Research article

Dietary Exposure Assessment of Benzylpenicillin Residue in Pork Consumed by Age and Gender Groups in the Philippines

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Abstract Exposure assessment is one of the most important key components of the risk assessment process. Dietary intake of significant amounts of residue can lead to adverse health effects and development of antimicrobial resistance in the population. The study was conducted to determine exposure risk to antibiotic drug residues in pork consumed in the Philippines. The specific aim was to estimate dietary exposure of Benzylpenicillin residues by age and gender groups. Parameters such as food consumption, substances residue, body weight, ages, and gender groups were gathered from local and international institutions. Mathematical equations were used to calculate for Dietary Exposure from amount of drug residue multiplied by the mean food consumption and adjusted by body weight. The present study; dietary exposure of Benzylpenicillin residue for children from 1 to <3 years old had the highest exposed followed by adolescents, adults and infants while males were significantly higher than females ($p<0.05$). This is the first attempt to determine risk assessment of dietary exposure to antibiotic residue of different population groups in the Philippines. Improvement of mathematical models used in this study is proposed to better prioritize exposure assessment models for veterinary drug residues to ensure the safety of food produced from farm to table.

Keywords exposure assessment, drug residues, age-gender groups, consumption

INTRODUCTION

The use of risk assessment has gained steadily in importance and recognition as a scientifically-based approach for the development of food safety and quality standards. During recent years there has been increasing use of the word “risk” in connection with food safety (Sumner et al., 2004). Consequently, a risk assessment of the food safety implications (Gehring et al., 2005) may be made on the potential harm or risks of veterinary drug residues to the human consumer. The importance of risk assessment lies not only in its ability to estimate human risk, but also in its use as a framework for organizing data, as well as for allocating responsibility for analysis. As such according to World Health Organization (1995), it is important to understand that risk assessment is a process that can include a variety of mathematical models to estimate risks. Risk assessments also promote international trade by addressing new safety and quality challenges (Graf, 2005).

Exposure assessment is among the components of risk assessment (Codex Alimentarius Commission, 1999). Dietary exposure to veterinary drugs occurs when residues remain in food products derived from animals treated with a veterinary drug (Health Canada, 2003a). Dietary exposure models have been developed to predict human exposures to chemicals resulting from the consumption of contaminated food and residue levels and also for substances naturally occurring in them (Fryer, 2006). In 2003b, Health Canada primer on "Assessing exposure from pesticides in food" indicated that risk exposure from food can either result in short-term (i.e., acute) or long term (i.e., chronic) effects. In actual risk equations, it is possible that toxicity may be computed utilizing the estimation of consumer intake of drug residues in foods of animal origin, hence, this study on exposure assessment.

Thorough literature search revealed no available study on exposure assessment on veterinary drug residues in the Philippines. With the increase in reports of occurrence of risk of veterinary drug residues in foods of animal origin in the last two decades (Health Canada, 2003a; Sumner et al., 2004), there is a strong need to study exposure assessment of antibiotic residues. To date, there is no local study conducted on the exposure risk assessment for residual antibiotics in the Philippines. Thus, this study aims to make a "Dietary Exposure Assessment of Benzylpenicillin Residues in Pork Consumed by Age and Gender Groups in the Philippines".

The overall objective of the study is to determine exposure risk to antibiotic drug residues in pork consumed in the Philippines. The specific aim is to estimate the dietary exposure of Benzylpenicillin residues by ages and gender groups.

METHODOLOGY

The study was conducted using secondary data collected from local and international institutions for estimating dietary exposure assessment. For instance, local data like the report on veterinary drug residue (2003-2008) from National Meat Inspection Service, recommendation on Maximum Residue Limit (MRL) published by Bureau of Aquaculture Fisheries and Product Standard, the report of Food Consumption Survey in 2003 and Recommended Energy and Nutrient Intake in 2002 published by Food and Nutrition Research Institute (FNRI, 2003), the development of antimicrobial resistance from Research Institute for Tropical Medicine, Philippines. International data came from Codex Alimentarius Commission (CAC) on amount of antibiotic drug residues, the procedural guidelines on residues of veterinary drugs in food from JECFA, and from an updated report of the 32nd session of the Codex Veterinary Drug Residues in Food 2009.

Dietary modelling combines food consumption data with food chemical concentration data to estimate dietary exposure to food chemicals, or intake of nutrients. The Eq. (1) below, the basic dietary exposure model is of the form:

$$Dietary\ Exposure = \frac{Food\ Consumption \times Amount\ of\ drug\ residure}{Body\ weight} \qquad (1)$$

where food consumption is the amount of food people eating per capita per day expressed in mg/kg/day and amount of drug residue expressed in μg/kg BW/day.

RESULTS

The benzylpenicillin antibiotic have been test for consecutive years from 2006 to 2008 in the Philippines. The number of violations was determined using Microbial Inhibition Test and was measured using caliper method (NMIS, 2008). Positive benzylpenicillin residue results in NMIS were assumed to equivalent to HPLC LOQ 400 μg/kg (Heitzman, 1995) and dietary exposure was calculated using the following equation (3) which regarded computed using equation (2).

Eq. (2) the Mean Food Consumption Difference Age Groups is as follows;

$$The\ mean\ food\ consumption\ difference\ age\ groups = \frac{average\ weight\ difference\ age\ groups \times the\ mean\ food\ consumption\ per\ capita\ in\ the\ Philippines}{average\ weights} \qquad (2)$$

Eq. 3 Dietary Exposure of Benzylpenicillin Residue is as follows;

$$DE_{PEN} = \frac{\text{amount of benzylpenicillin residues of 3\% positive results} \times \text{mean food consumption difference age groups}}{\text{average weights differences age groups}} \quad (3)$$

Based on an update as of the 32nd session of the Codex Alimentarius Commission in 2009 first draft prepared by Dr. Macneil, a typical recommended dose by intramuscular injection (IM) in swine, cattle, horses, and sheep of a 300,000 unit/mL formulation is 6,600 units/mL BW. As a feed additive, a typical dosage for swine or poultry is 55 mg/kg in the diet. Intramammary treatment is typically by administration of 100,000 units per quarter. In the studies reported, 1 mg procaine benzylpenicillin is equivalent to 1667 IU (international units).

As at 50th report of JECFA in 1999, the Committee considered residues of procaine benzylpenicillin to be equivalent to residues of benzylpenicillin. Dietary Exposure (DE) was calculated using equation (1) following the mean one-day per capita food consumption in the Philippines and by island groups, food groups and adjusted 55-kg person. The DE of Benzylpenicillin Residue was calculated by the amount of benzylpenicillin of 3% positive results multiplied the food consumption difference age groups and adjusted by average weight difference age groups.

Table 1 shows that DE of benzylpenicillin residue for children from 1 to 3 years old had the highest value at 0.002923 µg/kg bw/day. Such value was calculated as 5 µg/kg of amount residues × mean one-day per capita pork consumption of 0.0076 kg ÷ 13 kg of average children weights. Likewise, average DE for children (0.002913 µg/kg bw/day) was higher than adolescents (0.0029096 µg/kg bw/day), followed by adults (0.002909 µg/kg bw/day) and infants (0.002903 µg/kg bw/day). Also, DE for males was significantly lower than females (p-value=0.034).

Table 1 Dietary exposure of benzylpenicillin residue of 3% of positive results intake of fresh pork in the Philippines

Age Groups	Average Weight (kg)	Amount Residue (µg/kg)	Mean One-Day Per Capita Pork Consumption (g)	Dietary Exposure (µg /kg bw/day)
1. Infants, month				
Birth- <6 (3)	6	5	3.5	0.002917
6-<12 (9)	9		5.2	0.002889
2. Children, year				
1-3 (2.5)	13		7.6	0.002923
4-6 (5.5)	19	5	11.1	0.002921
7-9 (8.5)	24		13.9	0.002896
3. Adolescents, M, year				
10-12 (11.5)	34		19.8	0.002911
13-15 (14.5)	50	5	29.1	0.002910
16-18 (17.5)	58		33.7	0.002905
4. Adolescents, F, year				
10-12 (11.5)	35		20.4	0.002914
13-15 (14.5)	49	5	28.5	0.002908
16-18 (17.5)	50		29.1	0.002910
5. Adults, M, year				
19-49	59		34.3	0.002907
50-64	59	5	34.3	0.002907
65 and over	59		34.3	0.002907
6. Adults, F, year				
19-49	51		29.7	0.002911
50-64	51	5	29.7	0.002911
65 and over	51		29.7	0.002911

DISCUSSION

To determine the risk of dietary exposure of DE_{PEN} residue using mathematical model gives an estimate of the risk of having toxicity among the populations. In the present study is a first step in determining the most important fields for generation new data to estimate more accurately the proportion of the population at risk of toxicity and development of antimicrobial resistance due to a given the amount of antibiotic residue of dietary intake in pork consumption.

Exposure was calculated for the populations in the Philippines based on the consumption per capita (as a major factor), followed by the amount substance residue and body weight. For instance, Steve (2009) and Kroes et al., (2002) where dietary exposure assessments have been taken, relevant food consumption data have been utilized. E.g., Ock and Hee (2002) reported estimation of dietary pesticide risks, following the setting up of food consumption and pesticide residue levels in the calculation of toxicological risk. E.g., assessment on dietary melamine exposure based on the maximum consumption of melamine and the median levels of melamine detected in the most contaminated food (Xu et al., 2009). This dietary modeling combines food consumption data with food residue concentration data to estimate dietary exposure level to contaminants heavy metal (Haeng et al., 2005).

The present study found that DE_{PEN} residue for children from 1 to 3 years old is the highest exposed followed by adolescents, adults and infants whilst males are significant for females in the Philippines. For instance, Kroes et al., (2002) reviewed on children, because of its higher food consumption rates per kg bw, is generally expected to have a higher exposure level and is therefore higher risk of the population. In this respect, children may be of special interest because of their higher intake level per kg bw due to growth processes (Kroes et al., 2002). A similar study on dietary exposure of children and teenagers to benzoates, sulphites, butylhydroxyanisol and butylhydroxytouen found that between 2 groups of students the younger subjects are more exposed when the exposure is expressed in kg of bw ($p<0.01$) (Soubra *et al.,* 2006). Another possible example was conducted on cumulative risk assessment of the exposure to organophosphorus and carbamate insecticide in the Dutch diet by Boon et al., (2008). For children the exposure (57 vs. 25 μg/kg BW/day) was higher than the total population (18 vs. 23 μg/kg BW/day). The resulting in exposure levels equal to 11% and 25% of the acute reference dose for the total population and young children respectively. Another similar study, Caldas et al., (2006) found that children exposure to acetylcholinesterase (AChE) inhibition pesticides is also of additional concern, as this population might be more sensitive to these compounds than adults. For children, the exposures were, on average, 2.4 times higher than the exposure found for the general population. Since the determination of dietary exposure to antibiotic residues in the present study shows no zero risk, i.e., there is a risk for possible adverse effects on the population. Another concern for use of antibiotics in agriculture and aquaculture is the risk for development of antimicrobial resistance. Currently, an antimicrobial resistance surveillance reference laboratory has been prepared with 435 isolates by the Antimicrobial Resistance Surveillance Program of Research Institute for Tropical Medicine. It is clear that the percentage of penicillin resistance is 25% Salmonella sp. (RITM, 2009).

CONCLUSION

Based on the finding of the present study, dietary exposure of benzylpenicillin have been detected in pork which children from 1 to 3 years old is more exposed and more risk, because of their higher food consumption rates per kg body weight, is generally expected to have a higher exposure level due to physical activity.

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REFERENCES

Boon, P.E., Van der Voet, H., Van Raaij, M.T. and Van Klaveren, J.D. 2008. Cumulative risk assessment of the exposure to organophosphorus and carbamate insecticide in the Dutch diet. Food and Chemical Toxicology, 46 (2008), 3090-3098.

Caldas, E.D., Boon, P.E. and Tressou, J. 2006. Probabilistic assessment of the cumulative acute exposure to organophosphorus and carbamate insecticide in the Brazilian diet. Toxicology, 222 (2006), 132-142.

Codex Alimentarius Commission. 1999. Procedural manual, tenth edition, Joint FAO/WHO Food Standards Programme, Food and Agriculture Organization of the United Nations, 1997. Definitions for "risk management" and "risk communication" were adopted as revised texts at the Twenty-third Session of the Codex Alimentarius Commission, July 1999.

FNRI. 2003. Food consumption survey. Food and Nutrition Research Institute. Philippines.

Fryer, M., Chris, C., Ferrier, H., Colvile, R. and Nieuwenhuijsen, M. 2006. Human exposure modelling for chemical risk assessment: a review of current approaches and research and policy implications. Environmental science and policy, 9 (2006), 261-274.

Gehring, R., Bayaes, R. and Riviere, J. 2005. Application of risk assessment and management principles to the extra label use of drugs in food-producing animals. College of Veterinary Medicine, North Carolina State University, Raleigh, N.C., U.S.A.

Graf, L. 2005. Introduction to chemical risks in food. Chemical Risk Analysis. Food Standard Australia and New Zealand.

Lee, H. S. Cho, Y.H., Park, S.O., Kye, S.H., Kim, B.H., Hahm, T.S., Kim, M., Lee, J.O. and Kim, C. 2005. Dietary exposure of the Korean population to arsenic, cadmium, lead and mercury. Journal of Food Composition and Analysis, 19 (2006) , S31-S37.

Health Canada. 2003a. Setting standards for maximum residue limits (MRLs) of veterinary drugs used in food-producing animals. Health Canada. Ontario, Canada.

Health Canada. 2003b. Assessing exposure from pesticides in food. Pest Management Regulatory Agency. Health Canada. Ontario, Canada.

Kroes, R., Muller, D., Lambe, J., Lowik, M., van Klaveren, J., Kleiner, J., Massey, R., Mayer, S., Urieta, I., Verger, P. and Visconti, A. 2002. Assessment of intake from the diet. Food and Chemical Toxicology, 40 (2002), 327-385.

NMIS. 2008. Veterinary drug residue monitoring program. Veterinary Drug Residue Section, Laboratory Services Division. NMIS. DA.

Ock Kyoung Chum and Hee Gon Kang. 2002. Estimation of risks of pesticide exposure, by food intake, to Koreans. Food and Chemical Toxicology, 41 (2003), 1063-1076.

RITM, 2009. The report on antimicrobial resistant surveillance program. Research Institute for Tropical Medicine. Philippines.

Sumner, J., Ross, T. and Ababouch, L. 2004. Application of risk assessment in the fish industry. Fisheries technical paper 442. Food and Agriculture Organization of the United Nation. Rome, Italy.

Soubra, L., Sarkis, D., Hilan, C. and Verger, Ph. 2006. Dietary exposure of children and teenagers to benzoates, sulphites, buthylhydroxyanisol (BHA) ad buthylhydroxytoluen (BHT) in Beirut (Lebanon). Regulatory Toxicology and Pharmacology, 47 (2007), 68-77.

WHO, 1995. Application of risk analysis to food standards issues. WHO/FNU/FOS/95.3, World Health Organization, Geneva, Switzerland.