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Using QUANTREG to Examine time and Drug on Histamine HA level in Mice

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ABSTRACT

Keywords: SAS, QUANTREG,

INTRODUCTION

SAS is a powerful statistical software program and that provides several efficient procedures to examine relationship between outcome and predictors. Quantile regression model to conditional quantiles of the response variable to different percentile. Quantile regression is useful when the rate of change in the conditional quantile. Flexibility for modeling data with heterogeneous conditional distributions is one of an advantage of quantile regression over ordinary regression model. Quantile Regression can be used in many fields, including biomedicine, econometrics, and ecology. The SAS QUANTREG procedure used to perform regression analysis when the assumption of ordinary regression does not meet. The QUANTREG procedure uses quantile regression to model the effects of covariates on the conditional quantiles of a response variable. SAS provides practical and efficient ways to analyze different type of data with heterogeneous conditional distributions. The purpose of this paper is to examine the slope of time on Histamine (HA) level in mice is different by drug (desipramine) as compared to control. All of slopes were significant (P<.001) except time slope at .75 (P=.864). The results indicated that group was not significant for quantile level .05 (P=.426) and quantile level .85 (P=.458). In addition, time was not significant for quantile level of .75 and .80 (P=.864 and .119), interaction was not significant for quantile level .05 (P=.242). SAS is a powerful statistical program to analyze complex statistical procedure.

PURPOSE

This experimental design study used to examine the *in vivo* effect of the drug (desipramine) on Histamine (HA) in mice. The purpose of this paper is to examine the slope of time on HA level in mice is different by drug (desipramine).

BACKGROUND

Ordinary least square regression (OLS) estimates the conditional mean response of the dependent variable (E(Y|X)) dependent on the independent variables (X). The ordinary regression model is one of the most common used statistical analysis. However, using ordinary regression model require several assumptions. When the data skewed, multimodal, or data with outliers the behavior at the conditional mean fails to fully capture the patterns in the data. When our assumptions in OLS model does not met, modeling the mean is not adequate, and interest is in the quantiles quantile regression model would be another option to examine data. Quantile regression is a statistical method intended to estimate, and conduct relationship about, conditional quantile functions. The quantile level is the probability that is associated with a quantile range from zero to one. Quantile regression used in many fields [(1-3)].

METHODS

This paper used an experimental study on five mice to examine the effect of drug on Histamine (HA) over time in mice. By utilizing the tool of fast-scan cyclic voltammetry, files were taken of HA levels in nanoamps

(nA) at 10Hz over 30 seconds, recording a file every .1 seconds and creating 300 data points per file. Once control files were recorded for each animal, saline, acting as the drug vehicle, was injected in each specimen to account for any changes in HA levels which may result in the drug vehicle injection. Following saline injections, the mice were then injected with desipramine. HA was measured immediately after injection for 30 minutes. The outcome define as HA and independent variables were time and group (control vs using drug). The interest is to examine if the slope of time on HA level in mice is different by drug. There was different drug used to examine the slope of HA level in mice. The result of one drug (desipramine) is presented and discussed in this paper. The results were examined for all animal and by each animal. PROC MEAN, UNIVARIATE, and FREQ used to describe response and independent variable. PROC QUANTREG procedure used to examine the relationship of time on the conditional quantiles of outcome by group. Two models were 4 quantiles (.25, .50, .75, .99) and 20 quantiles (.05 to 1 by .05). The data of slope with standard error created for two models for each animal by group. New variable created (slope + Standard error). Finally, PROC TTEST used to examine if there was difference on new slope for each animal by group. In this paper we showed only the result of quantile regression for animal 1. The same process used for other animals. All data analyses performed using SAS/STAT® version 9.4[4].

RESULTS

Table 1 shows mean, standard deviation, minimum, and maximum of Histamine HA level. The mean of HA level for drug group was higher (1.52) than control (1.27) for all animal.

Table 1: Mean, standard deviation, minimum, and maximum of Histamine (HA) level by group.

Analysis Variable: S HA					
control/drug	**N**	**Mean**	**Std Dev**	**Min**	**Max**
Control	1500	1.27	4.36	-5.57	16.05
Drug/desipramine	1500	1.52	4.01	-8.78	10.42

Table 2 shows mean, standard deviation, minimum, and maximum of HA level by group for each animal. The mean of HA level for drug group was lower (4.33) than control (6.91) for animal one (n1) whereas the mean of HA level for drug group was higher (4.40) than control (2.79) for animal five (n7).

Table 2: Mean, standard deviation, minimum, and maximum of HA level by group for each animal.

Analysis Variable: S HA						
animal number	**control/drug**	**N**	**Mean**	**Std Dev**	**Min**	**Max**
n1	Control	300	6.91	4.71	0.01	16.05
	Drug/desipramine	300	4.33	2.93	-0.48	10.42
n4	Control	300	-0.16	1.41	-1.27	4.05
	Drug/desipramine	300	-1.01	2.38	-3.73	4.49
n5	Control	300	-0.39	2.88	-3.04	8.44
	Drug/desipramine	300	0.28	4.46	-8.78	6.67
n6	Control	300	-2.02	2.63	-5.57	3.35
	Drug/desipramine	300	-0.37	2.85	-7.10	3.15
n7	Control	300	2.03	2.79	-1.86	10.54
	Drug/desipramine	300	4.40	3.23	-0.00	9.38

Table 3 displays the parameter estimates and standard error of quantile regression for first model by time, group, and time*group. All of slopes were significant (P<.001) except time slope at .75 (P=.864). The result showed the slopes were negative for times for first and second quantiles but slope for group were negative for first three quantiles. The interaction slope was positive for first quantile and were negative for last quantiles.

Table 3: Parameter Estimates for Quantile regression (first model) for all animal by time, group, and time*group.

Quantile Level	Time		Group		Time*Group	
	Beta	SE	Beta	SE	Beta	SE
.25	.07	.006	-.40	.129	.05	.009
.50	.12	.013	-1.01	.287	.07	.020
.75	-.01	.030	-3.14	.648	.24	.045
.99	-.33	.003	8.37	.065	-.28	.005

Table 4 displays the parameter estimates and standard error of quantile regression for second model by time, group, and time*group. All of slopes were positive for quantile level less than .75 time with range from -.24 to .14. In addition, most of slopes for group were negative with range from -3.13 to 8.30 The interaction slopes were positive for all quantile level except .95 with range from -.31 to .24. The results indicated that group was not significant for quantile level .05 (P=.426) and quantile level .85 (P=.458). In addition, time was not significant for quantile level of .75 and .80 (P=.864 and .119), interaction was not significant for quantile level .05 (P=.242).

Table 4: Parameter Estimates for Quantile regression (second model) for all animal by time, group, and time*group.

Quantile Level	Time		Group		Time*Group	
	Beta	SE	Beta	SE	Beta	SE
.05	.02	.002	-.04	.048	.004	.003
.10	.03	.002	-.11	.052	.019	.004
.15	.06	.004	-.18	.081	.027	.006
.20	.07	.005	-.29	.104	.045	.007
.25	.07	.006	-.40	.129	.051	.009
.30	.10	.006	-.38	.129	.033	.009
.35	.10	.008	-.44	.162	.028	.011
.40	.11	.009	-.65	.197	.037	.014
.45	.11	.011	-.91	.244	.052	.017
.50	.12	.013	-1.01	.287	.066	.020
.55	.14	.015	-1.17	.318	.065	.022
.60	.13	.019	-1.29	.407	.079	.028
.65	.09	.019	-2.15	.401	.137	.028
.70	.07	.023	-2.55	.498	.184	.035
.75	-.01	.030	-3.13	.648	.236	.045
.80	-.04	.026	-1.11	.545	.128	.038
.85	-.11	.018	-.29	.398	.010	.028
.90	-.19	.016	1.26	.346	.078	.024
.95	-.24	.010	8.30	.216	-.310	.015

Table 5 displays the parameter estimates and standard error of quantile regression for first model by group. All of slopes were significant (P<.0001). The result showed the slope for first quantile for control was positive (.15) as compare to drug (-.08). The slope for second quantile (.50) was similar for both control and drug. However, the slope for third and fourth quantiles were different by group.

Table 5: Parameter Estimates for Quantile regression (first model) animal 1 by group.

Parameter Estimates (.25)				
Parameter	Control Estimate	SE	Drug Estimate	SE
Intercept	0.5723	0.3369	5.3337	0.5539
TIME	0.1502	0.0195	-0.0843	0.0298

Parameter Estimates (.50)				
Parameter	Control Estimate	SE	Drug Estimate	SE
Intercept	11.9793	0.1610	9.8962	02066
TIME	-0.2713	0.0093	-0.2377	0.0111

Parameter Estimates (.75)				
Parameter	Control Estimate	SE	Drug Estimate	SE
Intercept	18.2995	0.2471	11.7823	0.0762
TIME	-0.5102	0.0143	-0.3095	0.0041

Parameter Estimates (.99)				
Parameter	Control Estimate	SE	Drug Estimate	SE
Intercept	21.7701	0.0059	14.8066	0.1103
TIME	-0.6150	0.0003	-0.4136	0.0059

Table 6 displays the parameter estimates and standard error of quantile regression for second model by group. All of slopes were significant (P<.0001). The result showed the slope for control is positive less than .40 as compare to drug .05. The result indicated difference in slope by group.

Table 6: Parameter Estimates for Quantile regression (second model) animal 1 by group

Quantile Level	Control Slope	SE	Drug Slope	SE
.05	.13	.0065	.07	.0073
.10	.13	.0130	.08	.0188
.15	.14	.0147	.04	.0299
.20	.14	.0176	.01	.0376
.25	.15	.0195	-.08	.0298
.30	.16	.0231	-.14	.0241

.35	**.17**	**.0270**	**-.18**	**.0170**
.40	**.16**	**.0349**	**-.21**	**.0132**
.45	**-.03**	**.0317**	**-.22**	**.0122**
.50	**-.27**	**.0093**	**-.23**	**.0111**
.55	**-.35**	**.0055**	**-.25**	**.0109**
.60	**-.37**	**.0116**	**-.27**	**.0096**
.65	**-.42**	**.0113**	**-.29**	**.0075**
.70	**-.46**	**.0157**	**-.30**	**.0037**
.75	**-.51**	**.0143**	**-.31**	**.0041**
.80	**-.55**	**.0142**	**-.31**	**.0048**
.85	**-.59**	**.0134**	**-.32**	**.0060**
.90	**-.62**	**.0078**	**-.36**	**.0046**
.95	**-.62**	**.0041**	**-.40**	**.0117**

CONCLUSION

SAS is a powerful statistical software program and that provides several efficient procedures to examine relationship between outcome and predictors. The SAS QUANTREG procedure used to perform regression analysis when the assumption of ordinary regression does not meet. We examined the slope of time on HA level in mice is different by drug using two models. All of slopes for first models were significant (P<.001) except time slope at .75 (P=.864). The result showed the slopes were negative for times for first and second quantiles but slope for group were negative for first three quantiles. The interaction slope was positive for first quantile and were negative for last quantiles. All of slopes for second models were positive for quantile level less than .75 time with range from -.24 to .14. In addition, most of slopes for group were negative with range from -3.13 to 8.30 The interaction slopes were positive for all quantile level except .95 with range from -.31 to .24. The results indicated that group was not significant for quantile level .05 (P=.426) and quantile level .85 (P=.458). In addition, time was not significant for quantile level of .75 and .80 (P=.864 and .119), interaction was not significant for quantile level .05 (P=.242). The analyze was done for each animal. SAS is a powerful statistical program to analyze complex statistical procedure.

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Appendix

SAS Syntax

```
proc format;
 value groupf 0="Control"    1="Drug/desipramine";
 value sgf  0=" below zero"   1=" above 0";
 value idf   1="n1"   2="n4" 3="n5" 4="n6"  5="n7";

data one;  set trans.des;
if 0<s<100 then sg=1;   else if S<0 then sg=0;
label
id ="animal number"
group="control/drug"
time="time"
s= "HA"
sg= "HA group" ;
format group groupf.  sg sgf. id idf.;     run;

proc sort data =one; by id time; run;

*** only HA value above baseline;
data two;  set one;  if sg=1; run;
proc sort data =two; by id time; run;

**** only value above baseline **;
 data control2;  set two;  if group=0; run;
proc sort data =control2; by id time; run;

data drug2; set two; if group=1;run;
proc sort data =drug2; by id time; run;

Ods rtf;ods listing close;
%macro quant (d,c,o,e,t);
proc quantreg ci=sparsity/iid algorithm=interior(tolerance=5.e-4)
   data=&d order=internal ;
   class &C;
   model &o = &e &c   &c*&e/   quantile= 0.25 .50 .75 .99   plot=quantplot;
   title 'Quantile regression ';      title3 '  2020'&t;run;
%mend quant;
%quant(two,group,s,time,quantiles);run;
 ods rtf close;ods listing;quit;run;


Ods rtf;
ods listing close;
%macro quantb (d,c,o,e,t);
proc quantreg ci=sparsity/iid algorithm=interior(tolerance=5.e-4)
   data=&d order=internal ;
```

```
    class &C;
  model &o = &e &c   &c*&e/   quantile= 0.05 to 1 by .05   plot=quantplot;
 ;title 'Quantile regression ';       title3 '  2020'&t;run;
%mend quantb;
%quantb(two,group,s,time,quantiles);run;
 ods rtf close;ods listing;quit;run;

*** For only animal 1;

ods rtf;ods listing close;
%macro quant (d,n,t);
proc quantreg ci=sparsity/iid algorithm=interior(tolerance=5.e-4)
  data=&d order=internal;   where id=&n;
     model s = time/   quantile= 0.25 .50 .75 .99   plot=quantplot;
  title 'Quantile regression for HA/all ';       title3 '  2020'&t;run;
%mend quant;
%quant(control2,1,pre animal n1);
%quant(drug2,1,post animal n1);run;
 ods rtf close; ods listing; quit; run;

*** quantile for 10 points **;

Ods rtf;ods listing close;
%macro quant (d,n,t);
proc quantreg ci=sparsity/iid algorithm=interior(tolerance=5.e-4)
  data=&d order=internal;   where id=&n;
    model s = time/   quantile= 0.05 to 1 by .05   plot=quantplot;
  title 'Frequency tables for  HA/all ';       title3 '  2020'&t;run;
%mend quant;
%quant(control2,1,pre animal n1);
%quant(drug2,1,post animal n1);run;
 ods rtf close;ods listing;quit;run;
```