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# Does the combination of erythropoietin and tapered oral corticosteroids improve recovery following iatrogenic nerve injury?

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ABSTRACT

*Introduction:* The reported prognosis for recovery after peripheral nerve injury is remarkably poor. Deficits may persist for years, resulting in significant functional disability. Both corticosteroids and Erythropoietin have been investigated as neuroprotective agents; however, their efficacy in total hip and knee arthroplasty is not known. The purpose of this study was to evaluate the effect of systemically-administered Erythropoietin and tapered oral corticosteroids on the recovery of postoperative nerve palsies in the setting of total hip and knee arthroplasty.
*Methods:* Eleven patients sustaining postoperative peripheral nerve injuries after total hip or knee arthroplasty were treated acutely with Erythropoietin and tapered oral steroids. Motor and sensory function was assessed clinically pre- and postoperatively until complete motor recovery or for a minimum of 1 year.
*Results:* Motor loss was complete in seven (64%) patients and partial in four (36%). Seven (64%) patients' symptoms affected the common peroneal nerve distribution and four (36%) had concomitant tibial nerve involvement. Eight (73%) patients experienced *full* motor recovery at an average of 39 days (range: 3–133 days), and three (27%) had near-complete motor recovery. At final follow up, no patient required assistive devices for ambulation.
*Conclusions:* Administration of Erythropoietin coupled with oral tapered steroids for patients sustaining iatrogenic nerve injuries in total hip and knee arthroplasty demonstrated faster and more complete recovery of motor and sensory function compared to previous reports in the literature. This study highlights the importance of further investigation to define the role of each in the setting of acute postoperative nerve palsies.
*Level of evidence:* Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.



## Introduction

Peripheral nerve injuries can result in devastating complications following total hip or total knee arthroplasty. The reported prevalence after either procedure ranges from 0.3% to 4% [1–13]. Compression, traction, laceration, ischemia, thermal injury, or a combination may contribute; however, the exact etiology often remains unclear [5,14]. The resultant neurologic deficit may be persistent, taking years to resolve if ever. A number of investigators examining the natural history of postoperative nerve palsies in total hip and total knee arthroplasty support a poor prognosis [4,15–18] with a high likelihood of compromising postoperative rehabilitation and ultimate functional outcome.

Therapies aimed at reversing post-operative palsies (or, at least, shortening their duration) have obvious clinical benefit. Erythropoietin, an endogenous hormone and FDA-approved drug for the treatment of anemia, has shown promise as a neuroprotective agent. It has subsequently been the subject of over 180 preclinical studies performed by many different independent research groups worldwide investigating its efficacy in the treatment of a wide range of neurological problems including cerebrovascular disease, traumatic brain injury, spinal cord injury, multiple sclerosis, cerebral malaria, Parkinson's disease, retinal degeneration, status epilepticus, amyotrophic lateral sclerosis, peripheral neuropathy, diabetic neuropathy, and peripheral nerve injury [19]. Human studies have been performed in the setting of cerebrovascular disease and chronic brain diseases; however, to our knowledge, no

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such investigation exists for peripheral nerve injury. Multiple animal studies have been performed since 2005 with promising results necessitating further investigation [20–28].

On the other hand, widespread use of corticosteroids in the treatment of nerve injury has been well-established. It has been studied clinically in several pathologic conditions, including acute spinal cord injury, traumatic optic neuropathy, facial nerve paralysis, compressive neuropathy (i.e. carpal tunnel syndrome), and neuropathic pain with variable efficacy [29–35]. No such clinical investigation has been performed for postoperative motor nerve palsy about the hip or knee, although multiple animal studies have suggested a potential therapeutic benefit [36–40].

The purpose of this study was *to retrospectively assess a series of 11 patients who underwent total hip or total knee arthroplasty between September 2008 and October 2013 who were found to have post-operative nerve palsies and were treated acutely with Erythropoietin and tapered oral corticosteroids.*

## Methods

Following approval from the Institutional Review Board, all patients receiving Erythropoietin during admission for total hip or knee arthroplasty by a single surgeon between January of 2005 and October of 2013 were identified via a review of pharmacy records. Upon review of the records, the indication for Erythropoietin therapy was determined. Of 62 records, eleven patients were given Erythropoietin in the setting of acute postoperative peripheral nerve palsy, and each was noted to be anemic. A course of tapered oral corticosteroids were also given to each patient.

Each patient was followed until complete neurologic recovery – defined as a return to preoperative strength – or for a minimum of 1 year. Two patients failed to follow up regularly, one with documented near complete recovery and one with full recovery. Thus determination of the healing time in these two patients was impossible. Accordingly, nine of eleven patients (82%) were included in the time to recovery determination. Final follow up occurred at an average of 437 days postoperatively with a range of 45 days to 1283 days.

The patient's neurologic status was focused on motor strength testing using a standard scale. The absence of motor function within a nerve distribution was defined as grade '0'. Normal strength was defined as grade '5'. Grade '1' was flicker, grade '2' full without gravity, grade '3' against gravity, and grade '4' against some resistance. Sensation was also evaluated and recorded as normal or abnormal based upon patient report.

Of the eleven patients, three were male and eight were female. The mean age at the time of surgery was 65 years (range: 40–77). All patients were noted to have preoperative grade 5 of 5 motor strength bilaterally and intact sensation. The most common indication for surgery was primary osteoarthritis in eight of eleven patients (73%). The remaining three patients (27%) had aseptic failure of prior arthroplasties requiring revision. Four patients underwent total hip arthroplasty, including all three revision cases. Seven patients underwent total knee replacement, all of which were primary surgeries. The patient's preoperative diagnosis, surgical procedure, laterality, neurological injury, additional complications, and postoperative treatment regimen were recorded; a summary of these findings is included in Table 1. One patient undergoing primary total hip arthroplasty developed a hematoma postoperatively requiring urgent evacuation, and one patient undergoing revision total hip arthroplasty developed a postoperative infection requiring removal of the implanted prosthesis. No other intraoperative or postoperative complications were noted.

## Results

Seven (64%) patients sustained complete motor loss (grade '0'), including three total hip and four total knee arthroplasty patients. Four (36%) patients sustained partial motor loss, including one total hip and three total knee arthroplasties. Injuries affecting the common peroneal nerve distribution were most frequent, accounting for deficits in seven (64%) patients. This included five total knee and two total hip patients. Four (36%) patients, including two total hip and two total knee arthroplasty patients, had concomitant tibial nerve involvement. No femoral or obturator nerve injuries were appreciated (Table 2).

The average time from the procedure to diagnosis of nerve palsy was 1.4 days (range: 1–3 days). Patients received Erythropoietin and a tapered oral methylprednisolone pack at an average of 1.4 days postoperatively (range: 1–3 days). The dose of Erythropoietin was not standardized, but was prescribed in consultation with a Hematologist.

Eight (73%) patients experienced *full* motor recovery–defined as grade 5 of 5 strength-by an average of 39 days (range: 3–133 days).

**Table 1**
Summary of patient cohort characteristics, including age, gender, preoperative diagnosis, laterality, joint involved, primary versus revision surgery, nerve injury based upon physical examination, and additional complications.

| Patient # | Age | Gender | Preoperative Diagnosis | Laterality | Joint | Primary vs. Revision | Neurologic Injury Distribution | Additional Complications |
|---|---|---|---|---|---|---|---|---|
| 1 | 70 | Female | Osteoarthritis | Left | Knee | Primary | Peroneal/Tibial | None |
| 2[a] | 77 | Female | Aseptic Failure of Arthroplasty | Right | Hip | Revision | Peroneal/Tibial | None |
| 3[a] | 40 | Male | Osteoarthritis | Right | Knee | Primary | Peroneal | None |
| 4[a] | 73 | Male | Osteoarthritis | Left | Hip | Primary | Peroneal/Tibial | DIC/Hematoma requiring immediate evacuation |
| 5 | 46 | Female | Aseptic Failure of Arthroplasty | Right | Hip | Revision | Peroneal | None |
| 6[a] | 70 | Female | Osteoarthritis | Left | Knee | Primary | Peroneal/Tibial | None |
| 7[a] | 63 | Male | Osteoarthritis | Right | Knee | Primary | Peroneal | None |
| 8 | 68 | Female | Osteoarthritis | Left | Knee | Primary | Peroneal | None |
| 9 | 62 | Female | Osteoarthritis | Right | Knee | Primary | Peroneal | None |
| 10[a] | 75 | Female | Aseptic Failure of Arthroplasty | Left | Hip | Revision | Peroneal | Postoperative Infection requiring revision |
| 11[a] | 70 | Female | Osteoarthritis | Right | Knee | Primary | Peroneal | None |

[a] Denotes complete motor palsy (grade 0).