Effect of Immuno Suppressent (Methylprednisolone) and Its Biochemical Changes in Rheumatoid Arthritis
G. SHANTHI, V. SIVAKUMARI, R. PRABHU AND S. GIRIDARAN

ABSTRACT
Rheumatoid arthritis is potentially crippling disease. Numerous pharmacologic agents are available for treatment of rheumatoid arthritis; the goal in therapy is relief of pain and inflammation, through modification of disease process. Several corticosteroids play an important role in the management of RA, among corticosteroids methylprednisolone shows beneficial effect. In this study the level of ADA activity, C-reactive protein and erythrocyte sedimentation rates are reduced after treatment with methylprednisolone compared to rheumatoid arthritis patients. This shows that methylprednisolone involves in several metabolism of inflammatory process. But it does not shown any significant changes in pain score compared to rheumatoid arthritis patients, this may be due to it does not involves in analgesic process. In rheumatoid arthritis pain and inflammation are important two symptoms. Based on present study it can be concluded that methylprednisolone has more anti-inflammatory effect compared to analgesic effect. So, while treating rheumatoid patient with methylprednisolone they should take care of pain of patient with some other pain killers like NSAIDS or potent opioids. The understanding of the pathophysiology of rheumatoid arthritis and precise knowledge of the possible triggers of the inflammation may open novel therapeutic approaches. Hence, the present study suggests the importance of measuring the biomarkers of inflammation assessed in the study not only to determine the severity of inflammation and the effect of treatment with drug.

Key words : Rheumatoid arthritis, ADA activity, C-reactive protein and erythrocyte.

Rheumatoid arthritis is a chronic inflammatory condition of unknown etiology affecting primarily the synovium, leading to joint damage and bone destruction (Haugeberg et al., 2003). Rheumatoid arthritis causes significant morbidity as a result of synovial inflammation, joint destruction and associated disability. It is classified as one of the autoimmune disease (Cassim et al., 2002). There is a prominent immunological dysfunction in the joints and many other tissues by accumulation of chronic inflammatory cells including T-cell and B-lymphocytes, monocytes and macrophages. It affects approximately 1-2% of World’s population (Deborah et al., 2002). In India, alone there are some 10 million people affected with rheumatoid arthritis and is associated with reduced life expectancy and is a major cause of chronic disability and handicap.

Methylprednisolone is an intermediate acting corticosteroid with an anti-inflammatory potency five times that of cortisol. Clinical situations that require parantaral administration of corticosteroids in large doses usually employ methylprednisolone (Wilson, 1974). As the prolonged half-life of dexamethasone produces a greater degree of hypothalamic-pituitary axis suppression as compared to methylprednisolone, the latter is preferred over dexamethasone in pulse corticosteroid therapy (Hari et al., 1998).

Methylprednisolone has serious side effects if taken long-term, including weight gain, glaucoma, osteoporosis and psychosis, especially when overdosed. The most serious side effect occurs after the adrenal glands cease natural production of cortisone, which methylprednisolone will replace. Abrupt cessation of the drug after this occurs can result in a condition known as Addisonian crisis, which can be fatal. To prevent this, the drug is usually prescribed with a tapering dosage, including a pre-dosed “dose pack” detailing a specific number of pills to take at designated times over a six day period (ACR Subcommittee, 2002).

MATERIALS AND METHODS
50 patients presenting rheumatoid arthritis attending Sounderrajah rheumatology Hospital, Chennai were included in the study. The diagnosis of rheumatoid arthritis was established by clinical analysis, ESR and pain scale at initial stage and after treatment with Methylprednisolone-4mg (Methone-4) procured from Icarus pharmaceuticals for
duration of 3 months. Equal number of age and sex matched healthy individuals with no known history of any disease were taken as control. All the subjects were examined clinically and information pertaining to age, sex, habits and health status was recorded in special case proforma. Blood samples were collected from both controls and patients for clinical estimation.

**ADA estimation:**

The serum was assayed immediately for ADA activity at 37°C by a spectrophotometric method using adenosine as the substrate. This method is based on the Bertholet reaction, that is, the formation of coloured indophenols complexes from ammonia liberated from adenosine and quantified spectrophotometrically at 630 nm (Galanti and Guisti, 1984). One unit of ADA is defined as the amount of enzyme required to release one micromole ammonia per minute from adenosine at standard assay conditions. The activity of ADA is expressed in units/liter.

**C-Reactive protein detection:**

For the detection of CRP in serum. Avitex-CRP kit was used which is arapid latex agglutination test. The test is based on the principle that avitex-CRP latex particles are coated with antibodies to human CRP, i.e. when the latex suspension is mixed with serum containing elevated CRP levels on a slide; clear agglutination is seen within 2 minutes. Avitex-CRP has detection limit of 6mg/litre of CRP in patient’s serum. the test is considered as positive when the CRP serum concentration is above 6mg/litre and negative when it is at 6mg/litre and below (Tam Lai-Shan et al., 2007).

**Erythrocyte sedimentation rate:**

ESR denotes the velocity of sedimentation of RBC per unit of time and is expressed in mm at the end of one hour. Using a 2 ml disposable syringe, 1.6 ml of venous blood is drawn and mixed with 0.4 ml 3.8% sodium citrate solution in a test tube. The Westergren’s tube is filled up to 0 mark with citrated blood and placed vertically, in the rack. The sedimentation of RBC in mm in one hour is observed (Evangelia et al., 2007).

<table>
<thead>
<tr>
<th>Normal range</th>
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<tr>
<td>Men</td>
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<td>0–15 mm/hr</td>
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<td>Women</td>
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<td>0–20 mm/hr</td>
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**Pain measurement:**

Pain is measured in rheumatoid patients based on Randall chronic pain scale. In that several level of pain is described by using a phrase which best tells what patients are able or unable to do, not how they feel. How they were feeling emotionally does affect their pain. Each of us may vary a lot in how much attention we pay to our pain at any given time depending on our particular emotional state at that moment. How or whether we respond to our pain at a given level is not consistent or predictable. Therefore, this part of the pain scale should reflect the patient’s ability to function. This pain scale is updated by doctor in every visit of the patient and recorded.

**Statistical analysis:**

The data of the study subjected to statistical analysis is expressed as mean ± S.D. Statistical comparison were performed by student “t” test using SPSS-7 package.

**RESULTS AND DISCUSSION**

To determine the biochemical changes in rheumatoid arthritis patients’ with effect of methylprednisolone treatment, the detailed clinical examination are performed by rheumatologist of the centre and 50 patients with confirmed diagnosis of rheumatoid arthritis were included in the study. Adenosine deaminase level, C-reactive protein, erythrocyte sedimentation rate and pain score were determined and evaluated. The results are presented in the following Table 1, 2, 3, 4 and 5.

**Age and sex**

Among 50 patients of rheumatoid arthritis 19 patients were males and 31 were females as shown in Table 1. The mean ± S.D. of age in males was 44.35±13.70 (years) and females was 44.14 ± 14.37 (years) and mean age of control males was 40.46±8.45 (years) and control females was 44.64 ± 12.96 (years).

| Table 1: Sex and mean age (years) of test group |
|-----------------|-------|-------|
| Group           | Control | Treatments |
| Sex             |       |         |
| Male            | 20     | 19      |
| Female          | 30     | 30      |
| Age             |       |         |
| Male            | 40.46±8.45 | 44.35±13.70 |
| Female          | 44.64±12.96 | 44.14±14.37 |

**Serum ADA levels:**

Mean ADA levels estimated in rheumatoid arthritis patients (before and after the treatment with methylprednisolone) and controls are presented in Table 2. The mean ± S.D. of ADA levels in serum of RA patients was 59 ± 79.21 and that of the control was 20.71 ± 5.63. After treatment with methylprednisolone -4 mg for 3
month, the mean ± S.D. of ADA levels in serum reduced to 32.68 ± 17.01. The difference in the mean values was statistically significant at p<0.01 compared to baseline patients i.e. before treatment. This shows that methylprednisolone treatment reduces the cell mediated immunity in rheumatoid patients. Because ADA is the marker of cell mediated immunity, the enzyme ADA involves metabolism of purine bases in the process of physiological activity is related to lymphocytic proliferation and differentiation.

In another report Sari et al. (2003) investigated the correlation between the activity of total ADA and clinical activity in patients rheumatoid arthritis and concluded that serum ADA activity is closely associated with rheumatoid arthritis and further suggested that these non-invasive investigations can be used as biochemical marker for inflammation which may provide additional information regarding disease activity along with the traditional indices such as ESR and CRP.

### Serum CRP level:

CRP level estimated in the rheumatoid patients (before and after treatment with methylprednisolone -4 mg) and controls are presented in Table 3. The mean ± S.D. of serum CRP level in RA patients was 22 ± 0.19 and that of the control was 3±0.8. But in treatment group the CRP level was decreased to 10.12 ± 0.2. The difference in the mean values was statistically significant at p<0.01 compared to before treatment. This may due to methylprednisolone reduces the rheumatoid arthritis induced inflammatory processes in the patients. It is evident that CRP is a prototypic marker of inflammation in rheumatoid arthritis and several diseases also. But the level of CRP is not decreased to the level of control group. This may be due to incomplete cessation of rheumatoid arthritis induced inflammation process in patients. Recent studies suggest that CRP may also contribute directly to the proinflammatory state. CRP stimulates monocytes release of inflammatory cytokines such as IL-1β, IL-6 and TNF-α and may also directly act as a proinflammatory stimulus to phagocytic cells (Klocke et al., 2003).

### ESR:

The mean ESR levels estimated in RA patients (before and after treatment with methylprednisolone) and control presented in Table 4. ESR is the index of inflammatory process during rheumatoid arthritis and ESR level was elevated to 48±9.6 compared to control 14.6 ± 8.7. After methylprednisolone treatment (4 mg twice daily for 3 months) there was a beneficial reduction in ESR level to 16.2 ± 2.3 and their mean values were statistically significant at p< 0.01. This may be due to anti autoimmune depressant properties of methylprednisolone in rheumatoid arthritis disease state. As referred in review of literature methylprednisolone involves several mechanisms to suppress the immunological effect of body during rheumatoid arthritis in patients.

### Pain score:

Pain felt by rheumatoid arthritis patient was recorded in forms of Randall chronic pain scale and presented in Table 5. The patients reported that there was no significant difference in pain score after methylprednisolone administration. This may be due to immunosuppressant effect of methylprednisolone without analgesic effect of the drug.

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REFERENCES


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