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Diabetic animals injected with human IgG-methylglyoxal-glucose complex elicit antibodies and shows increase in biochemical markers of rheumatoid arthritis: Correlation with data on diabetic patients of varying age and disease duration

Background & Aim: Naturally occurring proteins are significantly more immunogenic than oligosaccharides and polysaccharides. The study of modified-human IgG antigenicity is of particular interest due to the involvement of anti-IgG antibodies in the immunopathology of Rheumatoid Arthritis (RA). Human IgG show immunological behavior in its native conformation but glycation by ribose/deoxyribose/glucose/fructose/glyoxal/methylglyoxal etc. causes structural changes in the IgG and immunogenicity enhancement. In poorly controlled diabetes mellitus and in hyperglycaemia methylglyoxal formation is accelerated. In that scenario IgG being rich in lysine can be a soft target of heavy glycation by methylglyoxal/glucose duo. The glycation may progress to Amadori stage culminate into Advanced Glycation End products (AGE) and may further result in aggregate formation. The study aims to evaluate whether diabetic animals injected with IgG-methylglyoxal-glucose complex would elicit antibodies against the complex and also show increase in biochemical markers typical of RA. The sera of diabetes mellitus patients of different age and disease duration will also be analyzed for auto antibodies against IgG-methylglyoxal-glucose complex and markers of RA.

Method: Experimental diabetes would be induced into rabbits by alloxan. Next, the diabetic rabbits will be injected weekly for seven weeks with IgG-methyglyoxal-glucose complex. The induction of antibodies and its specificity would be evaluated by direct binding and specificity enzyme immunoassay, respectively. Rheumatoid Factor (RF), TNF-α, IL-1 and 6 and CRP level will be estimated in the rabbit sera as well as in the sera diabetic patients of different age and disease duration.

Result: Diabetic animals challenged with IgG-methylglyoxal-glucose complex induced high titer antibodies having excellent specificity towards the immunogens. The level of RF, TNF-α, IL-1 and 6 and CRP in immunogens injected diabetic sera was above respective cut-off values and significantly more as compared to values in the sera of healthy or diabetic rabbits. Furthermore, auto antibodies in sera of diabetic patients showed enhanced binding with IgG-methylglyoxal-glucose complex. In a significant number of cases, but not all that were included in this study, there was direct correlation between level of serum autoantibodies and age of the patients and duration of diabetes mellitus. Another important observation made during the study was that the sera which showed high level of autoantibodies also showed significantly high level of RF, TNF-α, IL-1 and 6 and CRP.

Conclusion: The results obtained so far suggests that IgG-methylglyoxal-glucose complex may have a role in the development of arthritis-like features in long term patients of diabetes mellitus. More biochemical parameters need to be analyzed in diabetic sera of immunized animals as well diabetes mellitus patients, including study of biochemical in joint fluid of healthy and immunized rabbits.

Biography

Khurshid Alam completed his PhD in 1993 from Aligarh Muslim University College of Medicine. He became Faculty in the same year and teaching to undergraduate, postgraduate and doctoral students since then. He has already supervised 10 PhD and 05 MD and successfully operated 06 research projects. He has published more than 80 papers in journals of international repute.

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