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RESEARCH ARTICLE

MAM14 IMMUNOTHERAPY NEW MODALITY TREAT AUTOIMMUNE DISORDERS FIRST TIME PUBLISHED DATA

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ABSTRACT

Background and Objective: There is no safe single treatment for autoimmune disorders until this writing. This new modality is challenging this notion with safe non toxic method named MAM14 immuno therapy. This new method have been tried on many types of autoimmune disorders in the last 25 years in our lab at Kuwait University Faculty of Medicine. In this article we demonstrate the difference of MAM14 on four out of the 14 autoimmune disorder studied compared to control who received conventional chemotherapy.

Patients and Methods: Data accumulated of 1400 patients compared to 1400 controls. For the present article the sample we chose 10 patients treated with MAM14 for each disease studied compared to 10 control patients from the same sickness but treated by conventional immunosuppressant chemotherapy: Cyclosporine, Methotrexate and Tacrolimus. MAM14 immunotherapy In brief is vaccination of patients by allogeneic stressed peripheral blood lymphocytes. Peripheral Blood Lymphocytes isolated from venous whole blood on ficollhypaque centrifugation. Cultured for 24 hours in sterile physiological enriched media. Vaccinated subcutaneously into forearm of patients. Vaccination given every 4 weeks for four visits. 4 autoimmune disorder included in this study namely insulin dependent diabetes mellitus, rheumatoid, multiple sclerosis and Uveitis. Total 40 treated by MAM14 method 10 patients of each disease compared to 10 control patients of the same disorder but on conventional chemotherapy. Prism Graphpad Biostatistical package was used for data analysis.

Result: Data accumulated showed significant improvement in signs and symptoms of the present autoimmune disorders studied. Namely insulin dependent diabetes mellitus, Rheumatoid Arthritis, Multiple Sclerosis and Uveitis.

Conclusion: MAM14 immunotherapy showed superior improvement and safety on the long run compared to control patients who receive conventional immunosuppressant. Mechanism postulated that culturing cells in vitro cause shedding of antigens ,these antigens direct auto reactive pathogenic T cells shift to regulatory protective T cells in the presence of peripheral stem cells Leading to restoring tolerance and switching off autoimmunity reaction.

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INTRODUCTION

There are more than 80 autoimmune disorder (Playfair and Chain, 2013) however, there is no single safe treatment for autoimmune disorders since corticosteroid era to all current chemotherapy or biotherapy immune suppressants (Roitts Essential Immunology, 12th edition). Autoimmune diseases occur when the body recognizes its own tissues as foreign and triggers the adaptive immune system to attack them (Medical Immunology, 2007). This reaction may occur in only one organ, such as a joint (as in rheumatoid or psoriatic arthritis), or across multiple organs , as in systemic lupus erythematosus (SLE) (Roitts Essential Immunology, 12th edition). Autoimmune diseases can cause physical impairment and a decreased quality of life (Medical Immunology, 2007). Although their exact cause remains unknown, experts suspect a combination of factors, such as genetics and the environment, play a role (Playfair and Chain, 2013; Roitts Essential Immunology, 12th edition; Medical Immunology, 2007). The National Institutes of Health estimate that up to 23 million Americans have autoimmune diseases, about 8 percent, making them more common than cancer or heart disease (Medical Immunology, 2007) These diseases often are marked by periods of remission alternating with incapacitating exacerbations (Roitts Essential Immunology, 12th edition).

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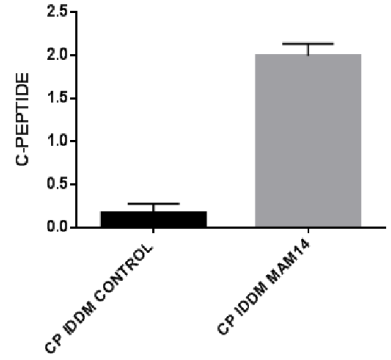
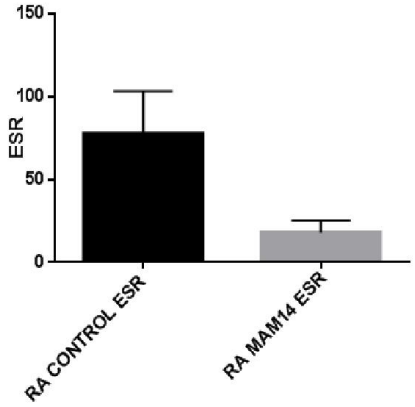
Because no known cure exists, treatment of autoimmune diseases focuses mainly on managing symptoms and achieving remission (Play fair and Chain, 2013). Recommendations include lifestyle modifications, such as regular exercise, a well-balanced diet, plenty of sleep, and stress control. Until recently, pharmacologic treatment was limited to analgesics, non steroidal anti-inflammatory drugs (NSAID), and corticosteroids. But since disease-modifying an tirheumatic drugs (DMARDs) were introduced (Medical Immunology, 2007) many patients have experienced better symptom control and improved quality of life. DMARDs essentially are either chemotherapy or biotherapy medications; many traditionally have been used to treat cancer. Their effectiveness against autoimmune diseases is thought to stem from their immunosuppressant or immune modulating properties. Both chemotherapy and biotherapy were found up not safe.

IDDM FIGURE 1 C-PEPTIDE MAM14 COPMPARED TO CONTROL



10 IDDM C-PEPTIDE MAM14 IMMUNOTHERAPY COMPARED TO 10 CONTROL
Mann whitney test P value 0.0001

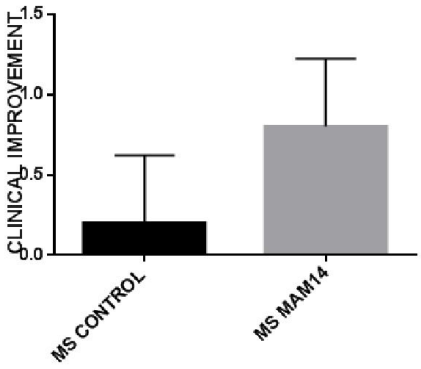
RA FIGURE 1 ESR TREATED COPMPARED TO CONTROL



10 RHEUMATOID ARTHRITIS ESR COMPARED TO 10 CONTROL
Mann Whitney test P value 0.0001

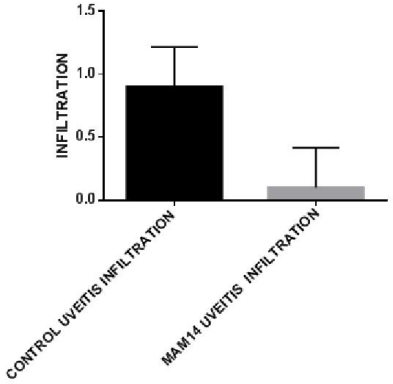
You have to assess patients before they enroll in these medication. Before treatment begins, also patient got to give informed consent. In the present revolutionary proposed treatment MAM14 immunotherapy we are uncovering a development which give treatment without the side effect encountered by conventional immune suppressants. In our laboratory from 1979-1999. Immuno gentics were employed to look for a mechanism of MAM14 immunotherapy (Saleh A Alharbi and Ali S. Alharbi, 2015; Alharbi and Ali S. Alharbi, 2015; Mark mccarty and Saleh A. Alharbi, 2013;

MS FIGURE 1 MAM14 TREATED COMPARED TO CONTROL



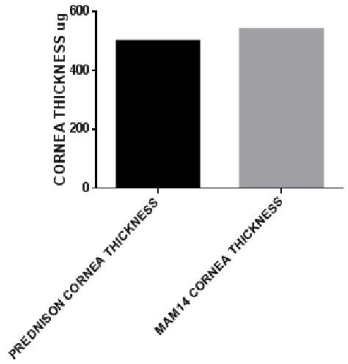
10 MS TREATED COMPARED TO 10 CONTROL
Mann Whitney P VALUE 0.0230

UVEITIS FIGURE 1 LYMPHOCYTE INFILTRATION COMPARED TO CONTROL
SLIT LAMP



10 UVEITIS MAM14 PATIENTS LYMPHOCYTE INFILTRATION REDUCED SIGNIFICANTLY
Mann Whitney test P value 0.0011

UVEITIS FIGURE 2 PREDNISONE CORNEA DEGRADATION NOTICED SIGNIFICANTLY COMPARED TO MAM14
Pachymeter



10 UVEITIS PREDNISONE TREATED CORNEA THICKNESS REDUCED SIGNIFICANTLY
Mann Whitney test P value 0.0011

Alharbi, Saleh, 2010; Al-Harbi and Levy, 1982; Levy *et al*., 1982; Levy *et al*., 1983; Levy *et al*., 1982; Al-Harbi, 1984; Levy *et al*., 1984; Fouad *et al*., 1994; Al-Harbie *et al*., 1994; Al-Harbi *et al*., 1994; Al-Harbi *et al*., 1995; Kaaba and Al-Harbi, 1995; Al-Harbi *et al*., 1996; Mahmoud *et al*., 1996; Al-Harbi and Haines, 1993; Al-Harbi and Haines, 2004). The treatment relied on immune regulation possibly through (PBL) antigen shedding (Pual H Black personal communication), (Peschon *et al*., 1998) in the presence of peripheral stem cells.

RESULTS

IDDM

MAM14 immunotherapy in the long run showed dramatic response in all 14 autoimmune diseases studied (n = 1400) compared to control (n = 1400) whom they received conventional chemotherapy namely methotrexate, Cyclosporine and Tacrolimus. Data presented in this article confined to only 4 group of autoimmune disorders out of 14 disorders. Consist of 10 IDDM, 10 Rheumatoid Arthritis, 10 Multiple Sclerosis and 10 Anterior Uveitis. Total patients presented here, 40 patients treated by MAM14 compared to 40 patients treated by conventional chemotherapy. Figure 1showed C-peptide significantly increased in IDDM treated by MAM14 immunotherapy compared to control IDDM treated by Cyclosporine.

Rheumatoid Arthritis

Figure 1 Rheumatoid Arthritis (RA) showed ESR lowered significantly in 10 RA treated by MAM14 immunotherapy compared to 10 control RA treated by conventional chemotherapy.

Multiple Sclerosis

Anterior Uveitis (Figure 1 and 2)

Figure 1 Uveitis lymphocyte infiltration examined by, Slit Lamp, reduced significantly in MAM14 immunotherapy treated patients compared to control uveitis treated by steroid eye drops. Figure 2 Uveitis showed significant degradation in cornea thickness, 500 micron, in prednisone eye drops treated patients compared to normal cornea thickness, 540 micron, in MAM14 immunotherapy treated patients.

Conclusion

MAM14 cause dramatic significant improvement in all signs and symptoms of autoimmune disorders studied so far (Saleh A Alharbi and Ali S Alharbi, 2015; Saleh A Alharbi and Ali S Alharbi, 2015; Alharbi and Haines, 1999; Alharbi and Haines, 2004). Autoimmune Disorders studied in our laboratory were 14 disorder totaling 1400 patients namely:

IDDM, Rheumatoid Arthritis, SLE, MS, Bronchial Asthm, Uveitis, Allergic Rhinitis, Psoriasis, Rheumatic Arthritis, Alopecia Areata, Autoimmune Thyroiditis, Eczema, pemphigus vulgaris and IgA nephropathy. Results compared to 14 control autoimmune disorder totaling 1400 patients of the same disease but treated by conventional immune suppressants. Mann Whitney test, used with a two- tailed T test for comparing P values of experiment and control. Data shown in this article are only 4 out of 14 autoimmune disorder namely: IDDM, Rheumatoid Arthritis, Multiple Sclerosis and Uveitis. From the graphs presented an examiner notice the superiority of MAM 14 immunotherapy compared to the conventional chemotherapy which is not safe with a limited benefit.

Notion of auto reactive T cell conversion to regulatory T cell is well known in immunology practice nowadays (Roitts Essential Immunology, 2007; Bettelli *et al*., 2006). Peripheral Blood Lymphocytes shed antigens when they are stressed in vitro. These antigens play a major role in converting detrimental autoreactive T cells into protective regulatory T cells in the presence of peripheral stem cells leading to switching autoimmunity reaction to tolerance leading to off the reaction. This will lead to ameliorating sign and symptom of autoimmunity causing patient relief without the necessity of anti- inflammatory drugs like NSAID OR conventional chemotherapy.

The precise mechanism that give rise to autoimmune disease remain incompletely understood (Playfair and Chain, 2013; Roitts Essential Immunology, 12th edition). Much of our current knowledge comes from the study of animal models, such as experimental allergic encephalitis and collagen-induced arthritis, in which autoimmunity is induced by direct immunization with self-proteins. These models have taught us much about how tolerance may be broken, but important differences remain between the corresponding animal and human diseases (Playfair and Chain, 2013; Roitts Essential Immunology, 12th edition). No cure exist for most autoimmune diseases and treatment is symptomatic (Playfair and Chain, 2013; Roitts Essential Immunology, 12th edition; Medical Immunology, 2007). The available chemotherapy or biotherapy are of limited success and their risk outweigh the benefit (Roitts Essential Immunology, 12th edition). The present MAM14 immunotherapy protocol solves the problem by dealing with converting detrimental auto reactive T cell to protective T regulatory cells (Playfair and Chain, 2013; Bettelli *et al.,* 2006) in the presence of shedding antigens (Paul H Black personal communication), (Peschon *et al*., 1998) especially in the presence of peripheral stem cells, restoring in this way self-tolerance which is needed to switch off-autoimmunity reaction. (Paul H. Black, personal communication)

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