«THE EFFICACY AND SAFETY OF SUCROFERRIC OXYHYDROXIDE VERSUS SEVELAMER CARBONATE IN DIALYSIS PATIENTS: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS»

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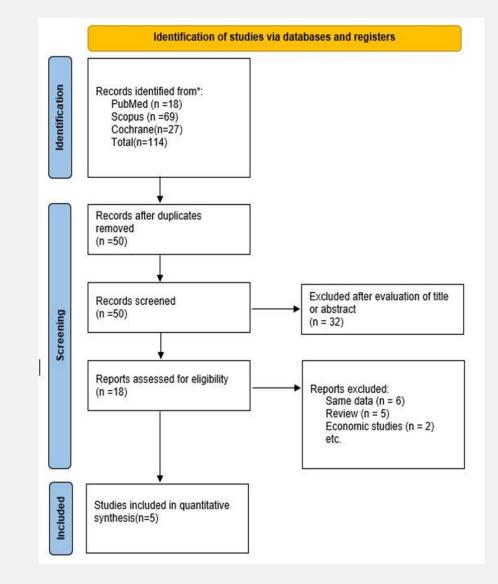
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INTRODUCTION –SCOPE OF THE STUDY

- Phosphate binders are commonly used in patients receiving renal replacement treatment (RRT), aiming to reduce and maintain serum phosphorus
- Chronic kidney disease-mineral and bone disorder (CKD-MBD) has been linked to reduced lifespan and worsened quality of life
- Sevelamer carbonate is the first non-absorbable, non-calcium phosphate binder that has demonstrated satisfactory control of serum phosphorus
- Sucroferric oxyhydroxide is an alternative iron phosphate binder that has the advantage of requiring fewer daily doses to achieve the therapeutic goal
- **Study aim**: to investigate the efficacy and safety of sucroferric oxyhydroxide versus sevelamer carbonate in dialysis patients

METHODS

- Data sources included MEDLINE(PubMed), Scopus, and the Cochrane Central Register of Controlled Clinical Trials from September 2014 to March 2021
- Inclusion criteria: all RCT comparing sucroferric oxyhydroxide versus sevelamer carbonate in adult population receiving RRT
- **5 RCTs** met the inclusion criteria and were analyzed in the meta-analysis
- There were no statistically significant differences in the basic characteristics of the patients between the studies
- Studies included patients undergoing hemodialysis as well as peritoneal dialysis
- Wuthrich's study contained 5 different arms of dosing and they were all included in the final analysis



METHODS

- Effect size was estimated by weighted mean differences (WMD) for continuous data and odds ratio (OR) for dichotomous data (adverse events)
- Heterogeneity was also assessed using the I^2 index as well as the Q statistic
- Based on these indicators, the choice of either the fixed(common) or random effects model was decided accordingly
- All data were analyzed using R-studio

RESULTS

- No statistically significant difference in the change of serum phosphorus serum levels was observed between the 2 drugs {MD: -0.05 mmol/l, 95% CI fixed effects model: -0.1 to 0.00, p-value: 0.0347}.
- As no significant degree of heterogeneity was found ($I^2 = 46\%$ and $\tau^2 = 0.0045$, p-value of Q-statistic=0.06) the fixed effects model was more appropriate
- The prediction interval (-0.25 to 0.12) suggests that future studies will prove that there will be no statistically significant difference between the 2 drugs

	Experimen	tal Control			Weight Weight
Study	Total Mean	SD Total Mean SD	Mean Difference	MD 95%-CI (c	ommon) (random)
Floege 2014	694 -0.70 0.6	500 347 -0.70 0.6300	<u>1</u>	0.00 [-0.08; 0.08]	37.5% 25.5%
Floege 2015	384 0.02 0.52	200 260 0.09 0.5800	¥	-0.07 [-0.16; 0.02]	32.9% 24.5%
Koiwa 2017	100 -0.90 0.5	800 92 -0.73 0.4500		-0.17 [-0.31; -0.03]	13.1% 16.8%
Wuthrich 2013 1.25g	26 -0.04 0.6	00 24 -0.34 0.4900		0.30 [-0.00; 0.60]	2.8% 5.7%
Wuthrich 2013 10.0g	25 -0.65 0.5	00 24 -0.34 0.4900		-0.31 [-0.61; -0.01]	2.7% 5.6%
Wuthrich 2013 12.5g	24 -0.55 0.4	700 24 -0.34 0.4900	- x 1 1	-0.21 [-0.48; 0.06]	3.4% 6.8%
Wuthrich 2013 5.0g	26 -0.35 0.5	700 24 -0.34 0.4900		-0.01 [-0.30; 0.28]	2.9% 5.9%
Wuthrich 2013 7.5g	25 -0.40 0.3	700 24 -0.34 0.4900		-0.06 [-0.30; 0.18]	4.2% 8.0%
Sprague 2018	48 -1.90 1.90	000 52 -2.20 1.8000		- 0.30 [-0.43; 1.03]	0.5% 1.1%
Common effect model	1352	871	•	-0.05 [-0.10; -0.00]	100.0%
Random effects model			\diamond	-0.06 [-0.17; 0.04]	- 100.0%
Prediction interval				[-0.25; 0.12]	
Heterogeneity: $I^2 = 46\%$, τ	$^{2} = 0.0045, p = 0.06$	1		- · · ·	
• , , ,		-	-0.5 0 0.5	1	

Forest plot, mean difference value of serum phosphorus

RESULTS

- No statistically significant difference in the occurrence of adverse events was observed between the two groups (OR:1.06, 95% CI:0.64-1.76, random effect model).
- A significant degree of heterogeneity was found $(I^2=87\%, \tau^2=0.37, p-value of Q-statistic<0.0001)$ indicating that the random effects model is more appropriate
- Due to the significant degree of heterogeneity the prediction interval is particularly wide (0.22 to 5.03) highlighting that future studies will not show differences in the incidence of adverse events between the 2 drugs

	Experin	nental	C	ontrol						Weight	Weight
Study	Events	Total	Events	Total		Odds Ratio)	OR	95%-CI	(common)	(random)
Floege 2014	588	707	264	348		i		1.57	[1.15; 2.15]	25.0%	15.8%
Floege 2015	189	391	205	267	-+			0.28	[0.20; 0.40]	52.9%	15.6%
Koiwa 2017	81	108	70	105		-		1.50	[0.83; 2.72]	7.5%	13.5%
Wuthrich 2013 1.25g	14	26	15	26	<u></u>		6	0.86	[0.29; 2.56]	2.9%	9.2%
Wuthrich 2013 10.0g	18	27	15	26			0	1.47	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	2.1%	9.0%
Wuthrich 2013 12.5g	17	24	15	26			-	1.78	[0.55; 5.77]	1.8%	8.6%
Wuthrich 2013 5.0g	16	26	15	26	1			1.17	[0.39; 3.56]	2.4%	9.1%
Wuthrich 2013 7.5g	13	25	15	26	8			0.79	and the second second	3.0%	9.1%
Sprague 2018	121	130	66	75			•	1.83	[0.69; 4.84]	2.4%	10.2%
Common effect model		1464		925				0.84	[0.70; 1.01]	100.0%	
Random effects model						\Rightarrow		1.06	[0.64; 1.76]	-	100.0%
Prediction interval					_		10. SZ		[0.22; 5.03]		
Heterogeneity: $I^2 = 87\%$, τ^2	² = 0.3723	3, p < 0	.01								
					0.2	0.5 1	2 5				

Forest plot, odds ratio -all adverse events

RESULTS-GASTROINTESTINAL AE

- Regarding gastrointestinal adverse events, a statistically significant difference was observed between the 2 drugs highlighting that sevelamer carbonate reduces the occurrence of gastrointestinal adverse events by 47% compared to sucroferric oxyhydroxide (OR=1.53 with 95% confidence interval 1.25-1.86 fixed effects model).
- As no significant degree of heterogeneity was found ($I^2 = 0\%$ and $\tau^2 = 0$, p-value of Q-statistic=0.70) the fixed effects model is more appropriate
- The prediction interval confirms that sevelamer carbonate is superior to sucroferric oxyhydroxide in reducing gastrointestinal adverse events in prospective studies (1.2– 1.93)

	Experin	nental	C	ontrol				Weight	Weight
Study	Events	Total	Events	Total	Odds Ratio	OR	95%-CI	(common)	(random)
Floege 2014	318	707	117	348	+	1.61	[1.24; 2.11]	52.5%	54.4%
Floege 2015	55	391	26	267	- <u>+</u>	1.52	[0.92; 2.49]	16.1%	15.9%
Koiwa 2017	29	108	22	105	- 4	1.38	[0.73; 2.61]	9.9%	9.7%
Wuthrich 2013 1.25g	3	26	3	26		1.00	[0.18; 5.48]	1.6%	1.3%
Wuthrich 2013 10.0g	8	27	3	26		3.23	[0.75; 13.89]	1.3%	1.8%
Wuthrich 2013 12.5g	4	24		26		1.53	[0.31; 7.69]	1.5%	1.5%
Wuthrich 2013 5.0g	8	26		26	- <u>-</u>	3.41	[0.79; 14.72]	1.3%	1.8%
Wuthrich 2013 7.5g	6	25	3	26		2.42	[0.53; 11.00]	1.4%	1.7%
Sprague 2018	56	130	33	75		0.96	[0.54; 1.71]	14.5%	11.8%
Common effect model		1464		925	\$	1.53	[1.25; 1.86]	100.0%	12
Random effects model					\	1.52	[1.25; 1.84]		100.0%
Prediction interval							[1.20; 1.93]		
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p = 0	.70							
					1 0.5 1 2 10				

Forest plot, odds ratio -gastrointestinal adverse events

LIMITATIONS OF THE STUDY

- The number of studies that met the inclusion criteria in the study was relatively small, thus increasing the possibility of publication bias and small study effect
- All the studies included in the research were open label which automatically reduces the quality of the studies
- No subgroup analysis was performed as the small number of studies did not allow further analysis

CONCLUSIONS

- No statistically significant reduction in serum phosphorus was highlighted in favor of any group, both interventions seem to have the same efficacy
- No statistically significant difference in the occurrence of all adverse events was observed between the two drugs
- Further analysis of adverse events highlighted that sevelamer carbonate might have a better safety profile than sucroferric sucroferric oxyhydroxide in the gastrointestinal tract
- More RCTs are needed to strengthen the result of the meta-analysis

THANK YOU FOR YOUR ATTENTION!