER STUDY

Exposure variable is the administration of iron dextran in an infusion bolus as a loading strategy.
Dependent variables will be the value of renal function by eGFR, hemoglobin, iron deficiency, renal function and safety parameters.

4.4 ETHICAL ASPECTS

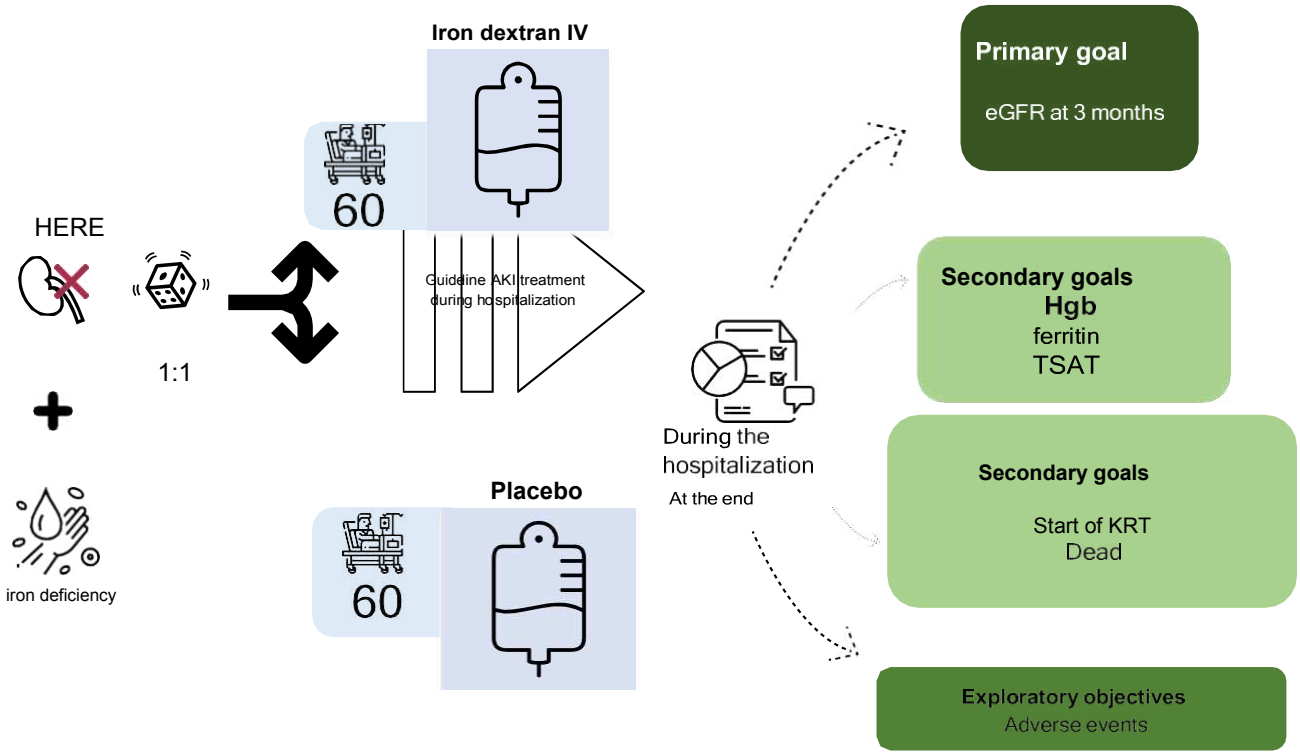
YO.	RESEARCH WITHOUT RISK RESEARCH WITH	
II.	MINIMAL RISK RESEARCH WITH RISK	xxxx
III.	GREATER THAN MINIMAL	

ANNEX LETTER OF CONSENT

Teaching Subdirectorate
Research Coordination

Letter of consent attached to the protocol

Visual summary of the study



5.1 SCHEDULE OF ACTIVITIES ATTACH

FORMAT

subd color	Year Teaching direction Research dination	2023										2022							2024
	Month	mtor	TO B. R.	m TOO AND	J RO No L	J TO RG. EITHER	S A P	EITH R D. yo	N EITH R uV	.D Yo C.	AND No AND	D B.	T EITHER G	DS AND P	EITHER D. you	No EITHER V	D. Yo C.	AND No.	D AND
	Definition of the question of investigation																		
	construction of approach of problem																		
	population selection study																		
	Database creation																		
	data collection																		
	data ordering																		

														[redacted]
Analysis of data														
Comparison with theoretical referents														
Final report of the investigation														

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