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Communicational Strategies to Prevent Mycotoxins Exposure and Improve Community Health in Developing Countries

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ABSTRACT

In the response to sequential outbreaks of serious and long-lasting effect of mycotoxins in developing countries which is responsible for deaths of people, strategies are required and transferred within the community. The aims of the paper is to pinpoint community wellbeing strategies for the reduction of mortality and morbidity incidences associated with the consumption of mycotoxins-contaminated food in the emerging countries and to shape an assimilated plan that supplementary successfully pools farming approaches and public health to the control of mycotoxins. Communicational strategies are important to address potential remedial points about mycotoxins and identify gaps in current information around critical and chronic human health effects of mycotoxins, reconnaissance and diet monitoring, and the ability of intervention strategies. Accordingly, different melodies should be emerged commencing the works and deserve immediate responsiveness such as; quantifying the effect on the health of human and the problem of infection because of mycotoxins experience; assembling an record and appraise the efficiency of on-going intervention strategies; improve and expand the disease investigation, nutrition monitoring, research laboratory, and community health reaction capability of exaggerated areas; and emerging a response practice that can be used in the happening of an eruption of mycotoxins effect.

Keywords: mycotoxins, exposure, strategy, health risk

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INTRODUCTION

Well-known within the agricultural community, mycotoxins have been studied for over forty years due to their widespread occurrence and their significant impact on crops [20,24,65,66,77,78]. Aflatoxins are toxic secondary metabolites produced by fungi. Mycotoxins are the most potent and potentially lethal metabolite and are a known human carcinogen. Mycotoxins can affect a wide range of commodities including cereals, oilseeds, spices, and tree nuts as well as milk, meat, and dried fruit. The major sources of exposure are maize and groundnuts as these are the foods that are most susceptible to contamination and consumed in the greatest amounts. The greatest risk for health impact lies within developing countries located in tropical regions, which rely on these commodities as their staple food source. Food insufficiency and lack of diversity substantially contribute to the susceptibility of individuals and communities to Mycotoxins. Mycotoxins have been recognized as significant contaminants by the agricultural production community since the 1960s and control strategies have mostly eliminated harmful exposures in developed countries [30]. The application of these strategies in developing countries is difficult, given differences in technology, agriculture, and trade practices, as well as other issues contributing to occurrence of aflatoxins and incidence of exposure. Consequently, over 5 billion people in developing countries worldwide are at risk of chronic exposure to mycotoxins through contaminated [65,66,78].

Mycotoxins associated health effects pervade the developing world despite the fact that these effects could be mitigated or prevented with the current state of agricultural knowledge and public health practice. Outbreaks of acute mycotoxins poisoning are a recurrent public health problem. In 2014, one of the largest, most severe mycotoxins outbreaks occurred in Developing countries followed by another outbreak in 2005 (CDC 2014). Given that diseases in the developing world often go unreported, the developing countries outbreaks are likely to be an underestimation of the problem; furthermore, the burden of disease attributable to chronic aflatoxin exposure (e.g. hepatocellular carcinoma, impaired growth, immune suppression) remains undefined. These outbreaks emphasize the need to quantify and control mycotoxins exposure in developing countries and highlight the potential role of public health. Contamination can occur at any stage of food production from pre-harvest to storage [79]. Factors that affect mycotoxins contamination include the climate of the region, the genotype of the crop planted, soil type, minimum and maximum daily temperatures, and daily net evaporation [2,5,6,22,23,54,79,]. Mycotoxins contamination is also promoted by stress or damage to the crop due to drought prior to harvest, insect activity, poor timing of harvest, heavy rains at harvest and post-harvest, and inadequate drying of the crop before storage [33,34, 53,54, 70,71,72]. Humidity, temperature, and aeration during drying and storage are also important factors.

The effects of mycotoxins on animal health have been observed in many species for over forty years [59,48] beginning with the documentation of Turkey X disease in 1960 [3]. The primary target of mycotoxins is the hepatic system. Acute effects include hemorrhagic necrosis of the liver and bile duct proliferation while chronic effects include hepatocellular carcinoma (HCC). In animals, suppression of immunity, growth retardation, and increased susceptibility to infectious disease due to mycotoxins exposure is well-documented [3,59,]. The effects of mycotoxins on humans, as with animals, are dependent upon dosage and duration of exposure. Acute exposure can result in mycotoxins, which manifests as severe, acute hepatotoxicity with a case fatality rate of approximately 25% (Cullen and Newberne 2014) [16]. Early symptoms of hepatotoxicity from aflatoxicosis can manifest as anorexia, malaise, and low-grade fever. Acute high level exposure can progress to potentially lethal hepatitis with vomiting, abdominal pain, jaundice, fulminant hepatic failure, and death. Outbreaks of acute mycotoxins are a recurring public health problem throughout the world (Krishnamachari, Bhat et al. 1985; Krishnamachari, Bhat et al. 1985; Ngindu, Johnson et al. 1992; Lye, Ghazali et al. 2005; CDC 2014) [10,41,42,45,50,]. Hepatocellular carcinoma (HCC) as a result of chronic exposure has been well documented, generally in association with hepatitis B virus or other risk factors [12, 35,52, 64,74,75,76,]. The International Agency for Research on Cancer (IARC) first recognized aflatoxins as carcinogenic in 1976 and has subsequently reaffirmed naturally occurring mixtures of aflatoxins and aflatoxin B1 as Group 1 carcinogens (carcinogenic to humans) (IARC 2012). Additional effects of chronic exposure have not been widely studied but are thought to include immunologic suppression, impaired growth, and nutritional interference [16,24, 78, 59,].

MYCOTOXINS CONCERNS IN DEVELOPING COUNTRIES

Although a few studies have provided estimates of daily exposure to mycotoxins during non-outbreak periods [31,38,57,74-76,], more information is needed concerning baseline levels of chronic exposure for vulnerable populations. This would allow for a better quantification of the health risks associated with chronic exposure and for a better estimate of the level of mycotoxins exposure necessary to trigger an outbreak. Such knowledge will enable the public health community to understand health effects associated with chronic exposure and allow for the evaluation of future public health and agricultural interventions.

PUBLIC HEALTH RISKS ASSOCIATED WITH CONSUMPTION OF MYCOTOXINS

HCC is the sixth most prevalent cancer worldwide with a higher incidence rate within developing countries [58]; however, the burden of HCC attributable to aflatoxins when accounting for other co-morbidities, such as hepatitis B (HBV), is not known. Several studies in China have indicated combined exposure to HBV and aflatoxins is associated with a much higher risk of HCC [6474-76,]. This interaction has not been studied in other high risk areas such as sub-Saharan Africa and the molecular mechanism of the interaction between HBV and aflatoxins is not known [70-72]. Quantifying the proportion of HCC attributable to aflatoxin exposure, to HBV, and to the interaction of aflatoxin exposure and HBV will help identify the best public health strategy to reduce HCC, including the benefits and limits of widespread HBV vaccination.

Additional health effects associated with chronic mycotoxins exposure have not been well studied. Without knowing the relationship between chronic exposure and health, the true human health impact and the resulting burden of disease in developing countries are not known. Preliminary evidence suggests that there may be an interaction between chronic mycotoxins exposure and malnutrition, immune suppression, impaired growth, and diseases such as malaria and HIV/AIDS. Experimental animal evidence suggests that chronic exposure to mycotoxins may lead to impaired immunity, reduced uptake of nutrients from the diet, and growth retardation [77,48]. Several studies of children in Benin and Togo have shown an association between mycotoxins albumin adduct levels and impaired growth [25-27]. In a recent study in Ghana, higher levels of aflatoxin B1-albumin adducts in plasma were associated with lower percentages of certain leukocyte immune phenotypes [38]. A study in Gambian children found an association between serum aflatoxin-albumin levels and reduced salivatory secretory IgA levels [70-72]. While the effects on immunity suggest the possible influence of mycotoxins on susceptibility to infectious disease, further investigation is needed. Quantifying the baseline levels of exposure and the associated burden of disease in developing countries is essential for determining the efficacy of interventions intended to reduce exposure to mycotoxins.

Evidence exists for the effectiveness of various interventions to reduce mycotoxins contamination of foods in developed countries, but it is unclear whether these are applicable in developing countries [78,6]. Because of inherent differences between local (subsistence farmer) and commercial markets, regulations and practices, such as Hazard Analysis and Critical Control Point (HACCP) (Pineiro 2011) [62], used in commercial markets may not directly apply to subsistence farmers. For example, while subsistence farmers consume their own grain, they also sell part of their harvest to local markets. They may later themselves purchase grain from these markets when their own supplies are depleted. Food commodities within these local markets are not tested for mycotoxins (Lewis, Onsongo et al. 2015) [43].

Table 1: Interventions for Preventing or Reducing Aflatoxin Exposure

Stage	Interventions	References
Pre-Harvest	Timing of planting; Crop planted; Genotype of seed planted; Irrigation; Insecticides; Competitive exclusion; Timing of harvest;	(Cotty and Bhatnagar 2014; Wilson and Payne 2014; Dorner, Cole et al. 2009; Brown, Chen et al. 2011; Chen, Brown et al. 2011; Cleveland, Dowd et al. 2013; Munkvold 2003)
Post-Harvest: Drying and Storage	Hand sorting; Drying on mats; Sun drying; Storing bags on wooden pallets or elevated off ground; Insecticides; Rodent control;	(Hell, Cardwell et al. 2010; Ono, Sasaki et al. 2012; Munkvold 2013; Fandohan, Gnonlonfin et al. 2015; Hawkins, Windham et al. 2005; Turner, Sylla et al. 2015)
Post-Harvest: Food Preparation	Hand sorting; Winnowing; Washing; Crushing and dehulling; Nixtamalization; Acidification; Chemoprotectant; Enterosorption;	(Price and Jorgensen 1995; Voss, Bacon et al. 2006; Elias-Orozco, Castellanos-Nava et al. 2012; Munkvold 2013; Kensler, Egner et al. 2014; Mendez-Albores, Arambula-Villa et al. 2014; Castells, Marin et al. 2015; Fandohan, Zoumenou et al. 2015; Mendez-Albores, Arambula-Villa et al. 2015; Wang, Luo et al. 2015)

While general principles of HACCP and other commercial practices may be applicable at the individual farmer level, appropriate adaptation of these principles into effective and sustainable strategies is essential and currently missing. An intervention to reduce exposure to aflatoxins can occur at various stages of food production and preparation (**Table 1**). Before crops are planted, efforts can be made to reduce the future burden of aflatoxins. Interventions can also occur before harvest, during harvest, and after harvest. The appropriate intervention or combination of interventions may differ depending on the crop and the country. Therefore further evaluation is needed with consideration towards the sustainability, cultural acceptability, economic feasibility, ethical implication, and overall effectiveness of potential interventions.

Pre-harvest mediations

The presence and growth of *fungi* on pre-harvested crops is dependent on the environment. Agricultural practices including proper irrigation and pest management can reduce mycotoxins contamination. Pre-harvest interventions include choosing crops with resistance to drought, disease, and pests and choosing strains of that crop which are genetically more resistant to the growth of the fungus and the production of mycotoxins [15,12,13]. Elimination of inoculum sources such as infected debris from the previous harvest may prevent infection of the crop [51]. A biopesticide, consisting of a non-aflatoxigenic strain of *Aspergillus*, may competitively exclude toxic strains from infecting the crop [19,13] however; the allergenic and human health aspects of the atoxigenic strain need to be evaluated.

Concerns at drying and storage

Before storage, crops should be properly dried to prevent the development of aflatoxins. Sorting and disposing of visible moldy or damaged kernels before storage is proven as an effective method for reducing of mycotoxins [22,23,70-72]. During storage, moisture, insect, and rodent control can prevent damage to the crop and reduce aflatoxin development.

Mycotoxins contamination of maize is influenced by the structure used for storage, the length of time in storage, and the form of maize stored (i.e. with husk, without husk, or as loose grain) [34]. A community-based intervention trial in east Africa focused on thorough drying and proper storage of groundnuts in subsistence farm villages and achieved a 60% reduction in mean aflatoxin levels in intervention villages [70-72].

Post-harvest concerns

Interventions during food preparation or consumption involve removing contaminated portions of food, diluting contaminated food with uncontaminated food, neutralizing mycotoxins present in food, or altering the bioavailability of the mycotoxins consumed. Mycotoxins are not largely affected by routine cooking temperatures, but simple food preparation methods such as sorting, washing, crushing, and dehulling may reduce aflatoxin levels (Lopez-Garcia and Park 2008; Park 2012; Fandohan, Zoumenou et al. 2015) [23, 44,55-58].

Traditional methods of cooking food with alkaline compounds (i.e. nixtamalization) have been used to reduce mycotoxins exposure; however, the chemical reaction may involve temporary inactivation of mycotoxins, a process that may reverse in the gastric acid of the stomach [21,22,23,63,46,47,]. These methods do not always transfer well to other communities due to lack of acceptance. However, the principles could be used to create culturally appropriate methods. Additional strategies for reducing aflatoxins, including enterosorption and chemo protection, attempt to reduce the effects of aflatoxin exposure or the bioavailable portion of aflatoxins in food. These strategies are expensive and therefore difficult to implement in poor communities. Enterosorption is the use of clay, such as NovaSil, with a high affinity for aflatoxins [60,61,75]. Clay has been used as an anti-caking additive in animal feed and has been shown to protect animals from ingested aflatoxins. Chemo protection is the use of chemical (e.g. Oltipraz, Chlorophylin) or dietary intervention (e.g., broccoli sprouts, green-tea) to alter the susceptibility of humans to carcinogens and has been considered as a strategy to reduce the risk of HCC in populations with high exposures to aflatoxins[4,39,74-76,40]. The efficacy, safety, and acceptability of enterosorption and chemo protection require further study.

Awareness and promotion

Raising awareness of aflatoxins and disseminating relevant information to individuals is an important part of any intervention strategy. During the 2005 developing countries outbreak, individuals who reported receiving information on drying and storage through an awareness campaign implemented by the Food and Agricultural Organization, the Ministry of Health, and the Ministry of Agriculture had lower serum mycotoxins levels than those who did not receive this information (CDC 2005). Awareness campaigns should utilize systems that are in place already for disseminating information to subsistence farmers. Such campaigns should also include the dissemination of information to non-governmental organizations, public service associations, health care providers, and schools. Given diversity in culture and remote location of villages, multiple means for disseminating information as part of an awareness campaign may be necessary to reach a broad range of people. Populations not receiving messages from current campaigns and appropriate methods for reaching those populations need to be identified. Reasons for failure or unwillingness to adopt recommendations should also be identified.

APPLICABLE RESEARCH LABORATORY FOR DEVELOPING COUNTRIES

Current methods allow for the detection of mycotoxins and mycotoxins metabolites at very low concentrations in food and biological media; however, the application of these methods within developing countries is limited by practical considerations such as resources and infrastructure. Methods for testing food and biological specimens need to be adapted to fit the surveillance and epidemiologic needs of developing countries. A simple screening method, adapted for developing countries, would benefit subsistence farmers as well as public health and agriculture institutions. Furthermore, these institutions would also benefit from sustainable yet reliable confirmatory methods for use in centralized laboratories.

At field level

Simple and inexpensive field screening methods are available to determine that food is sufficiently free of aflatoxins, but currently lack direct applicability to aflatoxin contamination issues in developing countries. Field methods can be performed with minimal training or equipment and can be performed on-site (i.e. at a farm or grain silo). Field methods for aflatoxin analysis allow for rapid confirmation or exclusion of possible exposure at a reasonable cost, thus allowing officials to quickly determine whether further evaluation and intervention is necessary. Such methods would prove beneficial in developing countries given that the remote location of villages and long distances to a centralized laboratory make it impractical to take samples from villages, analyze them in the laboratory, and then travel back to the village to deliver the results.

Improving the cost, durability, ease of transport, and usability of field methods (e.g., simplicity of use, use in the absence of electricity) is necessary to optimize the public health approach to aflatoxin exposure in developing countries. One field method which could be useful involves dipsticks, which are developed to measure up to the cutoff value for aflatoxins in food that corresponds with trade agreements or regulations (Delmulle, De Saeger et al. 2015) [18]. However, cutoff values in developed countries are markedly lower than typical food levels in developing countries. Such field tests could prove effective if the cutoff value was adjusted based on chronic exposure, health effects, and action levels necessary for developing countries. Field methods for the analysis of biological samples have not been developed. However, the same concept of using dipsticks can be applied to field tests for biological specimens.

At laboratory level

Laboratory methods, which are more precise yet also more labor intensive and costly, can be used to confirm results of field tests. These methods require instrumentation or techniques not suited to working on-site. They require regular maintenance of instrumentation, training of personnel, and a ready supply of reagents and materials [69]. The best laboratory method for testing either food or biological specimen is one that balances the need for quick, accurate results with limitations in resources and infrastructure. Current laboratory methods require further refinement to improve their usability in developing countries. Thin layer chromatography (TLC) is a well-suited laboratory method for testing food samples, given its reliability and simplicity [68,65,66], however, it is labor intensive and limited in the number of samples tested in a day.

Early Threatening Methods in Developing Countries

In order to prevent future outbreaks, developing countries need an early warning system which is able to detect potential food contamination events with adverse health effects (Figure 1) [55-58]. Public health surveillance is the ongoing, systematic collection, analysis, interpretation, and dissemination of data regarding a health-related event for use in public health action to reduce morbidity and mortality and to improve health. Important characteristics of any surveillance system include simplicity, flexibility, data quality, acceptability, sensitivity, positive predictive value, representativeness, timeliness, and stability (CDC 2011). To create an effective and sustainable system, health surveillance and food and biological monitoring strategies must be adapted to meet the needs of developing countries.

Early warning signs need to be validated and a response protocol needs to be developed. Previous outbreaks have been identified by physicians noticing an increase in cases of jaundice despite a lack of any organized or official reporting system. While a national reporting system for jaundice would prove beneficial for developing countries, the baseline rate of jaundice and all its possible causes are not known. In addition, aflatoxicosis confirmation tests using biological markers are limited. An early warning system should also involve monitoring aflatoxin levels in food sources or individuals in order to prevent or reduce the health impact. Monitoring aflatoxin levels in food or individuals to identify those at risk for disease is more difficult than monitoring rates of jaundice. However, food and biological monitoring may identify susceptibility sooner and allow for a more timely intervention. To maximize resources, monitoring or surveillance should target high-risk areas or populations and the most appropriate specimen-food, urine, or serum, should be collected. A rapid, field test that analyzes aflatoxin adducts in biological samples would be ideal for an early warning system that incorporates bio monitoring. Ultimately an early warning system should rely on multiple sources of information and triggers that would set in motion various responses for preventing or reducing an outbreak of mycotoxins.

Triggers for action could also be based upon other factors which indicate or influence mycotoxins contamination, such as reporting of death among livestock or domestic animals which are often given lower quality grain. Modeling of mycotoxins contamination based on weather conditions from planting to post-harvest could also serve as a trigger (de la Campa, Hooker et al. 2015). Such modeling would require further validation and an infrastructure for weather monitoring and dissemination of information. But, it may be the easier and less expensive trigger to implement and would also allow for the earliest intervention in preventing further mycotoxins development. An early warning system must also include a response protocol to prevent further aflatoxin exposure and associated health outcomes once a contaminated food source is identified. A protocol can only be effective if the infrastructure and funds to replace contaminated food exist and a method for identifying families in need has been determined. Inclusion of key members from various government agencies, the health care sector, and non-governmental organizations in an effective communication strategy and in all response efforts is necessary to ensure that an early warning system is successful.

INTERACTIONS AND CO-EXISTENCE OF MULTIPLE MYCOTOXINS

Food commodities affected by aflatoxins are also susceptible to other types of mycotoxins and multiple mycotoxins can co-exist in the same commodity[2,24,67]. Various cereals affected by aflatoxins are also susceptible to contamination by fumonisins, trichothecenes (especially deoxynivalenol), zearalenone, ochratoxin A and ergot alkaloids. Maize can be contaminated with aflatoxins, fumonisin, trichothecenes, zearalenone and, rarely, ochratoxin-A, while wheat can be contaminated with aflatoxins, trichothecenes, ochratoxin-A, ergot alkaloids and zearalenone. Therefore individuals may be exposed to various combinations of mycotoxins (CAST 2013) [7]. The health effects associated with exposure to multiple mycotoxins are not well documented. Related mycotoxins are thought to have an additive effect while unrelated mycotoxins may have a synergistic effect (Speijers and Speijers 2014) [67]. A better understanding of exposure to multiple mycotoxins and the health effects associated with the interactions of multiple mycotoxins would clarify the true health impact of mycotoxins.

CONCLUSIONS

While a great deal is known about mycotoxins, much is not known about mycotoxins exposure and the resulting health effects in developing countries. Even without a complete understanding of the public health problem caused by mycotoxins, it is clear that acute mycotoxins are preventable and chronic exposure can be reduced. The four recurrent themes that were evident throughout the workshop and warrant immediate attention are:

- Quantify the human health impacts and the burden of disease due to mycotoxins exposure,
- Compile an inventory, evaluate the efficacy, and disseminate results of on-going intervention strategies,
- Develop and augment the disease surveillance, food monitoring, laboratory, and public health response capacity of affected regions, and
- Develop a response protocol that can be used in the event of an outbreak of acute mycotoxins.

These steps will provide much needed knowledge about the pattern and resulting health effects of aflatoxin exposure and will enable the development of effective, culturally appropriate interventions for reducing chronic levels of exposure. Although mycotoxins exposure is not a new issue, it requires new strategies to address it effectively within developing countries, where mycotoxins exposure is intertwined with the issues of food insecurity and insufficiency. Collaboration between the agricultural and public health communities, between the local, regional, national, and international governing bodies, and between different disciplines within public health and agricultural is necessary to reduce mycotoxins exposure.

AVAILABILITY OF DATA

No data are associated with this article.

CONFLICT OF INTEREST

No competing interests were disclosed.

GRANT INFORMATION

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