A prospective, double-blind, randomized pilot study evaluating the effects of Toradol versesplacebo for pain control after donor nephrectomy.[820]

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Introduction

This is a randomized controlled trial (RCT) comparing placebo to toradol treatment for pain control after donor nephrectomy. The primary outcomes of interest include narcotic use and length of stay (LOS), where the hypothesis is that toradol will reduce post-operative narcotic use and LOS. The study was powered on the safety outcome allowing for a limited creatinine increase on post-operative day 1. The rationale being that regardless of toradol efficacy, if it was not safe to use then it would not be adopted into clinical practice.

Investigator's Description

Completed pilot study now need power calculation for a prospective, double-blind, randomized pilot study evaluating the effects of Toradol, and Lyrica verses placebo for pain control after donor nephrectomy.

Project Endpoints

Paper, ASTS abstract 11/22/17

Data

The raw data set is at: Campsen_Jeffrey_820_toradol_rct\Data\Raw\Torpedo II Study.xlsx, the analysis data set is: Campsen_Jeffrey_820_toradol_rct\Data\Torpedo II Study - Recoded.xlsx.

Exposure Variables

The variable "group" in the analysis data set describes the exposure group, toradol versus placebo.

Outcomes

cr.ratio = Construct this safety outcome of fold change in creatinine within the toradol group (pre-op/post op day 1), constructed from the variables cr.pre and cr.pod1.

cum.me = The post-operative narcotic usage outcome in morphine equivalents (ME).

postop.los = Hospital LOS.

Inclusion/Exclusion

None, all patients in the data set were included in the analysis

Research Objectives

1. Compare patient characteristics: age, height, weight, bmi, sex, race, operative time, side, opioid usage, hct pre, hct pacu, hct pod1, hct diff, hct ratio, cr pre, cr pod1, cr ratio, postop nausea, failed foley and postop LOS between toradol and control groups.
2. Assess the creatinine safety outcome using a non-inferiority test that the fold change is at most two-fold, or alternatively for the pre-surgery creatinine group to be ≥0.5 times the post-surgery.

Analyses

1. For the comparison of patient characteristics, we will use the R functions developed by our center to implement simple statistical tests selected from the following options: 1=t.test, 2=Wilcox, 3=Chi-square, 4=Fisher's exact, 5=Fisher's exact test with simulation, 6=Exact wilcoxon rank sum test. The following table indicates our results and which test was used for which variable.

Table 1. Summary by group.

Variable*	placebo (N=29)	Toradol (N=33)	P-value	Test
age - Mean (SD)	45.1 (12.2)	43.8 (11)	0.68	1
-Median (IQR)	44 (35, 53)	42 (34, 52)	-	-
-Range	(26, 69)	(25, 66)	-	-
height - Mean (SD)	171.6 (8.9)	169.9 (9.4)	0.47	1
-Median (IQR)	170.2 (166.4, 179)	170.2 (162.6, 172.7)	-	-
-Range	(154.9, 190.5)	(156, 195.6)	-	-
weight - Mean (SD)	79.6 (13.3)	77.7 (16.3)	0.62	1
-Median (IQR)	80.3 (70.5, 88.9)	77.4 (64.5, 88)	-	-
-Range	(56.2, 109)	(50.9, 123)	-	-
bmi - Mean (SD)	26.9 (3.2)	26.6 (4.7)	0.76	1
-Median (IQR)	27.3 (24, 28.9)	27.5 (22.1, 30)	-	-
-Range	(21, 33.4)	(17.1, 34.8)	-	-
sex -Female	17 (59%)	26 (79%)	0.086	3
Male	12 (41%)	7 (21%)	-	-
race -American Indian and Alaska Native	0 (0%)	1 (3%)	0.4	4
Black or African American	0 (0%)	1 (3%)	-	-
Other	3 (10%)	1 (3%)	-	-
White-Caucasion	26 (90%)	29 (91%)	-	-
ethnicity -Hispanic/Latino	2 (7%)	2 (6%)	>0.99	4
Not Hispanic/Latino	27 (93%)	29 (94%)	-	-
optime -Mean (SD)	129.3 (30)	124.7 (27.8)	-	-
-Median (IQR)	124 (110, 135)	116 (110, 128)	0.33	6
-Range	(80, 200)	(99, 245)	-	-
side -Left	20 (69%)	25 (76%)	0.55	3
Right	9 (31%)	8 (24%)	-	-
cum.me -Mean (SD)	62.9 (65.2)	31.1 (25.5)	-	-
-Median (IQR)	45 (25, 70.8)	27 (13, 42.3)	0.006	6

Variable*	placebo (N=29)	Toradol (N=33)	P-value	Test
-Range	(10.7, 343.8)	(0.7, 111)	-	-
hct.pre - Mean (SD)	44.1 (2.8)	43.5 (3)	0.4	1
-Median (IQR)	44.5 (42.1, 45.6)	43.1 (41.5, 44.8)	-	-
-Range	(38.3, 51)	(38.7, 50)	-	-
hct.pacu - Mean (SD)	41.8 (3.4)	39.9 (3.2)	0.023	1
-Median (IQR)	42.2 (39.4, 44.3)	39.5 (38.3, 40.8)	-	-
-Range	(34.9, 47)	(34.4, 48.3)	-	-
hct.pod1 - Mean (SD)	39.8 (3.5)	37.2 (2.7)	0.002	1
-Median (IQR)	40.1 (37.5, 42.4)	36.9 (35.9, 38.2)	-	-
-Range	(33.6, 45.7)	(32.6, 46.3)	-	-
hct.diff - Mean (SD)	4.3 (2.5)	6.3 (2.1)	0.002	1
-Median (IQR)	4.7 (2.5, 5.7)	6.4 (5, 7.3)	-	-
-Range	(-1.9, 9.5)	(1.7, 12.5)	-	-
hct.ratio - Mean (SD)	1.1 (0.1)	1.2 (0.1)	<0.001	1
-Median (IQR)	1.1 (1.1, 1.2)	1.2 (1.1, 1.2)	-	-
-Range	(1, 1.3)	(1, 1.3)	-	-
cr.pre - Mean (SD)	0.9 (0.1)	0.8 (0.2)	0.65	1
-Median (IQR)	0.9 (0.8, 0.9)	0.8 (0.7, 0.9)	-	-
-Range	(0.6, 1.1)	(0.6, 1.2)	-	-
cr.pod1 - Mean (SD)	1.3 (0.3)	1.3 (0.3)	0.87	1
-Median (IQR)	1.2 (1.1, 1.5)	1.2 (1.1, 1.4)	-	-
-Range	(0.8, 1.9)	(0.9, 1.9)	-	-
cr.ratio - Mean (SD)	0.7 (0.1)	0.6 (0.1)	0.19	1
-Median (IQR)	0.7 (0.6, 0.7)	0.6 (0.6, 0.7)	-	-
-Range	(0.5, 1)	(0.5, 0.8)	-	-
postop.nasea -N	5 (17%)	8 (24%)	0.5	3
Y	24 (83%)	25 (76%)	-	-
failedfoley -N	29 (100%)	32 (97%)	>0.99	4
Y	0 (0%)	1 (3%)	-	-
postop.los -Mean (SD)	56.1 (16)	50 (13.5)	-	-
-Median (IQR)	57.3 (50.6, 66.3)	51.5 (46.5, 56)	0.029	6
-Range	(26.4, 82.2)	(23.6, 81.1)	-	-

*Missing values: race =1, ethnicity =2,
Test: 1=t.test, 2=Wilcox, 3=Chi-square, 4=Fisher's exact, 5=Fisher's exact test with simulation, 6=Exact wilcoxon rank sum test

2. The safety analysis was conducted using a 1-sided t-test compared to a 0.5 fold change. Here are the results:

A one-sided t-test shows that the pre-surgery creatinine increase over the post-surgery measure $\left(\frac{\text{HCT Pre-OP}}{\text{HCT Post-OP Day 1}}\right)$ within the Toradol group has a mean fold change of 0.64 (95% CI: 0.62, 0.66), which is over the safety level of a 0.5 fold change (because this is pre/post). The p-value for this test is less than 0.0001, thus the Toradol group meets the safety threshold.

Power Calculation

The primary safety outcome is defined by a creatinine increase on post-operative day 1 of at most 100% (ie, twice the pre surgery measure) in the toradol group. To achieve 90% power at a 2.5% significance level for testing that the post-surgery creatinine increase is at most two-fold (where 1.5 fold is expected), or alternatively for the pre-surgery creatinine group to be ≥0.5 times the post-surgery, we need 17 subjects in the toradol group. This calculation was based on a non-inferiority test (one sided t-test).

Quality Control (QC) Plans

The analysis plan and code was reviewed by two independent statisticians.

SDBC Information

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