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Biologicals in Juvenile Idiopathic Arthritis

We share our experience with biological agents in children with juvenile idiopathic arthritis with an aim to highlight the adverse events and response to treatment. Out of a total of 10 children treated with biological agents, one patient had serious infection, all showed good response and none had tuberculosis. High cost was limiting factor for their use.

Keywords: *Arthritis, Etanercept, Treatment, Outcome.*

Better understanding of pathogenesis of juvenile idiopathic arthritis (JIA) have led to the use of a number of biological agents in last two decades [1]. Their high cost and potential adverse effects preclude them from being used as first-line agents in developing countries. Their most important adverse effect is infection, and in India, tuberculosis is of particular concern [2]. Aim of the present study was to evaluate the adverse events and response to biological agents in patients with JIA, and to provide description of challenges in way of treatment of JIA with biological agents.

We conducted chart review of all patients diagnosed to have JIA and treated with biological agents in our center. Diagnosis of JIA was based on International League of Associations for Rheumatology Criteria [3]. They were treated as per guidelines of American College of Rheumatology [4]. Selected patients who were refractory or had responded inadequately to conventional therapy, were explained the need of biological therapy. It was prescribed on an individual basis to those who could afford it. Screening for tuberculosis was done before the initiation of therapy. Patients were followed up every 4-12 weeks and the following information was extracted from their records: demographic profile, clinical phenotype, laboratory results, therapy, response and side effects. As available data might not suffice for standard outcome criteria [5,6], response to treatment was defined as complete response (no or minimal residual symptoms, with no requirement for supplementary agents to maintain clinical remission and normal laboratory study findings), no response (no or minimal clinical benefit), and partial response (intermediate between remission and absent response) [7].

Biological agents were given in 14 patients between March 2012 – July 2015. Four patients were excluded because total duration of follow up was less than 12 weeks in two, and discontinuation of therapy (because of financial constraints) in two patients. Before commencing biological agent, all 10 patients (7 males) were on disease modifying antirheumatoid drugs (DMARDS), and 7 were on systemic steroids. Mean (SD) age of study population at onset of disease and at commencing biological agents was 4.8 (2.7) and 7.3 (3.6) years, respectively. Median (range) duration of follow up following initiation of biological agents was 11 (range 4-41) months. Clinical profile of the patients who received biological agents are summarized in ***Table* I.**

Clinical response was seen in nine out of 10 patients. Eight patients achieved complete response, while one had partial response. Median (IQR) time to show response for systemic features was 15 (15,20) days, and for articular disease was 40 (30,75) days. Five out of 7 patients were free of steroids by three months. One patient suffered from bronchopneumonia necessitating systemic antibiotics, and another had minor reactions related to tocilizumab infusion. No case of tuberculosis, malignancy or death occurred while on treatment.

Experience with these agents in Indian patients is scant. With biological agents, substantial proportion of patients were able to discontinue systemic steroids. Efficacy to the biological agents in published literature (75-85%) is comparable to the present study [8-10]. Limitation of present set of data includes small number of patients, lack of standardized outcome criteria due to retrospective study design and use of biological agents in only those who could afford. Two patients had to stop treatment due to high cost. We conclude that biological agents can be used in children who fail conventional treatment without risk of increased incidence of infection.

Contributors: IS: Data collection, analysis and manuscript writing; LD: data collection and manuscript writing; NG: data collection and manuscript writing; SKK: data collection,

TABLE I CLINICAL PROFILE OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS WHO RECEIVED BIOLOGICAL AGENTS

Age (y) at onset/ at initiation of treatment	*Type of disease*	*Biological agent used**	*Outcome*	*Time to response (d)*	
				Systemic features	*Articular features*
3.6 /4.2	Systemic onset	Tocilizumab	No response	–	–
		Abatacept	No response	–	–
5/6	Systemic onset	Tocilizumab	Partial response	30	Still active
6/13.9	Polyarticular	Etanercept	Complete response	-	60
3/3.5	Systemic onset	Tocilizumab	Complete response	15	30
10.6 /13	Polyarticular	Etanercept	Complete response	-	50
2/4.1	Systemic onset	Tocilizumab	Complete response	15	30
7/8.3	Systemic onset	Etanercept	Complete response	15	30
4/5.1	Polyarticular	Etanercept	Complete response	-	150
1/8	Systemic onset	Tocilizumab	Complete response	20	90
6/7	Systemic onset	Etanercept	[#]Complete response	7	30

**Doses of biological agent used: Tocilizumab 8 mg/kg/dose q 2 weeks, if <30kg 12 mg/kg/dose (IV infusion, dose tapered to 4 weeks with clinical response, Etanercept-0.8 mg/kg q wk SC, Abatacept-10 mg/kg wk 0, 2, 4, then q 4 wk IV infusion; [#]Off medication for 1 year.*

analysis, manuscript writing, and will act as guarantor for the study

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ISHA SAINI, LESA DAWMAN, NEERJA GUPTA AND *SK KABRA

Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India

**skkabra@hotmail.com*

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