

# Corticosteroids for infectious mononucleosis

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## Abstract

**Question** Infectious mononucleosis (IM) is a common viral infection year round, and we see patients with it in our family medicine clinic frequently. With fatigue, fever, pharyngitis, and cervical or generalized lymphadenopathy causing prolonged illness and school absences, we always look for treatments that will shorten the duration of symptoms. Does treatment with corticosteroids benefit these children?

**Answer** Current evidence points to small and inconsistent benefits when using corticosteroids for symptom relief in children with IM. Corticosteroids alone or in combination with antiviral medications should not be given to children for common symptoms of IM. Corticosteroids should be reserved for those with impending airway obstruction, autoimmune complications, or other severe circumstances.

## Corticostéroïdes pour le traitement de la mononucléose infectieuse

### Résumé

**Question** La mononucléose infectieuse (MI) est une infection virale courante tout au long de l'année. Nous voyons souvent des patients qui en sont atteints à notre clinique de médecine familiale. Étant donné que la MI se manifeste par de la fatigue, de la fièvre, une pharyngite et une adénopathie cervicale ou généralisée causant une maladie et des absences de l'école prolongées, nous sommes toujours à l'affût de traitements qui réduiront la durée des symptômes. Le traitement par corticostéroïdes est-il bénéfique pour ces enfants?

**Réponse** Selon les données actuelles, le recours à des corticostéroïdes pour le soulagement des symptômes des enfants atteints de MI procurerait des bienfaits faibles et inégaux. On ne doit pas administrer des corticostéroïdes seuls ou en association avec des antiviraux aux enfants qui présentent des symptômes courants de MI. Il faut réserver les corticostéroïdes aux enfants chez qui l'obstruction des voies aériennes est imminente, ou à ceux qui présentent des complications auto-immunes ou qui sont confrontés à d'autres circonstances graves.

Almost the entire world population (>90%) has been infected with Epstein-Barr virus, the most common cause of infectious mononucleosis (IM).<sup>1</sup> Common symptoms of IM include fatigue, fever, pharyngitis, and cervical or generalized lymphadenopathy, but among young children these symptoms are frequently not reported.<sup>2,3</sup> Diagnosis is predominantly based on symptoms at presentation to a primary care provider, physical examination, and in some cases Forssman antibody testing. Transmission of IM is through saliva (hence the colloquial name *kissing disease*), blood, semen, blood transfusions, and organ transplantation.<sup>4-6</sup>

### Treatment

Once a diagnosis has been made clinically or through laboratory testing, treatment of IM includes rest, enhancing hydration, and addressing fever and pharyngitis. Pharmacologic options include nonsteroidal anti-inflammatory drugs, acetaminophen, and throat lozenges or sprays containing anesthetics such as benzocaine, phenol, or lidocaine.<sup>7,8</sup>

Antiviral medications such as acyclovir and valacyclovir have been shown to provide little to no symptom alleviation.<sup>9,10</sup> Combinations of prednisone and acyclovir have similarly shown overall varying to little effect.<sup>11</sup>

### Corticosteroid use in IM

Corticosteroids exert anti-inflammatory properties through interactions with inflammatory genes. Specifically, after binding with receptors, responsive elements alter inflammatory gene expression, which affects cytokines, chemokines, adhesion molecules, and inflammatory enzymes.<sup>12</sup> Corticosteroids as anti-inflammatory agents are recommended for patients with severe complications of IM such as airway obstruction, autoimmune hemolytic anemia, and thrombocytopenia.<sup>13</sup> Their use for symptom relief is not considered standard and has been shown to have varying degrees of efficacy.<sup>7,8</sup>

A Cochrane review examined 7 randomized controlled trials with a total of 362 participants with IM between 14 and 30 years old.<sup>14</sup> Two trials found corticosteroid treatment to be somewhat effective in alleviating pain from pharyngitis.<sup>15,16</sup> In a study of 24 participants from Indiana University in the United States,<sup>15</sup> Klein et al found a 10-mg starting dose of prednisolone or cortisone (tapered over 8 days) was associated with reduction of pain owing to pharyngitis at 12 hours (odds ratio [OR]=21.0, 95% CI 1.94 to 227.20) but not at 36 hours (OR=6.0, 95% CI 1.02 to 35.37).<sup>14</sup> In a trial from Montréal, Que,<sup>16</sup> Roy et al found that more children between 8 and 18 years old who received 0.3 mg/kg (up to 15 mg) of dexamethasone shortly after diagnosis in the emergency department reported relief of pain owing to


pharyngitis at 12 hours compared with those who received placebo (OR=4.2, 95% CI 1.08 to 16.32) but not at 24 hours (OR=2.85, 95% CI 0.78 to 10.47).<sup>14</sup> Corticosteroids combined with antiviral drugs have also shown minimal effect. In a study of 94 patients between 14 and 29 years old in Sweden and the United Kingdom,<sup>11</sup> Tynell et al found that 800 mg of oral acyclovir taken 5 times a day with 0.7 mg/kg prednisolone for 4 days (reduced by 0.1 mg/kg for 6 additional days) resulted in a reduction of pain owing to pharyngitis compared with placebo from days 2 to 4 (OR=0.31, 95% CI 0.09 to 1.08) but not at 14 days, when no patients experienced pain owing to pharyngitis.<sup>14</sup>

In another trial from the United Kingdom, Bolden compared the effects of prednisone and acetylsalicylic acid on fever in 38 university students.<sup>17</sup> The study used 2 prednisone regimens: 10 mg taken 4 times daily on days 1 and 2 reduced by 10 mg every 2 days until day 7, after which patients took 5 mg 3 times daily, tapered by 5 mg every 2 days until day 12; and 5 mg taken 4 times daily, tapered by 5 mg every 2 days until day 7, after which a placebo (lactose) was taken until day 12. There was no significant reduction in fever during the 6-day corticosteroid course, but a noticeable reduction was noted with the 12-day course ( $P=.05$ ).<sup>14,17</sup> Finally, in a study of 82 students between 14 and 30 years old at Harvard University in Cambridge, Mass, and Princeton University in New Jersey,<sup>18</sup> treatment with 2 mg of paramethasone taken orally (with the initial dose described as 8 tablets), tapered by 1 tablet per day upon symptom improvement, produced different results at each centre.<sup>14</sup> Among the Harvard students, fever lasted an average of 1.99 and 3.7 days in the treatment and control groups, respectively; among the Princeton students, fever lasted 12.8 and 8.2 days in the treatment and control groups.<sup>14</sup>

In 4 of the 7 studies analyzed in the Cochrane review,<sup>14</sup> no significant differences in symptom outcomes such as fever, pharyngitis, fatigue, or anorexia were reported with corticosteroid use.<sup>17-20</sup> Bolden, who studied the effects of 6- and 12-day courses of oral prednisone in 38 patients,<sup>17</sup> found no difference in psychiatric score and found a reduction in fever only with the 12-day course (mean difference -3.89, 95% CI -7.05 to -0.73).<sup>14</sup> Collins et al studied the use of 60 mg of oral prednisolone (N=47) among patients 18 to 28 years old with IM.<sup>19</sup> In evaluating fatigue, anorexia, difficulty swallowing, excessive pharyngeal secretions, concentration difficulties, decreased social activity, and loss of class time, no significant differences were found at 1 or 4 weeks between the treatment and control groups.<sup>14,19</sup> Finally, a study by Simon et al<sup>20</sup> included participants

2 to 28 years old who received either prednisolone (1 mg/kg/day) or placebo, each with valacyclovir (20 mg/kg/dose), an antiviral medication.<sup>14</sup> No significant differences were found between the treatment and control groups in the selected score for sore throat, swollen glands, fatigue, nausea, and chills or in a combined score including additional symptoms (selected OR=9.33, 95% CI 0.96 to 90.94; combined OR=2.00, 95% CI 0.38 to 10.51).<sup>14,20</sup>

## Conclusion

Timely reduction of pain in IM is important for patients. Available evidence points to small and inconsistent benefit when using corticosteroids for symptom relief. Corticosteroid use can be associated with adverse effects. Primary care physicians should likely avoid corticosteroids for common symptoms in children with IM and reserve these medications for children with severe complications, such as impending airway obstruction, autoimmune hemolytic anemia, and thrombocytopenia. 

### Competing interests

None declared

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### References

1. Tzellos S, Farrell PJ. Epstein-Barr virus sequence variation—biology and disease. *Pathogens* 2012;1(2):156-74.
2. Grose C. The many faces of infectious mononucleosis: the spectrum of Epstein-Barr virus infection in children. *Pediatr Rev* 1985;7(2):35-44.
3. Luzuriaga K, Sullivan JL. Infectious mononucleosis. *N Engl J Med* 2010;362(21):1993-2000. Erratum in: *N Engl J Med* 2010;363(15):1486.
4. Vetsika EK, Callan M. Infectious mononucleosis and Epstein-Barr virus. *Expert Rev Mol Med* 2004;6(2):3-16.
5. Pagano JS. Is Epstein-Barr virus transmitted sexually? [editorial]. *J Infect Dis* 2007;195(4):469-70. Epub 2007 Jan 10.
6. Alferri C, Tanner J, Carpentier L, Perpète C, Savoie A, Paradis K, et al. Epstein-Barr virus transmission from a blood donor to an organ transplant recipient with recovery of the same virus strain from the recipient's blood and oropharynx. *Blood* 1996;87(2):812-7.
7. Voulomanou EK, Rafailidis PI, Falagas ME. Current diagnosis and management of infectious mononucleosis. *Curr Opin Hematol* 2012;19(1):14-20.
8. Hellwig T, Jude K, Meyer B. Management options for infectious mononucleosis. *US Pharm* 2013;38(5):38-41.
9. Torre D, Tambini R. Acyclovir for treatment of infectious mononucleosis: a meta-analysis. *Scand J Infect Dis* 1999;31(6):543-7.
10. Balfour HH Jr, Hokanson KM, Schacherer RM, Fietzer CM, Schmeling DO, Holman CJ, et al. A virologic pilot study of valacyclovir in infectious mononucleosis. *J Clin Virol* 2007;39(1):16-21. Epub 2007 Mar 21.
11. Tynell E, Aurelius E, Brandell A, Julander I, Wood M, Yao QY, et al. Acyclovir and prednisolone treatment of acute infectious mononucleosis: a multicenter, double-blind, placebo-controlled study. *J Infect Dis* 1996;174(2):324-31.
12. Barnes PJ. How corticosteroids control inflammation: Quintiles Prize Lecture 2005. *Br J Pharmacol* 2006;148(3):245-54.
13. Jensen HB. Acute complications of Epstein-Barr virus infectious mononucleosis. *Curr Opin Pediatr* 2000;12(3):263-8.
14. Rezk E, Nofal YH, Hamzeh A, Aboujaib MF, Alkheder MA, Al Hammad MF. Steroids for symptom control in infectious mononucleosis. *Cochrane Database Syst Rev* 2015;(11):CD004402.
15. Klein EM, Cochran JF, Buck RL. The effects of short-term corticosteroid therapy on the symptoms of infectious mononucleosis pharyngotonsillitis: a double-blind study. *J Am Coll Health Assoc* 1969;17(5):446-52.
16. Roy M, Bailey B, Amre DK, Girodias JB, Bussièrès JF, Gaudreault P. Dexamethasone for the treatment of sore throat in children with suspected infectious mononucleosis: a randomized, double-blind, placebo-controlled, clinical trial. *Arch Pediatr Adolesc Med* 2004;158(3):250-4.
17. Bolden KJ. Corticosteroids in the treatment of infectious mononucleosis. An assessment using a double blind trial. *J R Coll Gen Pract* 1972;22(115):87-95.
18. Prout C, Dalrymple W. A double-blind study of eighty-two cases of infectious mononucleosis treated with corticosteroids. *J Am Coll Health Assoc* 1966;15(1):62-6.
19. Collins M, Fleisher G, Kreisberg J, Fager S. Role of steroids in the treatment of infectious mononucleosis in the ambulatory college student. *J Am Coll Health* 1984;33(3):101-5.
20. Simon MW, Deeter RG, Shahan B. The effect of valacyclovir and prednisolone in reducing symptoms of EBV illness in children: a double-blind, placebo-controlled study. *Int Pediatr* 2003;78(3):164-9.

Can Fam Physician 2023;69:101-2. DOI: 10.46747/cfp.6902101



Child Health Update is produced by the Pediatric Research in Emergency Therapeutics (PRETx) program (<http://www.pretx.org>) at the BC Children's Hospital in Vancouver, BC. Kyle Gomes is a member and Dr Ran D. Goldman is Director of the PRETx program. The mission of the PRETx program is to promote child health through evidence-based research in therapeutics in pediatric emergency medicine.

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