

Systematic Review: non-adherence and non-persistence in intravitreal treatment

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Suppl. 2: Studies evaluating pain and its risk factors during or after IVT

First author	Study type	Data acquisition	Number of patients/eyes	Objective	Results
Alattas[59]	prospective, uncontrolled	questionnaire	56	comparison of bimanual lid retraction versus metal speculum	bimanual lid retraction was associated with less discomfort
Chua[60]	consecutive case series	questionnaire	100	comparison of expected discomfort (before IVT) versus actual discomfort	actual discomfort was significantly less than expected discomfort
Cintra[61]	prospective, randomized	VAS	60	comparison of different methods of anesthesia (topical, subconjunctival, peribulbar)	less pain with peribulbar anesthesia compared to topical and subconjunctival
Cohen[62]	Prospective, single-blinded, randomized	interview	57	preference of anesthesia: subconjunctival versus topical	88% preferred subconjunctival anesthesia over topical
Gregori[48]	randomized	Interview, examination	50	discomfort and safety of subconjunctival versus topical lidocaine	both methods equally effective, less ocular irritation after topical

Gueler[63]	prospective, non-randomized	VAS	70	pain experience during injection with 30-gauge versus 27-gauge needles	30-gauge more tolerable than 27-gauge
Kaderli[64]	prospective, randomized	interview	28	comparison of different methods of anesthesia (topical, subconjunctival)	better pain control with subconjunctival, procedure itself more painful and hemorrhage
Karimi[46]	prospective, randomized	VAS	1004	correlation of injection site with pain	superotemporal most painful, superonasal least painful
Kozak[65]	crossover and consecutive groups	VAS	28	comparison of different methods of anesthesia (topical, subconjunctival)	no difference in pain scores, more chemosis and hemorrhage with subconjunctival
Lagstein[66]	prospective, randomized, double-blind	rating scale	39	comparison of pain under IVT with or without prior application of apraclonidine	prior application of topical apraclonidine significantly reduced pain
Loureiro[47]	cross-sectional, randomized	VAS	54	pain experience and intraocular during injection with 30-gauge versus 27-gauge needles	comparable pain/discomfort, lower IOP spikes after 27-gauge injection
Makri[67]	prospective, double-blinded, randomized	VAS, questionnaires	52	evaluation of analgesic effect of topical nepafenac	a single drop of topical nepafenac reduced pain at injection and up to 6 hours after
Massamba[68]	prospective interventional case series	VAS	112	evaluation of risk factors for pain	risk factors were: left eye, IVT location temporal superior quadrant. Not correlated: age, gender, number of injections, waiting time, history of cataract surgery
Moisseiev[69]	case series, matched control group	VAS	57	comparison of pain after Ozurdex versus bevacizumab	comparable discomfort for Ozurdex and bevaicumab injections
Rahimy[70]	prospective, randomized, crossover	questionnaire, VAS	36 patients	comparison of bimanual lid retraction versus metal speculum	patients favored bimanual retraction over speculum
Rifkin[71]	prospective, randomized	VAS	60	comparison of different methods of anesthesia (tetracaine, proparacaine, TetraVisc)	pain is generally mild, no differences between topical medication
Sanabria[72]	prospective, randomized, double-masked	VAS	156	comparison of different pre- and post-IVT regimes (tetracaine+naphazoline versus lidocaine; tobramycin versus tobramycin+diclofenac)	effects of different regimes comparable
Shiroma[73]	prospective, randomized	VAS	260	comparison of five different concentrations of lidocaine gel	lidocaine drops effective and safe at concentrations from 2 to 12%

Tailor[74]	prospective, interventional case series	questionnaire	42	evaluation of distress during the different steps of the injection process	injection itself with highest percentage of distress; application and removal of drape and lid speculum caused >50% of distress
Ulrich[75]	prospective, double-masked, randomized	scale 0-3	120	evaluation of discomfort with and without application of a single drop of nepafenac before IVT	statistically less pain 6 hours after IVT with nepafenac, no statistically significant differences at 1 and 24 hours
Van Asten[76]	randomized, crossover	VAS	36	comparison of pain after use of 30-G and 33-G needles	pain comparable with both sizes, but potentially less scleral damage after 33-G needle (less reflux)
Yau[77]	prospective, randomized, double-blinded	VAS	93	comparison of 0.5% tetracaine hydrochloride with or without 4% lidocaine pledget versus 4% cocaine drops	no statistically significant differences

VAS: visual analog scale