

Probiotics Reduce Azotemia In Göttingen Minipigs

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BACKGROUND

Previously we have demonstrated that oral administration of probiotics in freeze-dried form extended life span of 5/6th nephrectomized Sprague-Dawley rats. (*J Am Soc Nephrol* 14; 2003, poster # SU1044). These data suggested that a probiotic added to dietary food supplement could provide some beneficial effect in chronic renal failure (CRF) patients. We then tested this hypothesis in a larger animal model (Göttingen minipig, whose gut microbial ecology more closely approximates that of humans) in a trial of uremia therapy.

GOAL

The goal of this study was to evaluate effectiveness of Kibow Biotics® as a means of decreasing BUN and creatinine levels in 5/6th nephrectomized Göttingen minipigs.

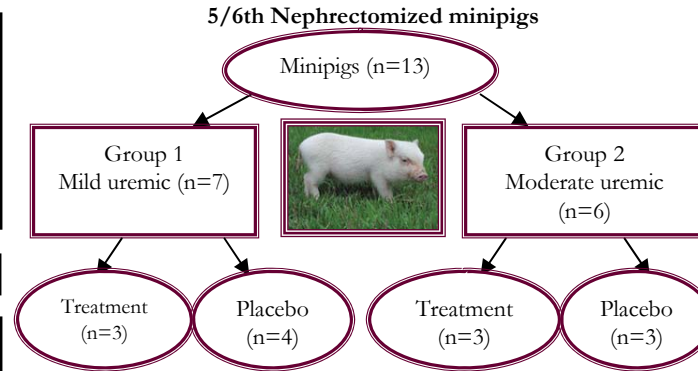
MATERIALS AND METHODS

- **Kibow Biotics®:** A proprietary blend of three screened, selected and proprietary grown food grade microbes – Generally Recognized As Safe (GRAS) by the United States Federal Drug Administration (USFDA).
 - **Design:** After a two-week stabilization phase, 13 pigs with mild to moderate uremia were grouped based on BUN levels (Fig. 1): Group 1 (mild uremia, 7 pigs) - BUN value < 90 mg/dl. Three pigs were fed Kibow Biotics®, the remaining four - placebo. Group 2 (moderate uremia, 6 pigs) - BUN value > 90 mg/dl. This group served as the CKD status group. Three pigs received Kibow Biotics®.
- Minipigs were housed individually and were monitored on a daily basis. Body weight (BW) changes, BUN, plasma creatinine (Cr), hemoglobin (Hb), hematocrit (Hct %), sodium and potassium concentration levels were measured and analyzed periodically. Feces were analyzed for bacterial content.
- **Statistical Analysis**
Data analysis by Student t-test
Data are expressed as mean ± Stdev.

Table 1 Composition of Kibow Biotics

Form Of Delivery	Microbial Component	Kibow Biotech Strain Number	Comment
Capsule	<i>Streptococcus thermophilus</i>	KB 35	Capsules were stored at 4 °C throughout the study.
	<i>Lactobacillus acidophilus</i>	KB 33	
	<i>Bifidobacterium longum</i>	KB 31	

Fig. 1: Distribution of Nephrectomized Minipigs fed Kibow Biotics



RESULTS

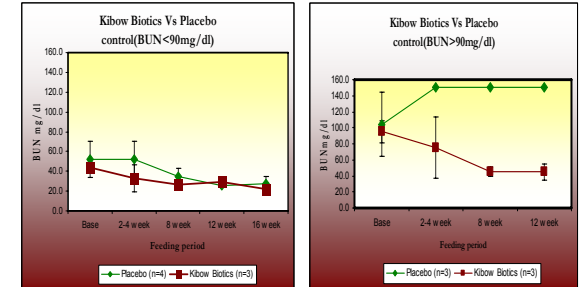
Table 2. Comparison of KIBOW BIOTICS with placebo group

Parameter	Norm. values (n=33)	Uremic status	Subgroup	Base	2-4 week	8 week	12 week
BUN, mg/dl	5.77 ±3.12	Group1	Placebo▲	52.0±18.4	52.0±18.4	34.8±7.7	25.9±1.9
			Treat▲	44.1±5.6	26.7±5.7	26.7±5.7	28.9±2.2
		Group2	Placebo▲	104.2±40.0	150.0±0.0	died	died
			Treat▲	95.3±13.6	75.1±37.9♦	45.7±5.8●	45.0±9.0●
Body weight, Kg	9.27 ±1.48	Group1	Placebo	9.43±0.56	10.0±1.27	11.41±1.42	11.89±2.10
			Treat	10.80±5.12	11.49±5.87	10.94±4.57	11.55±4.99
		Group2	placebo	9.98±0.03	7.72±1.84	died	died
			Treat	9.64±0.82	9.54±0.61	10.20±1.11	10.41±1.46
Cr, mg/dl	0.68 ±0.16	Group1	Placebo▲	2.70±0.3	1.94±0.4	1.86±0.5	1.95±0.61
			Treat▲	3.57±1.24	2.33±0.21	1.78±0.28	1.70±0.35
		Group2	placebo▲	4.59±3.4	4.51±3.03	died	died
			Treat▲	6.02±2.38	3.87±0.72	2.83±0.15	2.93±0.74
Hct %	40.90 ±3.35	Group1	Placebo▲	33.68±1.15	32.98±1.37	34.53±2.24	34.43±3.77
			Treat▲	35.47±5.32	34.16±4.86	34.83±4.55	35.55±3.88
		Group2	placebo▲	24.08±4.56	20.92±9.66	died	died
			Treat▲	32.03±3.44	30.70±5.38	28.39±1.92	31.00±3.52

Data are means and standard deviations of n samples

- ♦ Significantly different from placebo (p=0.009)
- significantly different from base line (p<0.05), Group1 (mild uremic levels, BUN<90mg/dl), Group2 (Moderate uremic levels, BUN >90mg/dl)
- ▲ significantly different from normal value (p<0.0001),

Fig. 2: Change in BUN (mg/dl) from baseline to 16 weeks



Data are means and standards deviations of n samples.

BW, BUN, Cr and Hct % were measured at regular intervals (monthly) throughout the study. No effect from administration of Kibow Biotics was noted in the Group 1 treatment subgroup – there was no significant difference (p=0.42) in BUN levels as compared with the placebo subgroup. All minipigs in Group 1 survived the study. The Group 2 placebo subgroup exhibited a significant increase (p=0.009) in BUN levels after 2-4 weeks (150±0 mg/dl), in contrast to Group 2 treatment subgroup levels (75.1±37.9 mg/dl). All minipigs in the placebo subgroup died by the fourth week of the study. The minipigs in the treatment subgroup survived and showed a significant (p=0.0016) decrease in BUN levels (from 95.3±13.6 to 45.0±5.0 mg/dl) after 8 weeks. No significant differences (p>0.01) in BW, Cr and Hct % were found between the two placebo subgroups. However, placebo minipigs in Group 2 exhibited a decrease in body weight from 9.98±0.03 to 7.72±1.84 kg, with Hct% 20.92±9.66 and Cr [2.33±0.21 mg/dl]. Surviving minipigs in Group 2 increased body weight from 9.64±0.82 to 10.41±1.46 kg, with a stable Hct% 31±3.52 and Cr [4.51±3.03 mg/dl].

CONCLUSIONS

We conclude that, Kibow Biotics fed as a daily treatment have the potential to decrease BUN levels and prolong survival in renal insufficiency. Study suggests further confirmation in larger trials.

Reference

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