NKR52_Meniere_PICO7_Steroid

Characteristics of studies

Characteristics of included studies

Lambert 2012

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Dexamethasone 1 ● *Age*: 53.0 ● *Boys (%)*: 57 Dexamethosone 2 ● *Age*: 55.5 ● *Boys (%)*: 44 Placebo ● *Age*: 47.0 ● *Boys (%)*: 36 **Included criteria:** Unilateral Meniere disease, AAO-OH. 2 or more episodes of vertigo per month for 2 months before the study lead-in period and 2 or more episodes of definitive vertigo during the last 4-week lead in-periode: Meniere disease 20 years. **Excluded criteria:** Exclusion criteria included infection in the ear, sinuses, or upper respiratory system; history of immunodeficiency disease or active or recent (G1 month before screening) middle ear disease; abnormality of the tympanic membrane in the affected ear that would preclude intratympanic injection; history of endo- lymphatic sac surgery; previous use of gentamicin in the affected ear; and use of systemic or intratympanic steroids within 1 month before screening. **Pretreatment:** No apparent differences at baseline
Interventions	**Intervention Characteristics** Dexamethasone 1 ● *Description*: A single 200-Kl intratympanic injection of OTO-104 was per- formed after application of phenol solution to the posterioinfer- ior quadrant of the tympanic membrane. A 26-gauge 3.5-inch spinal needle was inserted in the posterioinferior quadrant of the tympanic membrane, and drug material was injected near the round-window niche. 3 mg OTO-104 ● *Length of treatment*: 1 day ● *Longest follow-up efter endt behandling* : 12 weeks Dexamethosone 2 ● *Description*: A single 200-Kl intratympanic injection of OTO-104 was per- formed after application of phenol solution to the posterioinfer- ior quadrant of the tympanic membrane. A 26-gauge 3.5-inch spinal needle was inserted in the posterioinferior quadrant of the tympanic membrane, and drug material was injected near the round-window niche. 12 mg OTO-104 ● *Length of treatment*: 1 day ● *Longest follow-up efter endt behandling* : 12 weeks Placebo ● *Description*: A single 200-Kl intratympanic injection of OTO-104 was per- formed after application of phenol solution to the posterioinfer- ior quadrant of the tympanic membrane. A 26-gauge 3.5-inch spinal needle was inserted in the posterioinferior quadrant of the tympanic membrane, and drug material was injected near the round-window niche. Placebo ● *Length of treatment*: 1 day ● *Longest follow-up efter endt behandling* : 12 weeks
Outcomes	*Anfaldshyppighed, SD* ● **Outcome type**: ContinuousOutcome *Alvorlige bivirkninger, n* ● **Outcome type**: DichotomousOutcome *Sværhedsgraden af tinnitus, THI, SD* ● **Outcome type**: ContinuousOutcome
Identification	**Sponsorship source:** Supported in full by Otonomy, Inc. **Country:** USA **Setting:** 15 centers in the United States. **Authors name:** Paul R. Lambert **Institution:** Otonomy, Inc., **Email:** clebel@otonomy.com **Address:** Otonomy, Inc., 6275 Nancy Ridge Dr., Suite 100, San Diego, CA 92121, U.S.A.;
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Randomly assigned, unclear how
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Nothing mentioned
Blinding of participants and personnel (performance bias)	Low risk	Judgement Comment: Personnel was kept blinded
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Outcome assessors were blinded

Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: No other apparent sources of bias
Selective reporting (reporting bias)	Low risk	Judgement Comment: No other apparent sources of bias
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Lambert 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Dexamethasone ● *Age*: 54.8 ● *Boys (%)*: 45.5 Placebo ● *Age*: 55.3 ● *Boys (%)*: 50.6 **Included criteria:** Key patient inclusion criteria were the following: ages 18 to85 years diagnosed with definite unilateral Me´nie`re's disease(2); patient recorded at least two definitive (a score of 2 – 4 fromthe vertigo severity scale) vertigo episodes during the 4-weeklead-in period and completed at least 22 of 28 diary entriesduring screening; patient agreed to maintain their current treat-ments for Me´nie`re's disease; women of childbearing potentialhad a negative pregnancy test before randomization and tookadequate contraceptive precautions for the duration ofthe study. **Excluded criteria:** Patients were excluded from the study if they had any of thefollowing: infection in the sinuses or upper respiratory system;middle ear disease or a significant abnormality of the tympanicmembrane affecting the IT injection; a history of immunode-ficiency disease; previous use of IT gentamicin; previousendolymphatic sac surgery; tympanostomy tubes with evidenceof perforation or lack of closure; vertiginous migraine; dropattacks; systemic or IT steroids (within 1 month previous);experience of an adverse reaction to IT injection of steroids; orwomen who were pregnant or lactating. **Pretreatment:** Baseline demographics weregenerally balanced across both groups.
Interventions	**Intervention Characteristics** Dexamethasone ● *Description*: single 0.2 ml IT injection of 60 mg/ml on Day 1 ● *Length of treatment*: One injection ● *Longest follow-up efter endt behandling* : 3 months Placebo ● *Description*: injection of placebo on day 1 ● *Length of treatment*: One injection ● *Longest follow-up efter endt behandling* : 3 months
Outcomes	*Anfaldshyppighed, SD* ● **Outcome type**: ContinuousOutcome *Alvorlige bivirkninger, n* ● **Outcome type**: DichotomousOutcome *Livskvalitet, SF-36, SD* ● **Outcome type**: ContinuousOutcome *Activity of daily living, DHI, SD* ● **Outcome type**: ContinuousOutcome *Tone audometri, SD* ● **Outcome type**: ContinuousOutcome
Identification	**Sponsorship source:** The trial and analyses were financially supported by Otonomy, Inc. **Country:** USA **Setting:** Fifty-two academic and community otolaryngologycenters. **Comments:** clinicaltrials.gov Identifier NCT01412177 **Authors name:** Paul R. Lambert **Institution:** Medical University of South Carolina **Email:** lambertp@musc.edu **Address:** Paul R. Lambert,M.D., Medical University of South Carolina, Charleston, SC 29425
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "generated permuted block randomization algorithm. OTO-104" Quote: "Intervention Following the 4-week lead-in period, eligible patients were randomly assigned to receive either 12 mg OTO-104 or placebo on Day 1 using a 1:1 allocation ratio based on a computer- generated permuted block randomization algorithm."
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Nothing mentioned
Blinding of participants and personnel (performance bias)	Low risk	Quote: "The administering physicians were trained not to use video monitors or discuss the appearance of the injected materials that would unblind the study staff or patients."
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: The administering physicians were trained not to use video monitors or discuss the appearance of the injected materials that would unblind the study staff or patients.The physicians are not a part of the study staff??
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: No other apparent sources of bias

Selective reporting (reporting bias)	Low risk	Judgement Comment: Matches study protocol
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Footnotes

Characteristics of excluded studies

Albu 2015

Reason for exclusion	Wrong intervention

Casani 2012

Reason for exclusion	Wrong intervention

Jumaily 2017

Reason for exclusion	Wrong study design

Lambert 2015

Reason for exclusion	only abstract

Lambert 2017

Reason for exclusion	only abstract

Patel 2016

Reason for exclusion	Wrong intervention

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

Lambert 2012

Lambert, Paul R.; Nguyen, Shaun; Maxwell, Kenneth S.; Tucci, Debara L.; Lustig, Lawrence R.; Fletcher, Malcolm; Bear, Moraye; Lebel, Carl. A randomized, double-blind, placebo-controlled clinical study to assess safety and clinical activity of OTO-104 given as a single intratympanic injection in patients with unilateral Meniere's disease. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 2012;33(7):1257-65. [DOI: https://dx.doi.org/10.1097/MAO.0b013e318263d35d]

Lambert 2016

Lambert, Paul R.; Carey, John; Mikulec, Anthony A.; LeBel, Carl; Otonomy Meniere's, Study Group. Intratympanic Sustained-Exposure Dexamethasone Thermosensitive Gel for Symptoms of Meniere's Disease: Randomized Phase 2b Safety and Efficacy Trial. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 2016;37(10):1669-1676. [DOI:]

Excluded studies

Albu 2015

Intratympanic dexamethasone versus high dosage of betahistine in the treatment of intractable unilateral Meniere diseaseAmerican Journal of Otolaryngology 2015; 36(2):205-9United States 2015.

Casani 2012

Intratympanic treatment of intractable unilateral Meniere disease: gentamicin or dexamethasone? A randomized controlled trialOtolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 2012;146(3):430-7England 2012.

Jumaily 2017

Jumaily, Mejd; Faraji, Farhoud; Mikulec, Anthony A.. Intratympanic Triamcinolone and Dexamethasone in the Treatment of Meniere's Syndrome. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 2017;38 (3):386-391. [DOI: https://dx.doi.org/10.1097/MAO.0000000000001311]

Lambert 2015

Lambert P.R.; Carey J.P.; Mikulec A.; Lebel C.P.. Ph2b efficacy and safety of intratympanic OTO-104 in meniere's disease. Otolaryngology - Head and Neck Surgery (United States) 2015;153(1):108. [DOI: http://dx.doi.org/10.1177/0194599815593290f]

Lambert 2017

Lambert P.R.; Silverstein H.; LeBel C.; Bishop K.. OTO-104 in meniere's disease patients: Phase 3 results. Otolaryngology - Head and Neck Surgery (United States) 2017;157(1):P122-P123. [DOI: http://dx.doi.org/10.1177/0194599817717251]

Patel 2016

Intratympanic methylprednisolone versus gentamicin in patients with unilateral Meniere's disease: a randomised, double-blind, comparative effectiveness trialLancet (London, England) 2016;388(10061):2753-2762England 2016.

Studies awaiting classification

Ongoing studies

Other references

Additional references

Other published versions of this review

Classification pending references

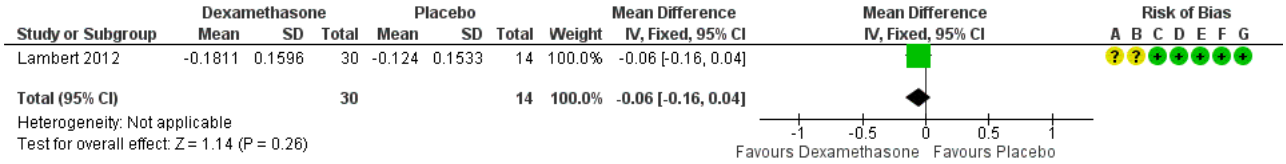
Data and analyses

1 Dexamethasone vs Placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Anfaldshyppighed. Mean change at month 3	1	44	Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.16, 0.04]
1.6 Alvorlige bivirkninger total	2	212	Risk Ratio (IV, Fixed, 95% CI)	Not estimable

Figures

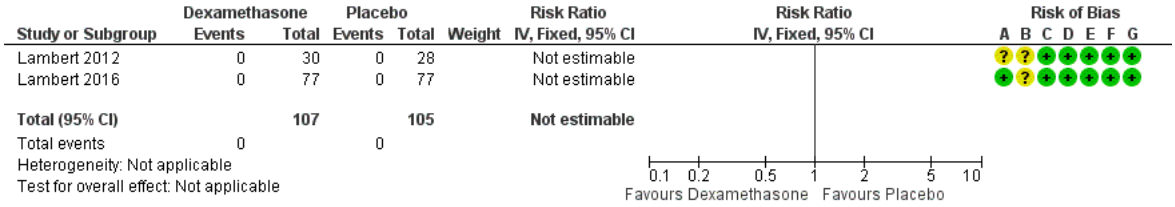
Figure 1 (Analysis 1.1)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Dexamethasone vs Placebo, outcome: 1.1 Anfaldshyppighed. Mean change at month 3.

Figure 2 (Analysis 1.6)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Dexamethasone vs Placebo, outcome: 1.6 Alvorlige bivirkninger total.