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Oral Phospholipidic Curcumin in Juvenile Idiopathic Arthritis-Associated Uveitis

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Purpose: To evaluate the efficacy and the safety of curcumin-phosphatidylcholine complex in children affected by juvenile idiopathic arthritis (JIA)-associated uveitis as an adjunctive treatment to their chronic systemic immunosuppressive therapy.

Methods: In this retrospective, longitudinal study, we treated patients affected by JIA-associated uveitis with residual low-grade inflammatory activity in the anterior chamber with one tablet of curcumin-phosphatidylcholine complex per day, over a year. Low-grade inflammatory activity was characterized by flare 1+ at slit-lamp examination and 10-50 photon counts per ms (ph/ms) at the FC500 Laser Flare Meter (LFM). Inactivity of uveitis was defined as complete disappearance of flare at the slit-lamp examination and values <10 ph/ms at LFM. Conversely, recurrence of the uveitis was defined as a one-step increase from baseline in anterior chamber cells levels or LFM measurements >50 ph/ms.

PT	SEX & AGE	JIA TYPE	AGE AT JIA ONSET	AGE AT UVEITIS ONSET	LATERALITY OF UVEITIS	COMPLICATIONS of UVEITIS	SYSTEMIC TREATMENT
1	F, 31	Oligo-extended, ANA+	2	12	Bilateral	BK	Adalimumab
2	M, 30	Oligo-extended, ANA+	2	2	Bilateral	Cataract	Golimumab
3	F, 25	Oligo-extended, ANA+	5	5	Bilateral	BK, IOL	MTX, Infliximab
4	F, 9	Oligo-persistent	5	6	Monolateral	/	MTX, Adalimumab
5	F, 9	Oligo-extended	5	5	Monolateral	/	MTX, Adalimumab
6	F, 11	Oligo-extended, ANA+	1	2	Bilateral	BK	MTX, Infliximab
7	F, 6	Oligo-persistent	3	6	Monolateral	/	MTX, Adalimumab
8	F, 30	Oligo-persistent	15	15	Bilateral	PS	MTX, Infliximab
9	M, 25	Oligo-extended, ANA+	6	7	Bilateral	PS	Golimumab
10	M, 6	Oligo-extended, ANA+	6	6	Monolateral	/	MTX, Adalimumab
11	F, 13	Oligo-extended	8	4	Bilateral	PS	MTX, Adalimumab
12	F, 29	Oligo-extended, ANA+	4	4	Bilateral	/	MTX, Infliximab
13	F, 11	Oligo-extended, ANA+	5	5	Monolateral	/	MTX, Adalimumab
14	F, 22	Oligo-extended	1	3	Bilateral	PS, cataract	MTX, Infliximab
15	M, 19	Oligo-extended	7	7	Bilateral	/	MTX, Adalimumab
16	F, 7	Oligo-extended, ANA+	1	3	Bilateral	Aphakia	MTX, Adalimumab
17	F, 12	Oligo-extended	2	3	Bilateral	PS	MTX, Adalimumab
18	M, 23	Oligo-extended, ANA+	9	4	Monolateral	BK	MTX, Golimumab
19	F, 22	Oligo-persistent	1	1	Bilateral	/	Rituximab
20	F, 17	Oligo-extended	2	5	Bilateral	IOL	MTX, Infliximab
21	F, 3	Oligo-extended, ANA+	1	2	Bilateral	/	MTX, Adalimumab
22	F, 22	Oligo-extended, ANA+	2	5	Bilateral	PS	MTX, Adalimumab
23	F, 26	Oligo-extended, ANA+	1	18	Bilateral	/	MTX, Adalimumab
24	F, 12	Oligo-persistent	1	5	Bilateral	PS	MTX, Adalimumab
25	M, 8	Oligo-extended	7	8	Monolateral	/	MTX, Adalimumab
26	F, 12	Oligo-extended, ANA+	5	8	Bilateral	PS	MTX, Infliximab
27	F, 31	Oligo-extended, ANA+	1	2	Bilateral	PS, cataract	Golimumab

Table 1. Patients' demographics, uveitis characteristics and current systemic treatment for JIA. ANA:antinuclear antibodies. BK:band keratopathy; IOL: intraocular lens; PS:posterior synechiae; MTX:methotrexate

Results: A total of 22 out of 27 patients (81%) achieved inactivity at the end of the study. Five patients (19%) did not show a significant reduction in anterior chamber flare, remaining stable throughout the follow-up. Only three episodes of flare-ups in three different patients were recorded. Overall, the treatment was well tolerated by all patients and no ocular discomfort, ocular side effects, or allergic reactions were registered.

MULTIPLE COMPARISONS	MEAN DIFFERENCE (ph/ms)	95% CI OF DIFFERENCES	P-VALUE
BASELINE VS. 1M	8.667	3.210 to 14.12	0.0006*
BASELINE VS. 3M	17.93	10.92 to 24.94	< 0.0001*
BASELINE VS. 6M	18.96	9.812 to 28.11	< 0.0001*
BASELINE VS. 9M	20.33	12.00 to 28.67	< 0.0001*
BASELINE VS. 12M	22.52	14.63 to 30.40	< 0.0001*
1M VS. 3M	9.259	3.843 to 14.68	0.0002*
1M VS. 6M	10.30	1.535 to 19.06	0.0145*
1M VS. 9M	11.67	3.316 to 20.02	0.0027*
1M VS. 12M	13.85	6.860 to 20.84	< 0.0001*
3M VS. 6M	1.037	-7.319 to 9.394	0.9988
3M VS. 9M	2.407	-3.403 to 8.218	0.7965
3M VS. 12M	4.593	0.7074 to 8.478	0.0137*
6M VS. 9M	1.370	-7.470 to 10.21	0.9966
6M VS. 12M	3.556	-3.244 to 10.36	0.6018
9M VS. 12M	2.185	-2.607 to 6.978	0.7261

Table 2. Semi-automated flare measurement of study population during the follow-up. Each value is expressed as mean ± standard deviation (SD). M: months; ph/ms: photon counts per ms; CI: confidence interval. All the p-values refer to repeated measure Analysis of Variance (ANOVA) with Tukey correction.* Statistically significant value.

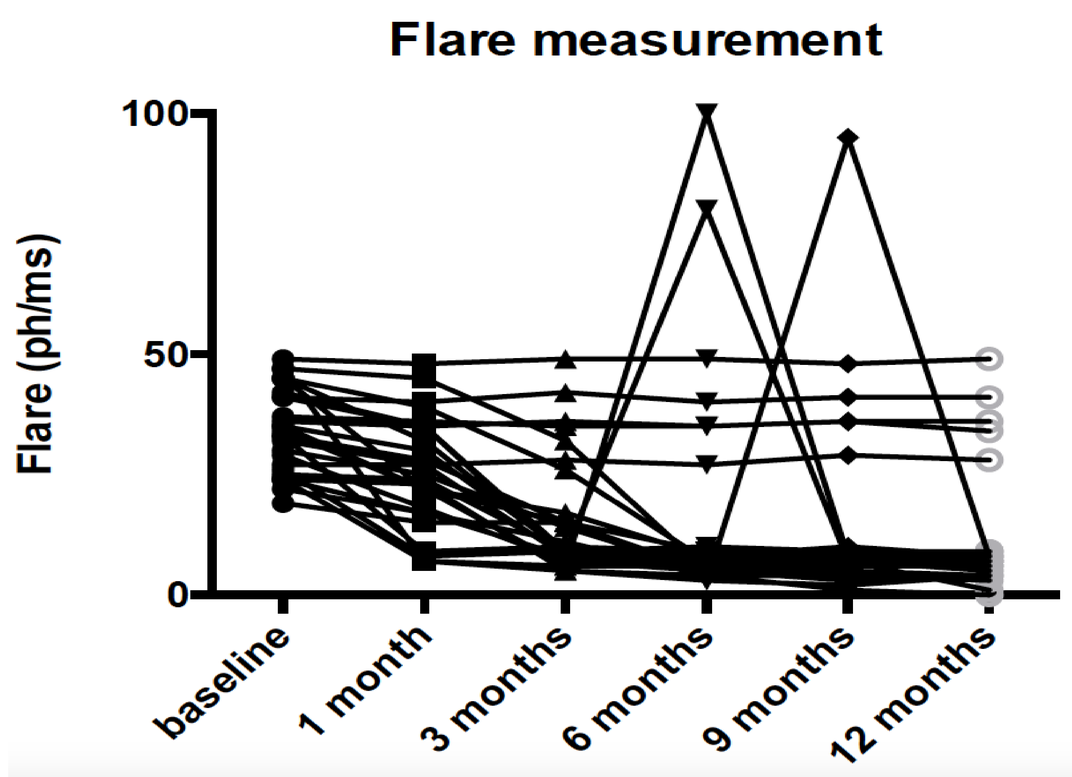

Figure 1. Semi-automated flare measurements of study population during the follow-up. Four patients reached inactivity of the uveitis at 1 month, 10 patients at 3 months, and 8 patients at 6 months, while 5 patients did not show a significant reduction in flare during the study. Three patients experienced a flare-up by the 9th month.

Conclusion: Adjunctive therapy with curcumin in patients affected by JIA-associated uveitis improves mild chronic anterior chamber flare and presents a good safety profile. Chronic low-grade anterior chamber inflammation in JIA uveitis patients should be minimized to avoid the development of sight-threatening complications in these patients.

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