Review Article

IMMUNO-MODULATORY EFFECT OF NUTRITION IN POULTY: IMPLICATIONS FOR FUTURE RESEARCH

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Introduction

In intensive poultry production systems, birds selected for a fast growth rate are raised in confinement at high stocking density. It is estimated that 85 to 90% of performance gains are due to genetic selection, whereas the other 10 to 15% are the consequence of improvements in nutrition and other management practices (Haven-stein et al., 2003). However, selection for growth rate and feed efficiency has resulted in a number of negative effects (Huff et al., 2009) such as reduced resistance to disease (Emmerson, 1997; Leshchinsky and Klasing, 2001) There are many nutrients capable for modulation of the immune system (Jankwoski et al., 2014).The concept of nutritional modulation involves using the specific nutrients to achieve a functional goal in general (Korver, 2012).Tryptophan, a nutritionally essential amino acid, is active in the regulation of immune responses in animals. The products of tryptophan metabolism, such as indoleamine 2,3-dioxygenase, kynurenine, quinolinic acid, and melatonin, may improve immunity in an organism and induce anti-inflammatory responses(Bai et al., 2017).The growth of thymus is relatively faster than the bird's body growth. Therefore, it is important to supply the required quantity of protein, particularly during the early growth phase. Deficiency of protein at this stage leads to the improper development of lymphoid organs. Several research workers have suggested there is a higher amino acid requirement for immunity than for growth. However, the influence of the level of protein in diet on the severity of the disease depends on the type of infective organism. The lesion score to E.coli inoculation decreased with an increase in protein level(18, 20.5 and 23%) I broiler diets. With Coccidiosis, the mortality decreased 32%-8% in chickens fed protein-deficient diets compared to those fed a normal protein level.

High dietary protein increases the activity of trypsin in the chicken gut. A high level of trypsin leads to the faster release of coccidian from oocyst, which will aggravate the disease symptoms.Dietary methionine level in excess of those required for maximum growth is essential for maximizing immunity. Methionine is required by the thymus-derived t-cell function. Methionine deficiency produces lymphocyte depletion and atrophy of bursa and increased susceptibility to Newcastle disease and Coccidiosis.Cysteine supplementation also stimulates cellular and humoral immunity.(70-84% as effective as methionine).Deficiency (16-50%) of branched-chain amino acids like isoleucine,leucine, and valine reduces the antibody titers against SRBC in broilers. Immunoglobulin containsa high concentration of valine and threonine. A deficiency of either of these amino acid reduces the immune response in chickens. A higher ratio between leucine to valine + isoleucine reduces immunity and structural antagonism between three amino acids. The absorption of valine and isoleucine are inhibited by a high leucine content in the diet.Increasing the dietary concentration of lysine improved the haemagglutination and agglutinin titers and IgG and IgM levels. Arginine is a substrate in the synthesis of nitric oxide, a cytotoxic product that is helpful in phagocytic activity of macrophages and kills bacteria and intracellular parasites.

Vitamins

Vitamins act as a cofactor in several metabolic functions in an immune reaction and therefore, deficiency of vitamins cause impairment of immunity.

Generally, higher levels of vitamins than the current recommendations will increase the immune response.

Vitamin A

This vitamin is important for maintaining the cellularity of the lymphoid organs and epithelial tissues and for enhancing both cellular and humoral immunity(Khan et al., 2012). Vitamin A helps in maintaining the mucous membrane of the natural orifices in healthy conditions to prevent the invasion of micro-organisms. Vitamin A directs the differentiation and development of B lymphocytes (Beisel, 1996). The concentration of Vitamin A in diet modulates the expression of retinoic acid receptors on lymphocytes in chickens. The productions of immunosuppressive agents (hydrocortisones) are reduced with a higher level of Vitamin A in the diets. Furthermore, deficiency of Vitamin A causes keratinization of basal cells of bursa and impairment in the response of T- lymphocytes. Therefore deficiency of Vitamin A impairs immunity by producing defective T and B- lymphocytes, impaired phagocytosis and reduced resistance to infection. Increased morbidity due to Newcastle disease virus has been reported due to deficiency of Vitamin A in the diet. The requirement for Vitamin A for maximum immunity i.e.lymphoid organ weight was higher than for the body weight gain in the chicken. An increase in Vitamin A from 12850 IU-42850 or 74045/kg decreased mortality due to E.Coli, and CRD in chickens and increased the rate of clearance of pathogens form blood. However, the beneficial effects of higher levels of Vitamin A depend on the concentration of other fat-soluble vitamins in the diet. An excessive level of Vitamin A interferes with the utilization of Vitamin D and E. The administration of 60 IU of Vitamin A /chick/day during a severe attack of Coccidiosis reduced mortality from 100% to almost zero. However, practical chick and young layer diets should contain 4000 and 200 IU/kg respectively. To minimize stress damage and also to prevent immune suppression, dietaryVitamin A levels should be increased to ten times the normal requirement. A combination of Vitamin A 14000 IU/Kg and Zinc 65mg/kg has been shown to enhance growth and both humoral and cell-mediated immunity in chickens.

Vitamin D

A receptor for 1, 25-dihydroxy vitamin D3 is present in peripheral monocytes. Vitamin-D3 is necessary for the differentiation of pro- monocytes and monocytes to macrophage and the proper phagocytic and cytotoxic activity of the macrophages. CMI decreased significantly in broiler chicks fed diets without any supplemental vitamin D3(Hoff et al., 2009).

Vitamin E

The immune system influenced by infection or vaccination – especially under stress condition is prone to damage by peroxides and superoxides(Khan et al,2012). Vitamins and Selenium protect the immune system under these situations. Vitamins protect the immune systems under this situation. Vitamin E protects the cell by keeping the lipoprotein fractions together in cell membranes and reduces the oxidative changes developed CMI. Vitamin E also enhances humoral immunity by favorably altering the proliferation and ratio of T helper cells. Selenium in glutathione peroxides together with Vitamin E acts as an antioxidant and reduces the concentration of free radicals in the cells. Vitamin E and Selenium play important role in lymphocytes blastogenesis. Deficiency of these nutrients reduces the phagocytic activity of the macrophages. The NRC recommendation for Vitamin E at 20 mg/kg is way below the level of 300 mg/kg that has been shown to increase the immune response and decrease mortality to E. coli, Newcastle disease, Infectious Bursal Disease and Coccidiosis. Increasing Vitamin E supplementation to 250 mg/kg was reported to prevent a drop in egg production in layers exposed to heat stress. The beneficial role of higher levels up to 300 mg/kg of Vitamin E on immunity is mediated through increasing the maturation of T cells. The same high level of Vitamin E reduced the lymphoid organ levels of prostaglandins, which cause suppression of CMI, and thus reduced antibody production. Both humoral and CMI responses in immunized chickens increased significantly with supplemental Vitamin E alone 200 v/s 80 mg /kg or in combination with Selenium 300 mg/kg Vitamin E and 1 mg/kg Selenium. Supplementation of Vitamin E 0.03 % in a breeder diet or by injection (2.5-3 mg/egg) to fertile eggs was reported to increase the immune response of chicks. Similarly, incorporation of Vitamin E in oil adjuvant vaccines (Newcastle disease and Infectious Bursal

Disease) induced more rapid and higher antibody titres than the controls.

Vitamin C

The synthesis of Vitamin C is inadequate in newly hatched chickens and in adult birds subjected to severe stress(Khan et al., 2012). Vitamin C enhances both humoral (SRBC and Newcastle disease) and CMI responses and increases the resistance of birds to *E. coli*, *Mycobacterium avium*, Newcastle disease, Infectious Bursal Disease, Marek's disease, etc. Vitamin C through its antioxidant properties maintains the stability of leukocyte membranes. It is also for the optimum functioning of neutrophils/granulocytes and thereby, it enhances the activity of neutrophils. Vitamin C protects the birds under the heat stress by reducing the synthesis of glucocorticoids. The immunosuppression caused by corticosterone and thermal stress was minimized by Vitamin C (0.1%) in chickens. Variation in the beneficial effects of Vitamin C supplementation has been attributed to the poor stability of the vitamin in some forms under poor but practical storage conditions.

Vitamin B complex

B complex vitamins play an important role in intermediate cell metabolism as co-factors for several enzymes involved in various metabolic reactions. Among the B complex vitamins, Vitamin B6 has been widely studied for its effect on immunity. It is important in the development and maintenance of lymphoid tissue. Deficiency of it (0.95 and 1.48 mg/kg) reduced the antibody response to SRBC and the production of IgG and IgM. Under conditions of heat stress, the administration of Vitamin B6, B2 and B12 has had positive effect on chicken immunity (Tamura et al., 1999).

Minerals

Certain minerals play and important role in immunomodulation through their effects on osmoregulation and by acting as co-factors and enzymatic catalysts and also by optimizing hormone function. Dietary concentrations of Na, Cl, Zn, Se, Mn, Cu, Fe and Co have all been shown to influence immune response. Generally the inorganic forms of the minerals are less well absorbed than the organic/chelated form. Therefore, a higher immune response has been observed when chelated minerals are supplemented in the diet.

Na and Cl

Na and Cl in addition to K play a key role in maintaining osmotic balance in extra and intra cellular fluids. During salt deficiency, chicken retain Na and Cl in the plasma, in addition to other plasma constituents, which may result in decreased immune response in birds fed low Na and Cl diets. Generally, antibody titres increased with higher level of Na (0.14%) or Cl (0.21%) in the diet. The humoral response decreased with less than 0.145% Na and 0.17% Cl. Supplementary salt as NaCl, 0.25, 0.5, 0.75% improved antibody titres against SRBC. However, excessive levels of Cl (0.25 and 0.36%) reduced the antibody response even at a higher Na level in the diet (0.24 or 0.40%). Increasing Cl as an immunomodulator under conditions of heat stress should be used only with great care (Cook, 1991).

Zn

The role of Zn on immunity is mediated through increasing the electrolyte and peripheral T-cell count; the activity of natural killer cells and neutrophils; macrophages production and antibody production; production of interferon and reducing viral penetration. Zn is also required for the proper functioning of thymulin which is involved in lymphocyte development, and metalloenzymeseg DNA and RNA polymerase. Deficiency of Zn impairs interleukin-2 production which plays a role in CMI as well as its role in maintaining the integrity of the lymphoid organs and T cell functions. Zn deficiency in a breeder diet decreased antibody titres to SRBC in their offsprings. Conversely, the antibody response increased significantly in the progeny where Zn was supplemented in the breeder diet (38-160 mg/kg). A few studies have indicated no significant benefits of supplementing Zn upto 220 mg/kg diet of breeders on humoral immunity or CMI(Park et al., 2004).

The discrepancy between the reports may be due to the differences in the concentration of zinc and other trace minerals in the basal diets used in the trails. Supplementation of Zn in the form of a methionine chelate to a breeder diet was more beneficial in the development of immune system organ and increasing antibody titers to SRBC and CMI in the progeny and specific antigens, e.g. *Salmonella enteriditis*, *E.Coli* in the parents (Beach et al., 1982).

Mn

Mn plays an important role in the development, repair and maintenance of the epithelial tissues. Mn dependent superoxide dismutase, present in the mitochondria, inactivates free radical produced within the cells. An organic form of this mineral helps to reduce the incidence of cellulitis and increase the antibody response to infectious bursal disease, Infectious bronchitis and Newcastle disease virus in the breeders (Cotran et al., 1999).

Cu

During the acute phase of an immune response, the liver cell produces, secrete APP in chickens which give Cu protection to birds against infections(Chamanza et al., 1999). Ceruloplasmin is one significant APP in chickens, and it needs Cu as a co-factor. Ceruloplasmin protects the birds by removing free radicals produced during phagocytosis (Cotran et al, 1999). Thus the Cu requirement increase during infection. Cu and Zn dependent SODM in the cytosol inactivates the free radicals. Generally, the requirement for Cu by chicks is higher when they are experiencing an acute phase response than when they are healthy. To increase bird health and wellbeing, additional levels of Cu (125-250mg/kg) can be supplemented to the diet. Cupric chloride is more effective in enhancing intestinal health and acting as an antimicrobial agent against *E.Coli* and salmonella than copper sulphate. Providing in a chelated form with amino acids is said to offer promise (Cohen, 1992).

Fe

The role of iron immunity can be appreciated by the sudden fall in iron concentration in the serum during the early phase of infection. Fe supplementation has been shown to increase the bactericidal activity of the macrophages in the liver and spleen of the affected chicks. The survival rates increased in the chicks inoculated with *Salmonella gallinarum* with additional supplementation of 100mg/kg Fe in diets containing 200mg/kg Fe (Berger, 1996).

Co and Cr

The beneficial effects cobalt on immunity has been attributed to its positive effects on protein synthesis and the function of the lymphoid organs. Supplementary feeding of 0.1or o.5 mcg/kg body weight enhanced the host defense function against infections or Newcastle disease vaccination in broiler chicksGuo et al, 1999).

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