

Evidence for the Use of Intramuscular Injections in Outpatient Practice

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There are few studies comparing the outcomes of patients who are treated with oral versus intramuscular antibiotics, corticosteroids, nonsteroidal anti-inflammatory drugs, or vitamin B₁₂. This may lead to confusion about when the intramuscular route is indicated. For example, intramuscular ceftriaxone for *Neisseria gonorrhoeae* infection and intramuscular penicillin G benzathine for *Treponema pallidum* infection are the treatments of choice. However, oral antibiotics are the treatment of choice for the outpatient treatment of pneumonia and most other outpatient bacterial infections. Oral corticosteroids are as effective as intramuscular corticosteroids and are well-tolerated by most patients. High daily doses of oral vitamin B₁₂ with ongoing clinical surveillance appear to be as effective as intramuscular treatment. Few data support choosing intramuscular ketorolac over an oral nonsteroidal anti-inflammatory drug unless the patient is unable to tolerate an oral medication. For other indications, the intramuscular route should be considered only when the delivery of a medication must be confirmed, such as when a patient cannot tolerate an oral medication, or when compliance is uncertain. (*Am Fam Physician*. 2009;79(4):297-300. Copyright © American Academy of Family Physicians.)

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Family physicians may choose to treat common bacterial infections, asthma, musculoskeletal pain, and vitamin B₁₂ deficiency with medications administered through the oral or intramuscular (IM) route. Because there are few studies comparing the outcomes of patients who are treated with oral medications versus IM medications, there may be confusion about when the IM route is appropriate.

In general, IM administration may be appropriate for patients with nausea, vomiting, diarrhea, or dehydration. It may also be appropriate when the physician needs to confirm the delivery of medication, such as when a patient has failed ongoing oral treatment, or when a patient is unreliable or uncooperative. The IM route is contraindicated when the medication is erratically absorbed, when there is concern for allergic reaction, or when there is a danger to the patient. Oral medications can be easier to administer than IM injections and are equally effective for treating many conditions. Oral medications do not cause pain or compromise the skin barrier. For most patients, the evidence does not support the IM route over the oral route for antibiotics, corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or

vitamin B₁₂, although IM antibiotics are indicated for some infections.

Antibiotics

After the discovery of penicillin in the early 1940s, "the shot" became associated with a dramatic reversal of illness. Since then, injections have continued to represent a powerful medical symbol.¹ Physicians and patients may perceive an injection as being more potent than standard oral treatment, and physicians may favor this route when treating a sick patient.¹ However, this approach is not supported by the literature.^{1,2}

The advantages of IM antibiotics are likely limited to situations when the delivery of a medication must be confirmed. For example, the IM route may be appropriate if a patient cannot tolerate an oral medication (e.g., because of emesis or an inability to swallow), or if the patient's compliance is uncertain (e.g., because of forgetfulness or unwillingness to take a medication).

The American Thoracic Society and the Infectious Diseases Society of America recommend oral antibiotics for the outpatient treatment of pneumonia.³ No IM antibiotics are approved by the U.S. Food and Drug Administration or specifically recommended

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References
Oral antibiotics are recommended for the outpatient treatment of pneumonia.	A	3
Intramuscular penicillin G benzathine is the recommended treatment of choice for <i>Treponema pallidum</i> infections, and intramuscular ceftriaxone (Rocephin) is recommended for <i>Neisseria gonorrhoeae</i> infections and pelvic inflammatory disease.	A	14, 16, 17
Intramuscular penicillin is the recommended treatment for group A beta-hemolytic streptococcal pharyngitis when the oral route cannot be used.	A	15
Intramuscular epinephrine is the recommended drug of choice for anaphylactic reactions.	A	30
Oral vitamin B ₁₂ at a dosage of 2,000 mcg per day is an effective treatment for B ₁₂ deficiency in the short term.	B	31-35
Intramuscular ketorolac (Toradol, no longer available for injection) is no more effective for pain syndromes than oral ibuprofen or other oral nonsteroidal anti-inflammatory agents.	B	40-43

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

for acute sinusitis,^{4,5} and most community-acquired methicillin-resistant *Staphylococcus aureus* skin infections remain susceptible to oral trimethoprim/sulfamethoxazole (Bactrim, Septra) and tetracycline.⁶

One systematic review found that there is no evidence that oral antibiotic therapy is less effective or slower than parenteral treatment for severe urinary tract infection in children and adults.⁷ Other studies have shown similar clinical effectiveness for a single dose of IM ceftriaxone (Rocephin) or 10 days of oral trimethoprim/sulfamethoxazole for urinary tract infections in febrile children.⁸⁻¹⁰ Several studies have shown that for children with otitis media, a single dose of IM ceftriaxone is no more effective in regard to rates of improvement, failure, or relapse than 10 days of oral amoxicillin, amoxicillin/clavulanate (Augmentin), or trimethoprim/sulfamethoxazole.¹¹⁻¹³

Although IM antibiotics have not been shown to be more effective or to lead to faster recovery, they are appropriate for specific indications. For example, IM penicillin G benzathine (Bicillin L-A) is the medication of choice to treat *Treponema pallidum*.¹⁴ IM penicillin G benzathine alone or in combination with penicillin G procaine (Bicillin C-R) is an effective treatment for group A beta-hemolytic streptococcal pharyngitis when the oral route cannot be used.¹⁵ The Centers for Disease Control and Prevention recommends 125 mg of IM ceftriaxone to treat *Neisseria gonorrhoeae* infections,¹⁶ and 250 mg of IM ceftriaxone plus seven to 14 days of oral doxycycline (Vibramycin) at a dosage of 100 mg twice daily to treat pelvic inflammatory disease and epididymitis.¹⁷

The perception that IM injections are more powerful or have an added psychologic effect is unproven and is an inadequate reason to choose injection when oral antibiotics are less expensive, less painful, and have fewer serious side effects.

Corticosteroids

For acute asthma exacerbation and croup, systemic corticosteroids are the recommended treatment.¹⁸⁻²⁷ Corticosteroids have been shown to lead to symptom improvement, fewer hospitalizations, and fewer return visits for both conditions.¹⁸⁻²⁷ Although much of the data regarding the treatment of asthma and croup are based on emergency department and hospital encounters, there is a growing body of evidence indicating that oral treatment and IM treatment are equally effective.²²⁻²⁷ One study also found that oral prednisolone (Prelone) is not inferior to IM prednisolone (Predalone; brand no longer available in the United States) in treatment for exacerbations of chronic obstructive pulmonary disease.²⁸

Multiple studies comparing IM administration of corticosteroids with oral administration have found no significant differences in outcomes between groups.^{20,22-26} Despite numerous trials evaluating doses, dosing frequencies, and routes of administration of various corticosteroids, there is no clear evidence for a superior formulation or administration route.^{20,22-26}

For children who are not able to swallow pills or who refuse a bad-tasting medication, a single long-acting IM-administered corticosteroid such as dexamethasone or methylprednisolone acetate (Depo-Medrol) eliminates nonadherence.²⁴ If the tolerability or compliance with a tapering dose of oral steroids are issues, the IM route is reasonable.^{23,29} However, oral corticosteroids eliminate the pain, anxiety, side effects, and costs associated with injections, and are generally well-tolerated by patients of all ages.^{22,25,26}

Some physicians believe that corticosteroids are the treatment of choice in acute anaphylaxis, although epinephrine is the recommended medication for anaphylactic reactions.³⁰ Epinephrine is absorbed more rapidly

intramuscularly than subcutaneously.³⁰ Corticosteroids may have some benefit in decreasing the uncommon occurrence of a protracted or biphasic reaction.³⁰ Whether delivered parenterally or orally, the effectiveness of administering corticosteroids for anaphylaxis is unclear.

Vitamin B₁₂

Until recently, the standard treatment for vitamin B₁₂ deficiency has been IM vitamin B₁₂.³¹⁻³⁵ However, because evidence indicates that patients with vitamin B₁₂ malabsorption (intrinsic factor deficiency) absorb only 1 to 2 percent of oral vitamin B₁₂,³²⁻³⁵ high-dose oral treatment has been investigated as an alternative to IM administration.³¹⁻³⁵

Trials of oral versus IM vitamin B₁₂ replacement therapy have found that oral vitamin B₁₂ in high doses appears to be as effective as IM administration in the short-term.³¹⁻³⁵ In one study, vitamin B₁₂ was administered orally at a dosage of 2,000 mcg per day for four months.³⁶ This resulted in a threefold increase in the level of serum vitamin B₁₂ compared with the monthly IM injection group. Other trials using oral dosages of less than 500 mcg per day have not shown a consistent response, which confirms the need for high-dose daily therapy.^{37,38} There have been no long-term outcome studies evaluating the effectiveness in treating or preventing anemia.

There are several reasons to consider oral vitamin B₁₂ administration instead of IM injection. An injection typically requires the patient to travel to a health care facility, which may be difficult for patients with disabilities and for older patients. Additionally, injections are more expensive and painful, and place health care professionals at risk of needle-stick injuries.³¹⁻³⁵ Although large long-term trials are needed to determine whether oral vitamin B₁₂ is as effective as IM treatment, high-dose oral vitamin B₁₂ treatment with ongoing clinical surveillance appears to be painless, effective, safe, cost-efficient, and convenient for most patients.³¹⁻³³

Ketorolac

All NSAIDs have the same mechanism of action, regardless of the route of administration.³⁹⁻⁴¹ The data do not support the practice of administering IM ketorolac (Toradol, no longer available for injection) for conditions such as migraine, gout, and musculoskeletal pain when oral NSAIDs are available and the patient can tolerate an oral medication.⁴⁰⁻⁴³ The few studies that have compared an oral NSAID such as ibuprofen to IM ketorolac have not demonstrated a significantly better response to the injection.⁴⁰⁻⁴³

Additionally, the evidence does not support the notion that IM ketorolac is more effective than oral NSAIDs for pain relief in patients with acute renal colic.^{44,45} Limited studies have shown that ketorolac is as effective as certain opioids for treating renal colic pain.^{40,41,44,45} However, data also indicate that oral NSAIDs generally offer at least equal analgesia when compared with opioids.^{40,44,45} No randomized, double-blind studies are available that directly compare oral NSAIDs with IM ketorolac. One study compared administration of a placebo injection to administration of a placebo oral agent and found that injections did not confer a selective placebo effect.⁴⁰

The risks of administering IM ketorolac include bruising, infection, hematoma, patient discomfort, and needle-stick injury.^{38,39} In addition, IM administration is significantly more expensive than oral ibuprofen.^{39,42} Because there is no outcome-based evidence for choosing IM ketorolac over an oral NSAID, and because there are increased costs and potential hazards with injections, IM ketorolac should be reserved for patients with acute pain who are unable to tolerate oral NSAIDs.³⁹⁻⁴²

Final Comment

Because of the broad nature of this topic, modes of administration were limited to the IM and oral routes. Similarly, medications such as diphenhydramine (Benadryl), opioid analgesics, ondansetron (Zofran), triptans, and others were not included. Definitive guidelines for choosing the IM route or oral route are unlikely to be forthcoming. The decision-making process involves assessing the clinical picture, knowing medication indications, and learning patient preferences. With few exceptions, there are no conclusive data that support the IM route as preferable to the oral route. The assumption that an IM injection is more powerful than the oral route is not supported by available data.

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