Anthropometric Effects of Intravenous Methylprednisolone Versus Oral Corticosteroids in the Treatment of Juvenile Dermatomyositis

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Introduction

Although juvenile idiopathic inflammatory myopathies are quite rare, juvenile dermatomyositis (JDM) is by far the most common inflammatory myopathy seen in children1 with a yearly incidence of 3 [1], children/million [2]. Before the introduction of treatment modalities nearly 50 years ago, the mortality rate of JDM was nearly 35%; it has now been reduced by approximately two-thirds [3]. While the exact etiology and pathogenesis are not fully understood, JDM is known to be a vasculopathy with known capillary lumen obliteration, perivascular atrophy, endothelial inflammation, tubuloreticular inclusions, and muscle degeneration and regeneration [4,5]. An array of factors has been implicated, including genetic predisposition, infectious agents and environmental triggers, complement-induced injury, major histocompatibility complex class expression, and expression of adhesion molecules increasing the inflammatory response [1]. The most widely used diagnostic criteria for JDM, as suggested by Bohan...
and Peter [6] include 4 parameters regarding muscle disease: elevated enzymes, abnormal electromyogram, abnormal biopsy, and proximal muscle weakness; as well as 1 criterion based on dermatologic features. Oral corticosteroids (OCS) have traditionally formed the backbone of JDM therapy as well as numerous other autoimmune, inflammatory, and neoplastic disorders due to their effects on the pathological inflammatory and immune mediators. Corticosteroids are such a frequently used treatment modality, that one study on asthma therapy suggested that nearly 1 in 10 children in Great Britain had been on OCS therapy at some point in their youth [7]. Unfortunately, along with their benefits, OCS can have significant side effects. Long-term effects include: Cushingoid features, weight gain, osteopenia with associate bone fractures and bone necrosis, hypothalamic-pituitary-adrenal axis suppression, peptic ulcer disease, intestinal perforation, hyperglycemia, hyperlipidemia, lipodystrophy, hypocalcemia, hypokalemia, infections, hypertension, cataracts, glaucoma, steroid-induced myopathies, depression, and psychosis [8,9]. OCS can also attenuate achievement of peak bone mass and stunt growth by alteration of gonadal function [10].

Intravenous steroid injections in supra-physiological “pulse” doses were first used in the treatment of renal graft rejections [11]. Since then, pulse dosing has been useful when rapid anti-inflammmatory or immunosuppressive effects are needed [12] in other conditions including lupus nephritis, severe glomerulonephritis, acute asthma attacks, vasculitides, dermatologic conditions, inflammatory bowel disease, acute spinal cord injuries, and hematologic disorders [12-16]. Pulse intravenous methylprednisolone (IVMP) therapy, either alone or with OCS, is thought to allow earlier remission and thus prevent the adverse, long-term sequelae of OCS usage [1]. Furthermore, a significant number of patients with JDM have bowel vascular complications including thrombus formation and vessel obliteration which may decrease absorption of OCS [17-20]. Miller [21] initially examined the response to IVMP in several juvenile rheumatological conditions, including JDM, and noted that all patients experienced temporary benefits, with the significant majority of patients either completely weaned off steroids, or requiring follow-up pulses every 1-2 weeks or further increased pulse intervals. The longest duration of IVMP pulse treatment was three years with no evidence of toxicity, and regression of Cushingoid features was seen in all patients [21]. IVMP has been shown to decrease creatine kinase (CK) levels and increase muscle strength in children [22], with similar results including an increased number of cases of remission in adults [23]. Matsubara et al. [24] also observed a decrease in inflammatory markers in adult muscle biopsies along with an increased number of regenerating fibers. Implementing IVMP in the therapeutic regimen was also shown to decrease the morbidity due to calcium deposition [9] which may have more long-term effects than the original myopathic insult, along with persistent muscle weakness and elevated enzyme activity [25]. Finally, when comparing the economic costs between OCS and IVMP, while OCS therapy was less expensive, the length of disease was considerably longer; the IVMP group had shorter disease durations as well as shorter hospitalizations and “appear[ed] to be cost-effective based on theoretical benchmark criteria” [26].

Few efforts have examined the effects of either method of therapy with respect to adverse outcomes measured via anthropometric parameters, along with scoring any change in functional status and abilities to carry out the activities of daily living. Specifically, we wanted to use continuous measures – height, weight, and body mass index (BMI) – to compare with age-adjusted normal children, as well as each other, along with a simple, objective measure, the modified Rankin scale [27,28] (MRS), to assess the level of functional disability in each patient. Although commonly used as an assessment of stroke disability in adults [29] the Rankin scale also has been previously utilized to categorize disability in children with JDM [30]. It is similar in ranking methodology to the KOSCHI scale (King’s Outcome Score for Childhood Head Injury) which has been validated for use in prospective studies in children [31]. Based on anecdotal clinical experience, we hypothesized that there would be fewer adverse anthropometric outcomes in children treated with IVMP yet similar outcomes in terms of recovery from flare-ups and subsequent functional disability. The data shown here were initially presented at the 2010 American Academy of Neurology annual meeting [32].

Methods

In the present study, we retrospectively examined the records of the pediatric neurology and rheumatology clinics from January 1995 until April 2009 at the University of Mississippi Medical Center (UMMC). Only patients with confirmed juvenile dermatomyositis, either via muscle biopsy or imaging studies, and less than 18-years old at treatment onset were included in this study. They were followed until either administrative censoring at age 19 (the age-limit for patients in the pediatric clinics) or clinically they had entered remission of their disease based on their symptoms (see Rankin scale below). The standard treatment protocol included steroid therapy (OCS or IVMP) and methotrexate (MTX). Based on the clinical course, patients were further treated with intravenous lG immunoglobulin (IVIG) if improvement wasn’t noted after initial therapy. Because variations in treatment occurred before the study began, many of the patients in our database had received multiple courses of treatment, including both OCS and IVMP; during relapses. For all patients, treatment group assignment was based on their latest round of treatment. Around the year 2000, the treatment protocol shifted in our clinic from using OCS as first-line therapy to using IVMP and MTX as first-line therapy, and then adding IVIG if additional pharmacological intervention was needed to induce remission of symptoms. Parameters of interest gathered from each patient included gender; age at which last treatment began, length of treatment, along with pre- and posttreatment weight and height. Furthermore, a categorical measure of disability (modified Rankin score, mRS) was assigned pre- and posttreatment, and also served as an indication of remission when pharmacotherapy was stopped. Specifically, zero denotes no symptoms; 1 represents no disability despite present symptomology and ability to perform daily activities; 2 corresponds to mild disability; 3 designates...
Results

As expected, a low number of cases were seen, even at the only statewide tertiary-care referral center during the 14-year period. Our goal in the present pilot study was to monitor the efficacy of therapy by attempting to quantify the side effects of OCS versus IVMP and serve as an impetus for future prospective or randomized studies, given these limitations. Of 39 possible cases, 14 patients had incomplete medical records, were ultimately given another diagnosis, or were lost to follow-up, and thus excluded from analysis (Figure 1).

Of the remaining 25 patients, 9 patients (8 females and 1 male) were assigned to the OCS treatment arm while 16 were given IVMP therapy (11 females and 5 males). Please note that data for the study focused on each patient’s last "regimen history" of therapy in determining whether they were placed in the OCS or IVMP group. Table 1 shows demographic and parameters obtained from medical records. Mean age at treatment onset for the entire group was 9.2 yrs ± 4.6 (SD) and mean treatment length was 24.4 mos ± 14.9 (SD). Treatment of two patients was stopped in the study due to reaching the age limit for inclusion in our clinic; this, however, coincided with remission of their symptoms (id = 4, 21). Within the OCS group, 7 patients had received MTX treatment and 1 had received IVIG, whereas in the IVMP group, 14 patients had received MTX and 4 patients had received IVIG. Thus, it was not possible to isolate only pure cases of OCS or IVMP usage (see Table 1).

Table 1: Demographic data for patients in the study. ID – identifier for purposes of the study only. Tx – treatment. Tx arm: IVMP (intravenous methylprednisolone) or OCS (oral corticosteroid). Tx supplement: MTX – methotrexate, IVIG – intravenous immunoglobulin, Pred – short course of oral steroids, Pulse x n – IVMP treatment n times. Percentiles based on age from standard CDC growth charts for particular growth parameter.

| ID | Tx arm | Sex | Age tx start (yr) | Tx length (mos) | Tx supplement | Pre-treatment | Post-treatment |
|----|--------|-----|------------------|-----------------|---------------|---------------|---------------|
|    |        |     |                  |                 |               | Weight (kg) | Height (cm) | BMI (kg/m²) | Rankin score | Weight (kg) | Height (cm) | BMI (kg/m²) | Rankin score |
| 1  | IVMP   | F   | 3.5              | 21              | MTX           | 16.4 (76.8) | 100 (71.3)  | 16.4 (75.8) | 3            | 22.2 (86.6) | 115.9 (89.0) | 16.5 (80.9) | 0            |

Figure 1: Patient flow diagram utilized within the study.
|   | OCS | F | 14.9 | 15 | MTX | 46.2 (23.9) | 157.5 (25.3) | 18.6 (32.1) | 1 | 50 (30.3) | 157.8 (22.7) | 20.1 (43.9) | 0 |
|---|-----|----|------|---|----|--------|-----------|-----------|---|---------|-----------|-----------|---|
| 3 | IVMP | F | 6.2 | 18 | IVIG, MTX | 22.6 (72.5) | 116.6 (57.7) | 16.6 (79.0) | 4 | 20.5 (10.5) | 117 (5.4) | 15.0 (33.1) | 0 |
| 4 | OCS | F | 13.7 | 45 | Pulse x 1 | 40 (13.6) | 150 (7.3) | 17.8 (29.8) | 4 | 73 (90.8) | 152.4 (5.1) | 31.4 (96.3) | 1 |
| 5 | IVMP | F | 5.8 | 4 | Pred, MTX | 16.1 (4.8) | 108 (11.9) | 13.8 (11.0) | 4 | 17.9 (14.1) | 113 (26.9) | 14.0 (15.7) | 1 |
| 6 | IVMP | F | 6.7 | 60 | Pred | 23.2 (6.5) | 117 (35.3) | 16.9 (80.4) | 3 | 36.4 (29.8) | 144 (24.8) | 17.6 (44.9) | 1 |
| 7 | IVMP | F | 8.1 | 7 | IVIG, MTX | 27 (60.5) | 132 (75.7) | 15.5 (42.6) | 3 | 36.5 (90.2) | 138 (85.3) | 19.2 (87.0) | 0 |
| 8 | IVMP | M | 8.9 | 4 | MTX | 29.0 (56.9) | 141 (90.5) | 14.6 (14.9) | 3 | 32.7 (71.6) | 146 (95.6) | 15.3 (28.5) | 1 |
| 9 | IVMP | M | 12.8 | 4 | Pred, MTX, IVIG | 54.9 (83.9) | 149 (23.9) | 24.7 (94.7) | 3 | 57.7 (85.2) | 150 (185.9) | 25.6 (95.5) | 1 |
| 10 | IVMP | F | 4 | 16 | MTX, IVIG | 15.6 (44.6) | 99.5 (36.2) | 15.8 (64.0) | 2 | 19.3 (54.7) | 109 (34.9) | 16.2 (75.9) | 0 |
| 11 | IVMP | F | 11.3 | 32 | MTX, pred | 42.7 (67.2) | 150 (67.6) | 19.0 (67.5) | 1 | 67.7 (92.0) | 159 (41.1) | 26.8 (94.3) | 0 |
| 12 | IVMP | F | 15.6 | 24 | MTX | 56.6 (63.1) | 157 (20.4) | 23.0 (77.0) | 3 | 62.3 (73.0) | 160.5 (34.6) | 24.2 (78.3) | 0 |
| 13 | OCS | F | 16.7 | 37 | MTX | 49.5 (25.2) | 155 (11.4) | 26.6 (48.4) | 2 | 56 (41.0) | 155 (10.0) | 23.3 (66.9) | 0 |
| 14 | IVMP | F | 4.8 | 5 | MTX | 19.8 (81.6) | 104 (36.3) | 18.3 (95.6) | 1 | 20.5 (76.1) | 109 (48.9) | 17.3 (89.1) | 0 |
| 15 | OCS | F | 13.2 | 17 | Pred, Hydroxychloroquine | 39.8 (19.2) | 155 (32.8) | 16.6 (16.6) | 2 | 54.8 (63.4) | 160 (40.6) | 21.4 (69.0) | 1 |
| 16 | OCS | F | 5.9 | 26 | MTX | 43.3 (99.9) | 136.2 (99.9) | 23.3 (99.4) | 1 | 58.2 (99.9) | 146 (99.7) | 27.3 (99.3) | 0 |
| 17 | IVMP | F | 9.2 | 35 | MTX | 28.9 (45.9) | 132 (40.2) | 16.6 (54.4) | 3 | 60.2 (93.7) | 153.2 (56.1) | 25.6 (95.4) | 0 |
| 18 | OCS | M | 3 | 39 | Pred, MTX | 14.3 (47.4) | 93 (27.5) | 16.5 (67.0) | 3 | 21.4 (50.5) | 113.5 (23.2) | 16.6 (78.4) | 0 |
| 19 | IVMP | M | 12.2 | 32 | MTX | 50 (82.2) | 157.5 (84.3) | 20.2 (78.6) | 1 | 71.8 (90.0) | 171 (58.5) | 24.6 (90.1) | 0 |
| 20 | IVMP | F | 5.8 | 23 | MTX | 20.2 (56.1) | 112 (40.2) | 16.1 (72.1) | 2 | 32.2 (91.0) | 124.5 (41.0) | 20.8 (96.0) | 0 |
| 21 | OCS | F | 16.3 | 24 | Pulse x 2, MTX | 62.8 (78.1) | 165 (64.0) | 23.1 (75.2) | 3 | 72.4 (89.1) | 167 (72.3) | 26.0 (85.5) | 1 |
| 22 | IVMP | M | 2.6 | 14 | - | 13.2 (36.7) | 92 (49.8) | 15.6 (29.9) | 3 | 16.8 (69.3) | 102 (61.6) | 16.1 (64.8) | 0 |
| 23 | OCS | F | 7.5 | 24 | MTX | 26.5 (69.4) | 124 (43.7) | 17.2 (78.0) | 2 | 43.2 (92.7) | 138 (61.7) | 22.7 (95.3) | 0 |
| 24 | IVMP | M | 5.3 | 35 | MTX | 23.5 (92.3) | 120 (97.5) | 16.3 (75.6) | 1 | 37.5 (96.4) | 137 (90.8) | 20.0 (94.4) | 0 |
| 25 | OCS | F | 15.4 | 48 | Pulse x 1, IVIG, MTX | 48.4 (28.9) | 164 (60.7) | 18.0 (19.7) | 4 | 65.7 (74.2) | 167.6 (74.7) | 23.1 (66.1) | 1 |

Three patients in the OCS arm had to be given IVMP pulses in order to help minimize symptoms, whereas 2 patients in the IVMP arm were given a brief course of oral corticosteroids. Only 1 patient in the study received no other adjunct therapy besides IVMP, and 1 patient received an additional medication, hydroxychloroquine, to help control symptoms. Based on the MRS, pretreatment functional disability ranged from mild symptomology to moderately severe disability, whereas posttreatment improvements ranged from none to minimal symptomology, thus all individuals from both groups were considered to be in remission. No patient in either group qualified for the WHO’s definition of short stature (<3rd percentile), but id = 3 (IVMP) and 4 (OCS) were both near this threshold. The former’s negative shift in height percentile was particularly marked, going from 57.7 to 5.4. The maximum increase seen in either group was 18 percentile points. For weight percentiles, the aforementioned individual (id = 3) decreased 62 percentile points, while the maximum increases in either group were 77 (OCS) and 48 (IVMP) percentile points. With respect to BMI.
percentiles posttreatment, 3/9 OCS patients would be considered obese by CDC and WHO standards (≥ 95th percentile), with 1 additional individual labeled as at risk for being overweight (≥ 85th percentile), whereas only 1 individual was obese pretreatment (p = 0.157). Similarly for the IVMP group, only 1/16 was obese pretreatment whereas 3/16 were obese posttreatment (p = 0.317). Finally, comparing obese individuals between the two groups, the differences were insignificant for both pretreatment (p = 0.600) and posttreatment (p = 0.630) (Table 2).

Table 2: Parameters of interest based on treatment arm. * denotes significance at p ≤ 0.05.

| Parameter                      | OCS (n = 9) | IVMP (n = 16) | p-value |
|--------------------------------|-------------|---------------|---------|
| Sex, No (%)                    |             |               |         |
| Female                         | 8           | 11            | -0.364  |
| Male                           | 1           | 5             | -0.317  |
| Time parameters, median (IQR)  |             |               |         |
| Age at treatment start (yrs)   | 13.7 (7.5–15.4) | 6.5 (5.1–10.3) | 0.036* |
| Treatment length (mos)         | 26 (24.0–39.0) | 19.5 (6.0–32.0) | 0.061  |
| Pretreatment parameters, median (IQR) |             |               |         |
| Weight (kg)                    | 43.3 (39.8–48.4) | 23.4 (18.1–35.9) | 0.089  |
| Weight percentile              | 28.9 (23.9–69.4) | 64.2 (51.0–79.2) | 0.017  |
| Height (cm)                    | 155 (136.2–157.5) | 118.5 (106.0–145.0) | 0.157  |
| Height percentile              | 32.8 (25.3–60.7) | 45 (35.8–73.5) | 0.031* |
| BMI (kg/m²)                    | 18 (17.2–20.6) | 16.5 (15.7–18.7) | 0.054  |
| BMI percentile                 | 48.4 (29.8–75.2) | 73.9 (48.5–78.8) | 0.038  |
| Rankin score                   | 2 (2–3)     | 3 (1.5–3)     | 0.059  |
| Posttreatment parameters, median (IQR) |             |               |         |
| Weight (kg)                    | 56 (50.0–65.0) | 34.6 (20.5–59.0) | 0.048* |
| Weight percentile              | 74.2 (50.5–90.8) | 80.7 (62.0–90.6) | 0.099  |
| Height (cm)                    | 155 (146.0–160.0) | 137.5 (114.5–151.6) | 0.062  |
| Height percentile              | 40.6 (22.7–72.3) | 45 (30.8–73.5) | 0.017  |
| BMI (kg/m²)                    | 23.1 (21.4–26.0) | 18.4 (16.2–24.4) | 0.048* |
| BMI percentile                 | 78.4 (66.9–95.3) | 84 (54.8–94.4) | 0.034  |
| Rankin score                   | 0 (0–1)     | 0 (0–1)       | 0.327  |
| Differences between post- and pretreatment, median (IQR) |             |               |         |
| Weight (kg)                    | 14.9 (7.1–16.6) | 5.8 (3.2–13.6) | 0.079  |
| Weight percentile              | 16 (6.0–44.0) | 10 (2.5–27.5) | 0.308  |
| Height (cm)                    | 3.6 (2.0–9.8) | 9.3 (5.0–14.7) | 0.148  |
| Height percentile              | 0 (-2.0–8.0) | 3 (-9–13.5) | 0.755  |
| BMI (kg/m²)                    | 4 (2.7–5.1) | 0.9 (0.4–1.1) | 0.084  |
| BMI percentile                 | 17 (11.0–46.0) | 12 (1.0–25.5) | 0.223  |
| Rankin score                   | -2 (-3–1)   | -2 (-3–1.5)   | 0.531  |

Table 2 shows comparisons of parameters of interest between the IVMP and OCS groups. As expected based on the female-predominance seen with this condition, JDM was seen more often in females than males (3.17: 1), but the difference was not statistically significant. The distribution for median age at treatment onset (unadjusted for previous treatment, see Discussion) was significantly less for the IVMP than OCS, 6.5 yrs versus 13.7 yrs. Median treatment length to remission of symptoms was borderline significant between the two groups, with IVMP requiring 19.5 mos versus 26 mos for OCS (p = 0.061). This is further illustrated in Figure 2.

**Figure 2:** Kaplan-Meier estimates of the probability of time to remission for OCS versus IVMP. The number (#) at risk for an event during each 10-month time period are shown at the bottom for each group.
Because the median ages between the two groups were significantly different (see Table 2), differences in height, weight, and BMI would not be unexpected. Pretreatment, significant differences were noted in height with borderline differences in BMI. No significant differences were noted in the pretreatment percentiles for weight, height, or BMI, nor the initial MRS. Posttreatment, there were significant differences in weight and BMI, along with borderline differences in height. There were no differences in any of the percentile measures nor the final MRS.

With respect to comparison of changes post- and pretreatment, weight and BMI were borderline significant, with the IVMP group gaining less weight and less of an increase in BMI. Of primary interest was not only the change across groups, as noted above, but also the change seen within each arm of the study, pre- and posttreatment (Figure 3).

**Figure 3:** Kernel density plots of pretreatment and posttreatment percentiles for (A) weight, (B) height, and (C) BMI stratified by treatment modality. * denotes significance based on p-value 0.05.
Figure 3 shows kernel density plots for the anthropometric percentiles. In Panel A, while the weight distributions and medians changed (see also Table 2) from pre- to posttreatment for both the OCS (28.9 percentile to 74.2 percentile) and IVMP (64.2 percentile to 80.7 percentile) groups, the change was significant only for the OCS group (p = 0.009). Neither group showed a significant change in height percentile over the course of treatment (Panel B). Finally, significant increases in BMI percentiles (Panel C) were noted for the OCS group (48.4 percentile to 78.4 percentile, p = 0.011), but not for the IVMP group (73.9 percentile to 84.0 percentile).

Next, using the Somers’ D parameter, 95% confidence intervals were then calculated for the most “age-adjusted” parameters of interest as shown in Table 3.

**Table 3:** Change in various parameters between treatment groups using Somer’s D parameter to calculate confidence intervals. The reference group for comparison for each parameter is OCS. See text for further explanation. * denotes significance at p ≤ 0.05.

| Parameter               | Probability of Change | p-value | 95% CI (%) |
|-------------------------|-----------------------|---------|------------|
| Change in BMI percentile| -29.9                 | 0.222   | -77.8      | 18.1       |
| Change in height percent | -7.6                  | 0.757   | -56.1      | 40.9       |
| Change in weight percent | -25                   | 0.321   | -74.3      | 24.3       |
| Change in mRS           | -14.6                 | 0.536   | -60.8      | 31.6       |
| Change in p50 wt for ht | -52.8                 | 0.008*  | -91.2      | -13.7      |
| Change in p50 BMI        | -45.8                 | 0.028*  | -86.6      | -5         |

Given a randomly-chosen individual in the OCS group and another randomly-chosen individual in the IVMP group, the IVMP patient was 29.9% less likely to have a greater positive change in BMI percentile than vice versa, with confidence limits from 77.8% less to 18.1% more. However, this result was not significant.

Similar negative predictors were calculated for height and weight percentiles along with mRS, but also were not significant as note by the p-values and CIs (Figure 4).

Figure 4 shows box plots for the changes in p50 weight for height and p50 BMI. From both panels, it’s evident that the IVMP group had a greater spread of values from the positive and negative whiskers along with a larger IQR as compared to the OCS group. Given a randomly-chosen individual from each group, the change in p50 weight for height is 52.8% less likely to have a greater positive change in the IVMP group than vice versa, with confidence limits ranging from 91.2% less to 13.7% less. Similarly, the change in p50 BMI is 45.8% less likely to have a greater positive change in the IVMP group than vice versa, with confidence limits ranging from 86.6% less to 5% less.

**Discussion**

In this retrospective study, we observed that both IVMP and OCS were efficacious in inducing remission, yet there were several important differences between the two groups. Clear differences were noted in the distributions of age at start of current treatment, along with pretreatment height, and posttreatment weight and BMI, all of which need to be considered within the context of age (see below). Borderline significant differences were seen in the distributions of treatment time, pretreatment weight and BMI, and change in weight and BMI from pretreatment to posttreatment. With respect to age, because differences were noted in the distributions of age at the start of current treatments, absolute heights, weights, and even BMIs between the two groups cannot be directly compared because each of these parameters increases with age in adolescents. Instead, examining growth percentiles more accurately assesses changes in each individual. Generally, as “normal” children develop, they should not deviate greatly from earlier percentile measurements. In fact, significant changes above and below earlier percentile measurements can alert pediatricians to possible abnormalities in growth and development. Presently, significant increases were seen in both weight and BMI percentiles for the OCS group but not for any of the measures for the IVMP group. While we examined only the endpoints, Ramanan and colleagues noted that the addition of MTX to OCS therapy compared to just OCS alone caused an increase in height velocity and less of an increase in BMI (see below) in a 1-year period.

Two “age-adjusted” references for comparison used in our study were the 50th percentile weight, given a certain height and age, as well as the 50th percentile BMI for a given age. The change in the differences from the corresponding values for post- and pretreatment were then used to determine, if given a randomly-chosen individual from each group, the likelihood of a greater or lesser change in a parameter in the IVMP individual with respect to the OCS individual as compared to vice versa. The likelihood of negative predictors in an IVMP-chosen individual were significant for both the aforementioned parameters, implying the posttreatment weights and BMIs were likely higher in the OCS group. With respect to disease duration, it was difficult to compare...
directly with other studies due to variations in endpoint definitions. Santiago et al noted a mean disease duration of 46.5 mos (SD 31.5 mos) with no distinction made between the two treatments [35], whereas Collison et al noted a mean steroid treatment duration of 53.1 mos (SD 40.5 mos) [36]. It was unclear, however, if this latter measure was for just this episode or was a lifetime cumulative dosage, and whether this involved OCS, IVMP, or both. Pachman and colleagues directly compared OCS with IVMP in 25 patients and noted significantly shorter periods of functional impairment between the two groups. 3.6 yrs versus 0.8, respectively [22]. Al-Mayouf et al noted a mean treatment duration of 23.5 months for 12 patients on combined OCS, MTX, and intermittent IVMP therapy.

In terms of examining functional outcomes of disease, both the Disease Activity Score (DAS) [37] (Bode) and the Childhood Health Assessment Questionnaire (CHAQ) have been suggested as a valid core set to monitor JDM disease activity [38]. However, they either require parents to have filled out a detailed questionnaire a priori [38] or the clinicians to complete an extensive 28-point joint examination [37], and thus were not usable in this retrospective study. Instead, we used the mRS which is a simple measure of assessing functional disability quickly in the clinic and from information available in patient charts for retrospective analysis [30,39]. Although not yet validated in the pediatric population [40,41] it has been utilized in pediatric patients in assessing stroke [42,43] intracranial hemorrhage [44], central venous thrombosis in Bechet’s disease [45] arteriovenous malformations [46] and neurotrauma [47]. Our retrospective assessment of IVMP and OCS therapy showed positive results in that no individual suffered from bone fractures, life-threatening infections, cataracts, calcinosis, or death in either group. These are possible adverse outcomes in JDM flare-ups, especially due to corticosteroid therapy. In fact, all of the patients in this study had either complete or near-complete resolution of their symptoms after treatment as shown by the mRS results, with no difference between the two groups. Our lack of side effects is in marked comparison to other studies, in which calcinosis and fractures were frequently seen [3,35,48,49].

While our study provides useful data to show the possible benefits of using IVMP versus OCS therapy, there are several caveats that need mentioning. Regarding our protocol, an informal change was noted circa 2000 from OCS as primary intervention to IVMP and MTX therapy. We unfortunately cannot rule out a selection bias – patients who appeared sicker at onset in previous flare-ups might have been treated more aggressively with both interventions and other anti-rheumatic treatments (MTX, hydroxychloroquine, IVIG, etc.), along with differences in individual clinician preferences (see below). Furthermore, while the treatment length was generally shorter for the IVMP group, they were also younger in age as compared to the OCS group. While not explicitly noted, the OCS group was more likely to be comprised of individuals who were relapsing, since median age of initial disease diagnosis is near 6 – 7 years of age. While we didn’t see the side effects seen in others, long-term outcomes in these individuals is unknown, especially in those who have shifted out of the pediatric population and are no longer followed by our clinic. Furthermore, we did not stratify by disease subtype, [19,50] i.e., monocyclic, chronic polycyclic, or chronic, active disease – these could respond differently in terms of treatment and outcomes (other schemes of clinicopathological classification exist [1]). It is unlikely, however, that we had any patients with the last subtype since long-term complications are often seen in those individuals.

Other parameters of interest that we did not examine were bone mineral density (BMD) [51,52] and the effects of cumulative glucocorticoid intake, [53] especially since many records from outside referral sources were incomplete. Thus, the extent of prior pharmacotherapy and its additive effects on the present study cannot be ruled out. Sinha and Bagga suggested that sustained lower quantitative doses of OCS are cumulatively more toxic than those of larger, but less frequently occurring doses of IVMP [54]. With respect to BMD, Castro et al [53] only observed a correlation between low BMD and corresponding low weights in Brazilian girls with JDM, and not other variables such as age, stature, Tanner stage, or cumulative glucocorticoid dosage. In fact, they assert that weight is likely the “best predictor of bone mass” [53]. This fact could help explain the lack of bone-related side effects in our patients. Alsufyani et al [51] reached a similar conclusion with no consistent relationship noted between BMD and steroid therapy. In a study in adult women with DM (mean age 48.4 yrs, standard deviation 16.3 yrs), Haugeberg and colleagues, however, noted that IVMP treatment led to high rates of bone loss, but no similar correlation was shown for OCS therapy [55]. But, the normal female population in that age group has a different basal hormonal state than in adolescents.

Finally, it is understood that our sample size lacks power to draw any definitive conclusions. Moreover, in the OCS group, we had only 1 male individual, precluding any inferences to be made based on gender between the groups, and all our patients were from a single referral center. While the aforementioned are all recognizable limitations of our work, to our best knowledge, ours is the first study to specifically examine one of the main issues of steroid usage – the effects on various growth parameters – and compare them between OCS and IVMP treatments based on an easily usable functional scoring scale, the mRS. The usage of IVMP has increased considerably in the past decade in order to help induce a rapid remission from symptomatic JDM flare-ups. Unfortunately, the incidence of JDM is low enough to preclude any randomized control trial (RCT) to investigate any medications, including corticosteroids, for its treatment [56]. Furthermore, the paucity of standardized measures to assess therapeutic responses have further hindered stringent evaluation of drug therapies [38]. In fact, there is currently no exact protocol for clinicians to follow, although there has been some recent consensus based on retrospective studies and anecdotal evidence to utilize some form of corticosteroid therapy (OCS and/or IVMP) along with MTX [56]. Another important point to consider is economic feasibility. While initially the costs versus benefits ratio might seem to forsake initiation of any widespread RCTs, an economic analysis of this
disease (along with another study dealing with rheumatological disorders in general [57]) showed that based on theoretical measures, IVMP is the more cost-effective option with OCS treatment being initially cheaper, but lasting considerably longer [26]. Even in adults, studies have shown that IVMP led to greater likelihood of remission and better outcomes as compared to OCS [23,58]; it is hoped that investigations such as ours will spur the interest for prospective cohort and even RCT.

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Conflict of interest

No conflict of interest.

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