



Review article

Systematic review of intralesional Cidofovir dosing regimens in the treatment of recurrent respiratory papillomatosis

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ABSTRACT

Objective: Surgical management of recurrent respiratory papillomatosis (RRP) usually involves resection via microlaryngoscopy. Intralesional injection of cidofovir has been shown to be an effective adjuvant treatment, but remains unlicensed. United Kingdom General Medical Council guidelines recommend the prescribing doctor should “be satisfied that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy”.

This study reviews the published dosing regimens of intralesional cidofovir in the treatment of RRP in order to provide a precedent for those that wish to prescribe it.

Methods: A systematic review of the literature was undertaken using Medline, EMBASE and CINAHL. Articles describing the use of intralesional cidofovir for RRP were reviewed. Information regarding cidofovir concentration, volume, total dose, number of treatments, interval between treatments, overall treatment period and follow up was extracted.

Results: Fifty-one articles were identified. Concentration of cidofovir injected ranged from 0.0001 mg/ml to 37.5 mg/ml, with 5 to 7.5 mg/ml being the most common. The volume of cidofovir solution injection ranged from 0.1 to 20 ml. The total dose per injection ranged from 0.15 to 105 mg. There was wide variation in dosing regimens with different intervals between endoscopies, number of injections and total doses delivered.

Conclusions: Based on this published literature, the precedent for prescribing intralesional cidofovir supports a concentration of 5 to 7.5 mg/ml. Volumes up to 5 ml per injection are routinely used. Total dose and frequency of cidofovir administration is highly variable. The need for repeat doses of cidofovir should be judged on an individual basis.

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1. Introduction

Recurrent respiratory papillomatosis (RRP) is characterised by recurrent formation of non-keratinised, squamous papillomata within the epithelium of the upper aerodigestive tract. DNA studies have identified human papilloma virus (mostly types 6 & 11) as a

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Table 1

Summary of reviewed articles. Unless otherwise stated, numbers are central tendency values (mean or median). Numbers in parentheses represent ranges.

Principle author	Year	Study type	Number	Concentration/ml	Volume ml	Number of injections	Frequency	Dose per injection mg	Cumulative dose mg	Therapy period	F/U period
Ablanedo-Terrazas	2012	Case series	9 children	5	2.3 (0.4–19)	5	4–6 weeks	26.5 (2–95)	132.4 (67.5–218.5)	4 months	27.1 months (19.7–32.1)
Graupp	2012	Case series	26 adults 8 children	(7.5–15)		3.6 (1–11)	4–6 weeks	34.7 (4–105)	126.2 (15–435)	(0.0–5.5 years)	1–8 years
Mikolajczak	2012	Case series	8 adults	6.1	2 (1.2–2.3)	5	4–8 weeks	13 (8–15)			15.7 months (12–18)
DeFatta	2012	Single case report	1 adult	15		4	8 weeks				
Boltezar	2011	Case series	1 child 8 adults	(2.5–7.5)		3.4 (1–9)	Mean 2.8 months		(10–75)		(7–22 months)
Wierzbicka	2011	Case series	6 children 26 adults	5	3 (1–12)	2.5 (1–7)	Every 4 weeks	Max 3/kg	39.7 (10–165)	5.5 (1–16 months)	(2–21 months)
Carney Man	2010 2010	Case series Single case report	4 adults 1 adult	5 (5–15)	<3 (6–8)	7	(5–9 weeks)	Max 15 (30–90)	(300–350)	6 months	
Gupta	2010	Case series	13 adults	5	(1–5)	(1–18)		(5–25)			
Sajan	2010	Case series	7 children	7.5 (5–10)	(0.2–3)		(1–4 months)				
Bielecki	2009	Case series	10 children	(5–10)		8.8 (6–14)	4 weeks	(1–5/kg)		9.9 months (6–15)	6 months
Carvalho	2009	Case series	23 children 44 adults				Initially 3 endoscopies at 2 week intervals 2 Weeks				
Lott	2009	Single case report	1 child	5		13				36 months	48 months
Verguts	2009	Case series	30 adults (over 12)	5	(2–4)	(1–85)	Every 2–6 weeks	(10–20)			
Major	2008	Single case report	1 child	(5–10)		7	Every 2 weeks	1/kg		55 weeks	117 weeks
Poetker	2008	Case series	2 (age not stated)	0.0001		1	Once				
McMurray	2008	Double blind placebo controlled study	8 adults 2 children	(0.3–5)	(0.5–3)	2.9 (NA)	Max of 6 treatments per year	(0.15–15)		12 months	
Loyo	2008	Single case report	1 neonate	5	1	8	(6–12 weeks)	(3.75–5)	(30–40)		22 months
Tanna	2008	Case series	13 adults			16 (NA)	(Between 2–12 weekly)				
Shi	2008	Case series	4 adults 1 child	7.5	(2–6)	Initially 2–3 every 3 weeks	Every 3 weeks	(15–45)			
Lindsay	2008	Case series	10 children	5				Max 25 per dose			
Hawkes	2008	Case series	2 children								
Pudszuhn	2006	Case series	8 adults 2 children	5	1 ml per subsite, up to 4	Mean 4.3. 2–7 times in 2–15 months	Every 4 weeks	Max 20 per injection.	33.9 (9–80)		
Chung	2006	Case series	11 children	(5–10) (5 went to higher dose)	(0.2–3.0 of 5, then 1.0–3.0 10)	Initially 4 (6 pts), then 4 more (5pts) 3 monthly, then increase to 2 weekly. Mean 4.5 (1–11)	Every month	(1–30)	73.8 (52–107)	8 months	
Naiman (nat Hx)	2006	Case series	19 adults	(5–7)		Mean 7.25 (2–26)	Monthly then 2 weekly				
Naiman (paeds)	2006	Case series	16 children	(5–7.5)			Monthly then 2 weekly				
Sheahan	2006	Case series	4 children	5	3.9 (2–6)	Mean 10.5 (8–18) in 10.5 (7–16) months	(Every 3–5 weeks)	(10–30)	204.8 (NA)	10.5 months (7–16)	

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