

Regional limb perfusions

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Regional limb perfusion (RLP) is a technique to deliver an antibiotics or other medication to a selected region of the limb through the venous system. Regional limb perfusions have changed and improved treatment of septic synovial structures in the distal limb in horses. Extremely high tissue and synovial fluid concentrations can be achieved with minimal systemic drug levels, thus maximizing effect of the drug administered while decreasing the odds of systemic side effects. RLPs are easily performed in the field and are cost effective.

Several techniques can be employed to perform RLPs in horses. Usually, the intravenous technique is preferred, but intraosseous RLP can be utilized as well if needed. The volume injected is usually between 10-60 ml total. For treatment of septic synovial structures or as a preventative measure in distal limb trauma/wounds, we usually prefer a concentration dependent antibiotic. In most cases the procedure can be performed in the standing, sedated patient. If the patient is already being anesthetized for surgery or another reason, RLP can be performed under general anesthesia. A wide rubber tourniquet is applied and a catheter is inserted into an available vessel (or IO administration) and 1/3 systemic dose (+/- mepivacaine, +/- saline or LRS). A quick prep can be performed over the vessel site, and a butterfly or short angiocatheter is used to administer the perfusion. Gauze should be applied over the puncture site with tape or Vetrap after the catheter is removed; leakage of blood or perfusate will occur if not due to the increased pressure created from the perfusate injection. While originally it was theorized that volume is needed for efficacy, as it pressurizes venous system, in more recent work, there is some question as to the exact volume needed and if a concentration gradient is more important the simply volume. The tourniquet is removed in 15-30 minutes. Surpass can be used over the injection site if it becomes inflamed and/or if repeated RLPs need to be administered.

If there is need to perform an intraosseous RLP, sedation is used and a local block performed over a suitable long bone (cannon, tibia, radius most common). A 4.0 mm drill bit is used to enter the medullary cavity, and the male end of an extension set will seat nicely into the hole drilled in the cortex. A hemostat can be used to clean the portal before use on subsequent days. It does typically become harder to inject each day as the drilled fills in. IO RLP may be helpful in select cases with severe limb swelling or thrombosis, laceration of vessel, etc.

Antimicrobial selection for RLP includes choosing a drug that is safe to administer intravenously. The ideal antimicrobial is bactericidal, concentration dependent and has low tissue toxicity. Commonly used antimicrobials include Gentamicin (250 mg-1 g), Amikacin (250 mg-1 g), and Ceftiofur (500 mg-1 g). The frequency and duration of RLP administrations recommended varies, but at our clinic typically administer RLPs once a day for 3 days.

Some cases that are more severe or highly contaminated may have 3 days of perfusions, then every other day treatment for 2-4 more treatments. Some have reported performing perfusions twice a day for severe cases, and we do perform RLPs twice a day in some instances. Similarly, if there is little contamination/not in joint we may perform only one treatment. I recommend using findings at presentation, progress, and response to therapy to decide the exact frequency and duration of RLP treatments.

Reasons for failure to achieve high antibiotic concentrations (> 10 times MIC) in the tissues or fluid of interest include: Inadequate tourniquet pressure, inadequate/poor placement, low antimicrobial dose, rate and site of injection, individual variation in limb vasculature, movement of animal, body weight discrepancies affecting dose.

RLPs are appropriate for open/septic joints, osteomyelitis, wounds and may be a good technique for delivery of other treatments. They are easy to perform and can be done standing. Intravenous technique preferred in most cases. Aminoglycosides are appropriate for most cases, but many antimicrobials can be used.

*See reference list below and Appendix A for evidence-based analysis of RLP use.

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Appendix A – credit to Dr. Paul Merkatoris (Large Animal Surgery Resident – Iowa State University)

First author	Title	Year	Journal	Topic/Category	Time (min)	GA or SS	Tourniquet	Perioperative anesthesia	Anesthetic volume	Total Vol (ml)	Catheter vs venipuncture	Joints	Antibiotic	Dose	Other Drug/Route	Dose	Conclusion
Stashal	Comparison of low tourniquet application time for regional intravenous limb perfusions with amikacin in sedated or anesthetized horses	2015	Veterinary Journal	MMB tourniquet time	20 vs 30	GA vs SS	Prismatic (50 mmHg)	PNE, median, ulnar, musculocutaneous	Lidocaine, 35 ml	60	28 ga butterfly catheter, cephalic	MC, PC	Amikacin	1000 mg		1000 mg	Recommended 20-minute tourniquet time is effective between 20 and 30 minute tourniquet time; recommended standing sedation for RLP of MCP vs cephalic vein
Blath	The effect of mepivacaine hydrochloride on the threshold during amikacin regional limb perfusion in the horse	2016	Veterinary Surgery	MMB regional anesthetic	30	SS	Esmarch tourniquet	Perifascial	Mepivacaine, 25 ml	60	28 ga butterfly catheter, cephalic	MC	Amikacin	1000 mg		1000 mg	Recommend use of mepivacaine in RLP; significant increase in the magnitude of analgesic effect on amikacin action of synovial fluid
Una	Treatment of pythiosis in equine limb using regional limb perfusion with amikacin	2012	Veterinary Surgery	Perifascial study	45	GA, SS	Esmarch	Perifascial		60	20, 22, or 24 ga	Amphotericin B	50 mg			50 mg	IVLP with amphotericin B is effective
Una	Evaluation of intravenous regional perfusion with amphotericin B and dimethyl sulfoxide to treat pythiosis	2015	BMC Veterinary Research	Perifascial study	45	GA, SS	Esmarch tourniquet	Perifascial		60	20, 22, or 24 ga	Amphotericin B	50 mg			50 mg	Effective and inexpensive for treatment of distal limb pythiosis in horses
Hands-Minkels	Effect of intravenous regional perfusion of distal limb with amikacin sulfate on wound healing by second intention in horses	2015	Veterinary Surgery	Wound healing	20	SS	Esmarch tourniquet	Perifascial		60	28 ga butterfly	Amikacin	5 mg/kg			5 mg/kg	Three consecutive daily IVLP did not inhibit wound healing
Hand	Effect of dose on intra-articular amikacin sulfate concentrations following an arthrocentesis regional limb perfusion	2016	Veterinary Surgery	Dose	20	SS	Prismatic (50 mmHg)	PNE, median, ulnar, musculocutaneous	Mepivacaine, 30 ml	60	28 ga butterfly	Amikacin	5 mg/kg			5 mg/kg	IVLP may not concentrate amikacin at wound bed; IVLP of distal limb with amikacin in experimentally created wounds
Anter	Morphine pre-emptive analgesia on postoperative intravenous regional limb perfusion in standing horses	2015	Veterinary Surgery	PK of morphine and agent	30	SS	Esmarch tourniquet	Perifascial		50	21 ga x 1.9 cm catheter	MC	Genamycin	1000 mg		1000 mg	Measurable levels of synovial morphine and genamycin concentrations similar to those previously reported
Ph	Pharmacokinetics of perfacortin in arthrocentesis regional limb perfusion in standing horses	2012	Canadian Veterinary Journal	MMB volume	30	SS	Prismatic (50 mmHg)	Perifascial		100	22 ga x 30 vs 60 ga K23 cm; 20 ga x 4 cm PFE; 20 ga x 4.2 cm PFE; 16 ga x 10 cm P.U.	MCP	Genamycin	500 mg		500 mg	No significant difference in synovial concentration (1000 to 4000 mg/ml) over 120 minutes for higher concentration in low volume; low volume perfusion may be beneficial
Beer	Effect of intravenous regional perfusion with amikacin sulfate on wound healing in horses	2012	Veterinary Surgery	MMB use of catheter	30	SS, GA	Esmarch tourniquet	Perifascial		100	20 ga x 4 cm PFE; 20 ga x 4.2 cm PFE; 16 ga x 10 cm P.U.	MCP	Genamycin	500 mg		500 mg	Including catheter facilitates long-term access
Beer	Evaluation of regional limb perfusion with amikacin sulfate in horses with pythiosis	2013	Journal of Vet Pharm and Therapeutics	PK of erythromycin	30	SS	Prismatic (50 mmHg)	PNE, median, ulnar, musculocutaneous common peroneal, tibial	Mepivacaine, 10 ml/nerve	100	20 ga x 4 cm PFE; 20 ga x 4.2 cm PFE; 16 ga x 10 cm P.U.	MCP	Erythromycin	2000 mg		2000 mg	Therapeutic concentrations achieved; use when specifically indicated due to severe complication in 1/12 horses
Beer	Evaluation of the pharmacokinetics of imipenem following regional limb perfusion using the intravenous regional limb perfusion technique	2017	Research in Veterinary Science	PK of imipenem	30	SS	Esmarch tourniquet	Perifascial		100	20 ga x 4 cm PFE; 20 ga x 4.2 cm PFE; 16 ga x 10 cm P.U.	MCP	Imipenem	500 mg		500 mg	Recommended regimen for re-sealed cases; high concentrations achieved
Boyer	Pharmacokinetics of amikacin sulfate in horses with pythiosis	2016	Veterinary Record	MMB tourniquet time	10 vs 30	SS	Esmarch tourniquet	PNE, median, ulnar, musculocutaneous	Mepivacaine, 20 ml	60	22 ga x 2.5 cm catheter, cephalic	MC, MCP	Amikacin	2000 mg		2000 mg	10-minute may be sufficient; no difference between synovial concentration at 5 min and 24 hours post
Demard	Pharmacokinetics, pharmacodynamics, and local tolerance at injection site of marbofloxacin administered by regional intravenous limb perfusion	2013	Veterinary Surgery	PK of marbofloxacin	30	SS	Esmarch tourniquet	Perifascial		60	25 ga butterfly	RC	Marbofloxacin	0.67 mg/kg		0.67 mg/kg	The studied dose should be considered effective; no adverse effects observed
Alme	Clinical and pharmacokinetic effects of regional or general anesthesia on intravenous regional limb perfusion with amikacin in horses	2014	Equine Veterinary Journal	MMB regional anesthetic	30	GA vs SS	Esmarch tourniquet	Perifascial, PNE, median, ulnar, musculocutaneous	Lidocaine, 20 ml vs 35 ml	50	28 ga butterfly,	MC	Amikacin	1000 mg		1000 mg	PNE recommended for standing IVLP; PNE > IV regional anesthesia; PNE, IV had no effect on regional PK parameters
Over	Effect of intravenous regional perfusion with amikacin sulfate on wound healing in horses	2016	Veterinary Surgery	MMB volume	30	SS	Prismatic (50 mmHg)	PNE, median, ulnar, musculocutaneous	Mepivacaine, 8 ml/nerve	100	18, 20, 22, 24 ga butterfly, cephalic	RC, DPM	Amikacin	1000 mg		1000 mg	More synovial concentrations achieved; 15-min perfusions were preferred; low volume concentrations needed with 10, 20, and 130 ml perfusions; no leakage with DPM; minimal with 38, 60, and 130 ml perfusions
Ido	Pharmacokinetics of amikacin sulfate in horses with pythiosis	2016	Canadian Veterinary Journal	PK of amikacin and Nafamoc	30	SS	Prismatic (50 mmHg)	PNE, median, ulnar, musculocutaneous		60	20 ga x 24 mm catheter, cephalic	MCP	Amikacin	2000 mg		2000 mg	Recommended combinations studied; higher clearly within 12 hours
Reif	The effect of perfacortin volume on amikacin concentrations in synovial fluid following equine regional limb perfusion	2016	Veterinary Surgery	MMB volume	30	SS	Esmarch tourniquet	Perifascial		30, 60, 120	20 ga x 32 mm catheter, cephalic	MCP	Amikacin	2000 mg		2000 mg	Recommended high (100 ml) volume; higher synovial concentrations with 100 ml perfusions; no adverse effects observed
Reif	Pharmacokinetics of ceftriaxone in regional limb perfusion in adult horses	2017	Veterinary Surgery	PK of ceftriaxone	30	SS	Esmarch tourniquet	Perifascial		60	20 ga x 2 cm catheter,	MCP	Ceftriaxone	2000 mg		2000 mg	Synovial concentration decreases below MIC within 6 hours; adequate PK (concentration with single proximal and distal tourniquets, adequate PK concentrations with proximal and distal; recommend 2 tourniquets with low volume perfusion for RC)
Horowitz	Effect of tourniquet number and designation on amikacin concentrations in the radiocarpal and distal interphalangeal joints after low volume intravenous regional limb perfusion in horses	2017	Veterinary Surgery	MMB tourniquet use	30	SS	Prismatic (50 mmHg), distal tourniquet	PNE, median, ulnar, musculocutaneous	Mepivacaine, 8 ml/nerve	10	28 ga butterfly, cephalic	RC, DPM	Amikacin	1000 mg		1000 mg	Do not recommend using combination; combination of amikacin with ticarcillin/clavulanate decrease concentration and activity of amikacin
Reif	Accumulation of amikacin in synovial fluid after regional limb perfusion of amikacin sulfate above the recommended dose in horses	2014	Veterinary Surgery	Perifascial study	30	SS	Esmarch tourniquet	Perifascial		60	25 ga butterfly	MC	Amikacin	2500 mg		2500 mg	7.6