

NÉVRALGIE POST-HERPÉTIQUE

Dr Suzie Paquet, HMR
Cours sciences de base
13 avril 2023

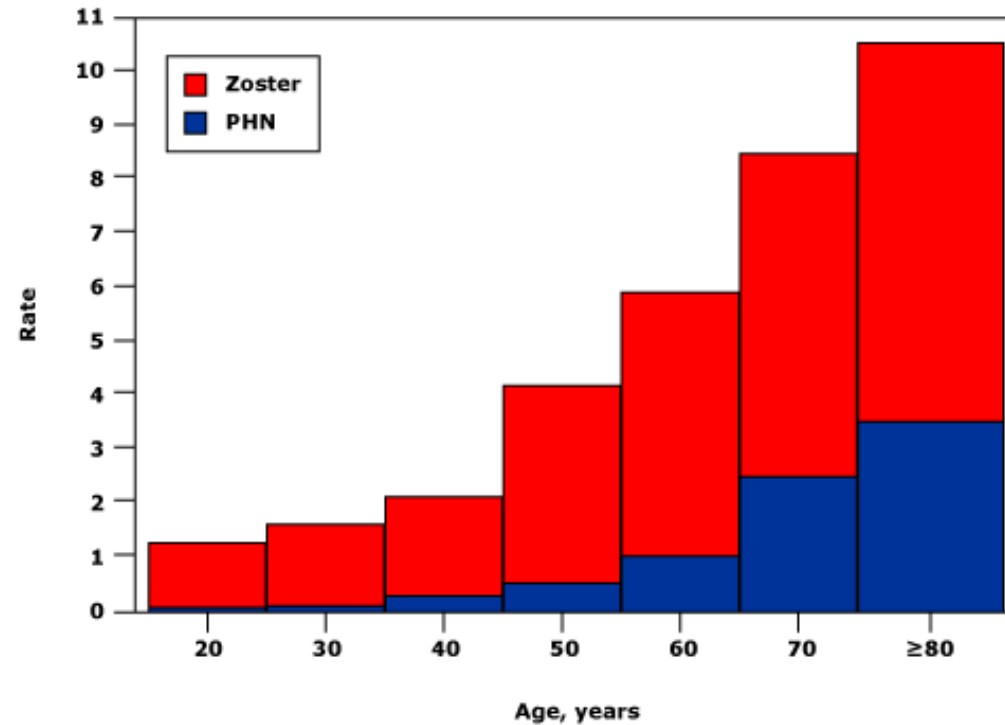
PLAN

- Introduction
- Épidémiologie
- Zona
- Névralgie post-herpétique
- Traitements
- Prévention
- Conclusion

ÉPIDÉMIOLOGIE

- USA : 1.2 millions/an causant une morbidité substantielle
- Au Québec : 27000 cas de zona/an et 600 hospitalisations/an.
- 30% des gens auront un zona dans leur vie
- L'incidence augmente partout dans le monde, cause non élucidée.
- Probabilité de développer une névralgie post herpétique augmente avec l'âge.
- 7% chez les patients de 60-69 ans
- 18% chez les plus de 70 ans .
- [Helgason S, Petursson G, Gudmundsson S, Sigurdsson JA. Prevalence of postherpetic neuralgia after a first episode of herpes zoster: prospective study with long term follow up. BMJ 2000; 321:794.](#)

Rates* of zoster and PHN[¶] by age - United States



PHN: postherpetic neuralgia.

* Per 1000 person-years.

¶ Defined as ≥ 30 days of pain.

Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of Herpes Zoster: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2008; 57:1.

PRÉSENTATION CLINIQUE (VZV)

- Varicella-zoster virus (VZV) cause 2 maladies distinctes
- 1) Primo infection : varicelle (rash prurigineux) jeune âge
 - infection légère en majorité
 - Après la primo-infection VZV, latence au niveau des ganglions sensitifs et autonomiques
- 2) Réactivation : Zona

RÉACTIVATION

- Mécanismes de réactivation peu compris
- Réactivation de la forme latente avec réplication du virus
- Atteinte localisée au niveau d'un ganglion sensitif, d'un nerf + dermatome cutané associé
- Douleur radiculaire unilatérale + rash
- Généralement limitée à un dermatome innervé par une seule racine ou un seul nerf crânien.

ZONA PRÉSENTATION CLINIQUE

- Douleur dans le dermatome atteint 48-72h avant l'apparition du rash
- rash maculopapulaire qui devient vésiculaire
- Guérison cutanée en 2-3 semaines
- Atteinte thoracique (T4-T6), cervicale et des nerfs trijumeau le + fréquent
- Incidence et sévérité augmentent avec l'âge



Figure 1. Classical herpes zoster in the left T4 dermatome. Note the concentration of lesions in areas of the dermatome innervated by the posterior primary division and the lateral branch of the anterior primary division of the left T4 spinal nerve. Source: Levin et al [2].



MANIFESTATIONS CLINIQUES



Figure 1. Clinical features of herpes zoster. (A and B) Typical maculopapular lesions that progress to vesicles. (C and D) Although lesions are typically confined to only one dermatome, they often cross dermatomes in immunosuppressed patients.

NÉVRALGIE ASSOCIÉE AU ZONA

- 3 phases de douleur :
 - 1) Névralgie aiguë qui précède et accompagne l'éruption cutanée et qui peut persister jusqu'à 30 jours.
 - 2) Névralgie subaiguë douleur persistante malgré la guérison des lésions cutanées mais se résolvent < 3 mois.
 - 3) Névralgie post-herpétique réfère à la douleur persistante après 3 mois.

NÉVRALGIES POST HERPÉTIQUE PATHOPHYSIOLOGIE

- Inflammation hémorragique du nerf périphérique, de la racine dorsale et du ganglion dorsal.
- L'inflammation associée avec le zona produit de la fibrose et des changements structuraux au niveau des nerfs.
- Activités spontanées des nerfs qui maintiennent la douleur malgré l'absence de dommage tissulaire actif.
- Les changements qui contribuent à la douleur persistante incluent:
 - Hyperexcitabilité au niveau ganglionnaire
 - Altération dans l'expression génique neuronale post infection

PATHOPHYSIOLOGIE

- Autopsies de patients avec douleur persistante :
 - Atrophie au niveau de la corne dorsale
 - Perte cellulaire, axonale et de myéline avec fibrose des ganglions sensitifs
 - Perte axonale et de myéline marquée dans le nerf et au niveau de la racine sensitive

NÉVRALGIE POST HERPÉTIQUE

- Principale complication du zona (5% à 40% des patients)
- Douleur neuropathique importante accompagnée de dysesthésies plus de 90 jours dans territoire atteint.
- Allodynie (90%)
- Hyperesthésie.
- Prurit, démangeaisons
- Paresthésies

NÉVRALGIE POST HERPÉTIQUE

- Limite la qualité de vie des patients avec atteinte du sommeil et de l'humeur.
- Peut perdurer des mois, des années et devenir chronique (30% des patients avec névralgie post-herpétique)
- Douleur difficile à traiter souvent réfractaire aux traitements avec atteinte majeur du fonctionnement.
- Importance de la prévention!!! : **antiviraux et vaccins**

AUTRES COMPLICATIONS

- Atteinte oculaire
- Surinfection bactérienne
- Complications neurologiques : encéphalite, paralysie, myélite transverse, guillain-barré, ACV
- Atteinte disséminée cutanée et atteinte organique chez les immunosupprimés
- HZ est associé à une perte de > 60000 QoL années et 2.4 milliards \$ en coûts médicaux et perte de productivité aux USA.

NÉVRALGIE POST HERPÉTIQUE

FACTEURS DE RISQUE

- Les 3 majeurs facteurs de risque pour névralgie post-herpétique
 - Âge >60 ans
 - Douleur sévère et incapacitante avec le zona
 - Rash plus sévère et important

RÉCIDIVES

- Immunité diminue avec le temps
- 5% de récurrences après un 1^{er} épisode de zona et jusqu'à 12% chez les immunosupprimés.
- Il est donc recommandé de recevoir le vaccin 12 mois après un zona

- Traitements Zona aigu

Table 1. Pharmacologic Therapies for Acute Herpes Zoster

| Agent | Dosage (adult) | Adverse effects | Notes | Cost* |
|--|---|--|--|---|
| Antivirals | | | | |
| Acyclovir | 800 mg orally five times per day for seven days | Diarrhea, encephalopathy, erythema multiforme, headache, malaise, nausea, Stevens-Johnson syndrome, vomiting | Dosing adjustments required for immunocompromised patients (10 mg per kg intravenously every eight hours) and for patients with creatinine clearance \leq 50 mL per minute per 1.73 m ² (0.83 mL per second per m ²) Approved for use in children (10 mg per kg intravenously every eight hours) | \$20 for 45 800-mg generic tablets |
| Famciclovir | 500 mg orally three times per day for seven days | Confusion, headache, nausea, Stevens-Johnson syndrome | Dosing adjustment required for patients with creatinine clearance \leq 60 mL per minute per 1.73 m ² (1.00 mL per second per m ²) | \$32 for 21 500-mg generic tablets (\$522 for brand name) |
| Valacyclovir (Valtrex) | 1,000 mg orally three times per day for seven days | Similar to acyclovir | Dosing adjustment required for patients with creatinine clearance \leq 50 mL per minute per 1.73 m ² | \$24 for 21 1,000-mg generic tablets (\$424 for brand name) |
| Adjunctive therapy | | | | |
| Corticosteroids (e.g., prednisone, prednisolone) | Prednisolone: 40 mg orally per day (days 1 to 6), 30 mg per day (days 7 to 10), 20 mg per day (days 11 to 14), 10 mg per day (days 15 to 18), 5 mg per day (days 19 to 21) Prednisone: 60 mg orally per day (days 1 to 7), 30 mg per day (days 8 to 14), 15 mg per day (days 15 to 21) | Dyspepsia, nausea, vomiting | Associated with accelerated time to crusting and healing of lesions and resolution of pain; no benefit in preventing postherpetic neuralgia | Varies |
| Analgesics | | | | |
| Acetaminophen | 325 to 1,000 mg orally every four to six hours as needed (maximum: 4,000 mg per day) | Headache, hepatotoxicity, hypersensitivity, nausea, rash | Infant and child dosage: 10 to 15 mg per kg orally every four to six hours as needed (maximum: 4,000 mg per day) | \$7 for 100 generic tablets |
| Nonsteroidal anti-inflammatory drugs (e.g., ibuprofen) | 400 mg orally every four to six hours as needed (maximum: 2,400 mg per day) | Abdominal discomfort, dyspepsia, gastrointestinal bleeding and perforation, myocardial infarction, nausea | Infant and child dosage (six months and older): 5 to 10 mg per kg orally every six to eight hours as needed (maximum: 2,400 mg per day) | \$7 for 100 generic tablets |

*—Estimated retail cost for one treatment course based on information obtained at <http://www.goodrx.com> and <http://www.walgreens.com> (accessed April 4, 2017).

Information from references 1 and 10 through 13.

**Débuter le plus vite possible les antiviraux
Idéalement < 72h**

Herpes Zoster and Postherpetic Neuralgia: Prevention and Management
AARON SAGUIL, MD, MPH; SHAWN KANE, MD; and MICHAEL MERCADO, MD, F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland

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Table 1. Medical treatment of HZ.

| Drug | Dosage | Remarks |
|--------------|--------------------------------|--|
| Acyclovir | Adults: 5 × 800 mg/day p.o. | Limited bioavailability |
| | 3 × 500 mg/day i.v. | In uncomplicated HZ |
| | 3–5 × 10 mg/kg/day | In severe HZ, in case of immunosuppression |
| | | for 10 day, usually 5–7 days |
| | Children: 3 × 10 mg/kg/day | Maximum daily dosage 2,5 g |
| Brivudin | Adults: 125 mg once a day p.o. | For 5 days. |
| Valaciclovir | Adults: 3 × 1000 mg/day p.o. | For 7 days |
| Famciclovir | Adults: 3 × 250–500 mg/day | 2nd line in ACV-resistant patients |

Adjunctive therapy

| | | | | |
|--|--|--|---|--------------------------------|
| Corticosteroids (e.g., prednisone, prednisolone) | Prednisolone: 40 mg orally per day (days 1 to 6), 30 mg per day (days 7 to 10), 20 mg per day (days 11 to 14), 10 mg per day (days 15 to 18), 5 mg per day (days 19 to 21) Prednisone: 60 mg orally per day (days 1 to 7), 30 mg per day (days 8 to 14), 15 mg per day (days 15 to 21) | Dyspepsia, nausea, vomiting | Associated with accelerated time to crusting and healing of lesions and resolution of pain; no benefit in preventing postherpetic neuralgia | Varies |
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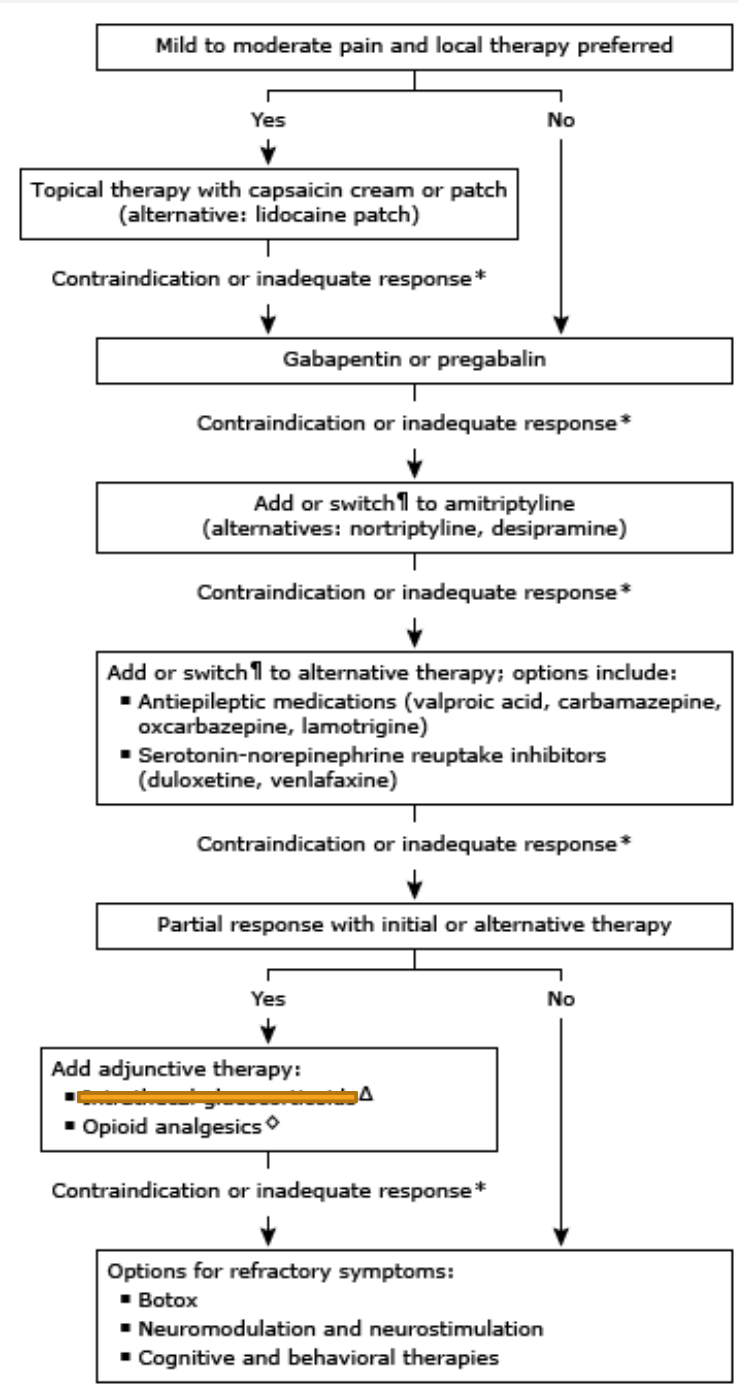
*—Estimated retail cost for one treatment course based on information obtained at <http://www.goodrx.com> and <http://www.walgreens.com> (accessed April 4, 2017).

Information from references 1, and 10 through 13.

Herpes Zoster and Postherpetic Neuralgia: Prevention and Management

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- Traitements névralgie
post-herpétique



* "Contraindication or inadequate response" includes patients who are unable to tolerate the medication, those who report partial relief after a trial of at least one month, and those who otherwise prefer an alternative option.

¶ "Add or switch" selection depends on whether initial agent provided partial versus no relief, the risk of adverse effects due to medication interactions from adding another agent, and patient/clinician preferences. Refer to the UpToDate topic for additional details.

Δ Not useful for patients with trigeminal region or other cranial pain.

◇ Opioids are generally reserved for short-term use in patients with intractable pain during the initial titration of other medications. The risks and benefits of using of opioid analgesic medications in this setting should be discussed with the patient before starting.

Table 2. Pharmacologic Therapies for Postherpetic Neuralgia

| <i>Agent</i> | <i>Dosage (adult)</i> | <i>Adverse effects</i> | <i>Notes</i> | <i>Cost*</i> |
|----------------------------|--|---|---|--|
| Topical treatments | | | | |
| Capsaicin 0.075% cream | Four applications per day | Erythema, pain on application, rash | Avoid contact with eyes and mucous membranes; 8% patch available for application by trained clinicians every three months | \$18 for 2-oz tube (over the counter) |
| Lidocaine 5% patch | Up to three patches per day | Blisters, local erythema, rash | Avoid in patients with allergy to amide local anesthetics | \$219 for 90 generic patches |
| Systemic treatments | | | | |
| Amitriptyline | Initial dose of 10 to 25 mg orally at bedtime, then increase by 10 to 25 mg per week to target of 75 to 150 mg per day | Blurred vision, constipation, dry mouth, sedation, urinary retention, weight gain | Taper gradually when discontinuing therapy; use caution in older adults; avoid in patients with cardiac arrhythmias, glaucoma, seizure disorder, or suicide risk; avoid concomitant use of tramadol, selective serotonin reuptake inhibitors, and serotonin-norepinephrine reuptake inhibitors (risk of serotonin syndrome) | \$4 for 30 75-mg generic tablets |
| Gabapentin (Neurontin) | 300 to 600 mg orally three times per day | Dizziness, peripheral edema, sedation, weight gain | Taper dose over seven days when discontinuing therapy; dosing adjustment required for patients with creatinine clearance ≤ 60 mL per minute per 1.73 m ² (1.00 mL per second per m ²) | \$13 for 90 300-mg generic capsules (\$406 for brand name) |
| Pregabalin (Lyrica) | 150 to 300 mg orally per day in two or three divided doses | Dizziness, peripheral edema, sedation, weight gain | Taper dose over seven days when discontinuing therapy; dosing adjustment required for patients with creatinine clearance ≤ 60 mL per minute per 1.73 m ² | \$395 for 60 75-mg brand name capsules (generic not available) |

*—Estimated retail price based on information obtained at <http://www.goodrx.com> and <http://www.walgreens.com> (accessed April 4, 2017).

Information from references 11, 27, 36, and 37.

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OPIACÉS

- Utilisation lors zona aigu si autres modalités de traitements non efficaces
 - Courte période
- Pas d'indication pour le traitement de la névralgie post-herpétique
 - Condition chronique
 - Risques surpassent les bénéfices
 - Petite période lors d'ajustements doses agents systémiques.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

| <i>Clinical recommendation</i> | <i>Evidence rating</i> | <i>References</i> |
|---|------------------------|-------------------|
| Although herpes zoster typically is diagnosed clinically, if laboratory confirmation is needed, polymerase chain reaction testing of vesicle or other fluids is preferred for diagnosis because of its high sensitivity (95%) and specificity (100%). | C | 7 |
| Acyclovir, valacyclovir (Valtrex), and famciclovir are effective treatments for herpes zoster and ideally should be started within 72 hours of the appearance of the rash to decrease the duration of symptoms and severity of pain. | B | 1, 2, 7, 14-16 |
| Capsaicin 8% patches, applied for 30 to 90 minutes, provide effective pain relief for patients with postherpetic neuralgia. | A | 40 |
| Gabapentin (Neurontin) and pregabalin (Lyrica) can be used for treatment of postherpetic neuralgia. | A | 42 |
| Amitriptyline, nortriptyline (Pamelor), and desipramine can be used for pain relief in patients with postherpetic neuralgia (number needed to treat = 3; 95% confidence interval, 2 to 4). | A | 26, 44 |
| The varicella zoster virus vaccine (Zostavax) should be given to patients 60 years and older, but it is contraindicated in those who are immunosuppressed, have human immunodeficiency virus infection and CD4 lymphocyte counts less than 200 per mm ³ (0.20 × 10 ⁹ per L), are undergoing cancer treatment, or who have cancer affecting the bones or lymphatic system. | A | 48, 50, 51 |

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort>.

TRAITEMENTS PHARMACOLOGIQUES

- Crèmes topiques
 - Lidocaine 5% ou 10% app locale q4h
 - Kétamine 2% + amitriptyline 5% app locale q4h
 - Capsaïcine
 - Crème 0,075% app locale 3 à 5x/jour
 - Patches 8%

TRAITEMENTS PHARMACOLOGIQUES

- Antidépresseurs tricycliques
 - Amitriptyline 10 mg HS ad 50mg à 150 mg
 - Desipramine 25 mg HS ad 150 mg
 - Nortriptyline 10 mg HS ad 150 mg
- Antiépileptiques
 - Prégabaline 75 mg BID ad 300 mg BID
 - Gabapentin 300 mg DIE ad 300 TID-600mg TID
- Titrer plus lentement pour les personnes âgées

TRAITEMENTS PHARMACOLOGIQUES

- ISRN
 - Duloxetine 60-120 mg die (initier 30 mg die)
 - Venlafaxine 150-225 mg die (initier à 75 mg die)
- Opiacés
 - Petite période lors d'ajustement et titration autres agents

TRAITEMENTS PHARMACOLOGIQUES

- Ajuster traitement selon patient
- Individualiser le traitement
- Plusieurs agents en concomitance seront souvent nécessaires.
- Comorbidités : trouble du sommeil, trouble de l'humeur, dépression
- Profil d'effets secondaires de chacun des médicaments

TRAITEMENTS NON PHARMACOLOGIQUES

- Acupuncture
- TENS
- Psychothérapie
- Méditation pleine conscience
- Hypnose

Definitions of grades of evidence:

TECHNIQUES INTERVENTIONNELLES

| Intervention | Strength of evidence |
|--|-----------------------------|
| 1. Intrathecal methylprednisolone | Very low |
| 2. Intercostal nerve chemical neurolysis | Low |
| 3. Epidural steroid injection | Low |
| 4. Pulsed RFA for intercostal nerve and dorsal root ganglion | Moderate |
| 5. Paravertebral steroid injection and chemical neurolysis | Low |
| 6. Stellate ganglion blocks and RFA | Moderate |
| 7. Spinal cord stimulation | Low |

TECHNIQUES INTERVENTIONNELLES CLINIQUE DE DOULEUR ACTUELLE

- Zona thoracique :
 - Bloc des nerfs intercostaux, RF pulsée, cryothérapie
- Zona cervical :
 - Bloc cervical superficiel, bloc stellaire
- Zona trigéminé :
 - Bloc n. supra-orbitaire, RF et cryothérapie
 - Bloc stellaire peut être tenté
 - Bloc n. mandibulaire
 - Bloc sphéno-palatin

PÉRIDURALE STÉROÏDES

- Avons longtemps pensé que les péridurales pouvaient diminuer le risque de développer une névralgie post herpétiques si effectuées en aigu.
- Dernières études avec des centaines de patients : pas de différences dans l'incidence de névralgie post herpétique.

Effect of Epidural Block in the Incidence of Postherpetic Neuralgia: A Population-Based Matched-Cohort Study
Jong-Yeop Kim^{1,2,*}, Jee-Young Hong^{1,*}, Inseok Ko¹, Minhye Chang³, Chi-Bum In^{2,3}

J Cutan Aesthet Surg. 2020 Oct-Dec; 13(4): 265–274. PMID: PMC8061658 doi: 10.4103/JCAS.JCAS_45_20: 10.4103/JCAS.JCAS_45_20

VACCINATION

- Diminue les risques de développer un Zona
- Diminue de 90% les risques de développer une névralgie post herpétique
- Recommandé aux adultes de plus de 50 ans
- Recommandé aux adultes immunosupprimés de plus de 18 ans
- Recommandé d'attendre 12 mois après un épisode de Zona

Table 1. Herpes Zoster Vaccines Licensed in the United States

| Characteristic | ZOSTAVAX (Zoster Vaccine Live; Merck) | SHINGRIX (Recombinant Zoster Vaccine; GlaxoSmithKline) |
|---|---|---|
| Vaccine type | Live-attenuated VZV (Oka/Merck); ≥19 400 PFU | Recombinant VZV gE, adjuvanted |
| Vaccine composition | Two components: 1. lyophilized vaccine 2. sterile diluent | Two components: 1. lyophilized gE antigen 2. AS01B adjuvant suspension |
| Storage | –50°C to –15°C | +2°C to +8°C |
| Shelf life | 18 months from the date of manufacture of the final filled container when stored at ≤ –15°C | 36 months from the date of manufacture when stored at +2°C to +8°C |
| Dosage and administration | 1 dose SQ in deltoid region of upper arm; 0.65 mL/dose | 2 doses IM in deltoid region of the upper arm, 2 to 6 months apart; 0.5 mL/dose |
| Reactogenicity | Low | High |
| Overall efficacy against incidence of HZ | 51.3% | 97.2% |
| Overall efficacy against incidence of PHN | 66.5% | 91.2% |
| Persistence of protection against HZ | Up to 8 years | ≥10 years (studied up to 10 years) |
| FDA approval | May 25, 2006 for adults aged ≥60 yoa; March 24, 2011 for adults aged 50–59 yoa | October 20, 2017 for adults aged ≥50 yoa July 23, 2021 for adults ≥18 yoa who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy |
| ACIP recommendations | For use in immunocompetent adults aged ≥60 years | (1) For use in immunocompetent adults aged ≥50 yoa; (2) For use in immunocompetent adults aged ≥50 yoa who previously received ZOSTAVAX; (3) Preferred over ZOSTAVAX. Should wait at least 8 weeks if previously administered ZOSTAVAX. |

Abbreviations: ACIP, Advisory Committee on Immunization Practices; FDA, US Food and Drug Administration; gE, glycoprotein E; HZ, herpes zoster; IM, intramuscular; PFU, plaque-forming units; PHN, postherpetic neuralgia; SQ, subcutaneous; VZV, varicella-zoster virus; yoa, years of age.

Herpes Zoster Vaccines

Ruth Harbecke,1,2 Jeffrey I. Cohen,3 and Michael N. Oxman1,2,4

CONCLUSION

- Prévention!!! Prévention !!!
- Syndrome douloureux chronique souvent réfractaire aux traitements avec atteinte fonctionnelle significative et impact sociétal.
- Vaccination chez tous les patients de plus de 50 ans et chez les immunosupprimés de plus de 18 ans.
- Antiviraux le plus vite possible (idéalement < 72h d'apparition du rash)
- Analgésie multimodale
- Clinique de douleur si NPH réfractaire malgré analgésie orale/topique/combinaison RX

- Questions ???

ÉTUDES EN COURS

STUDY PROTOCOL




Open Access

Effect of duloxetine premedication for postherpetic neuralgia within 72 h of herpes zoster reactivation [PROCESS]: a study protocol for a randomized controlled trial



Zheng Chen^{1†}, Niti Shrestha^{1†}, Chunmei Zhao^{1†}, Bifa Fan^{2*†} and Fang Luo^{1*†}

Efficacy and Safety of Pulsed Radiofrequency in Herpes Zoster Related Trigeminal Neuralgia: A Systematic Review and Meta-Analysis

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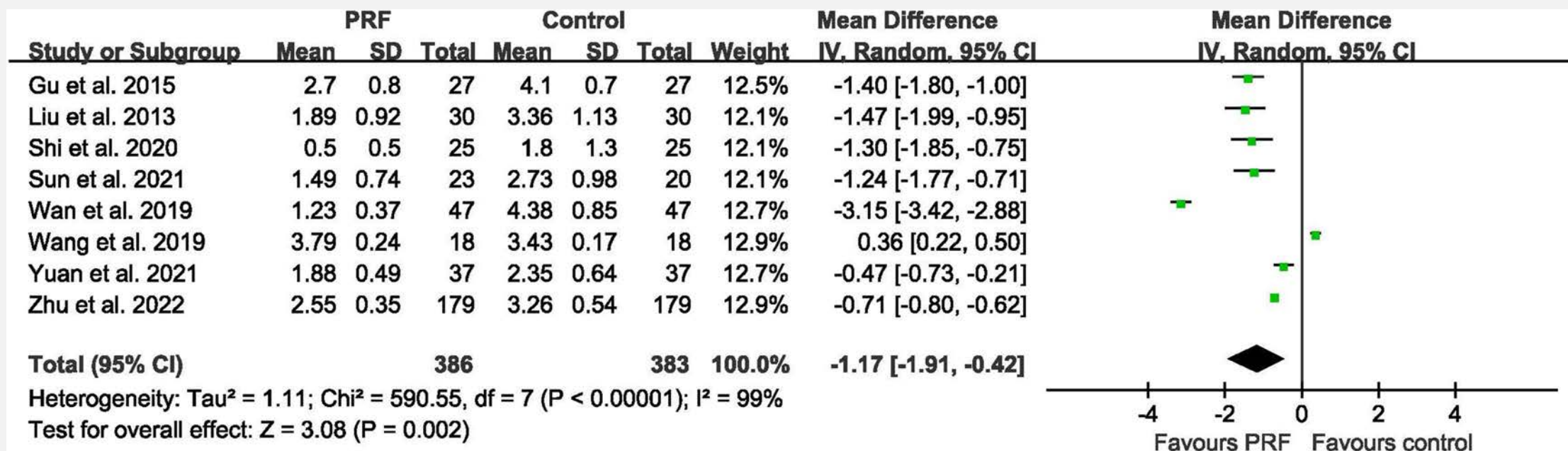


Figure 3 Comparison of PRF and control treatment: overall pain reduction at end of follow-up.

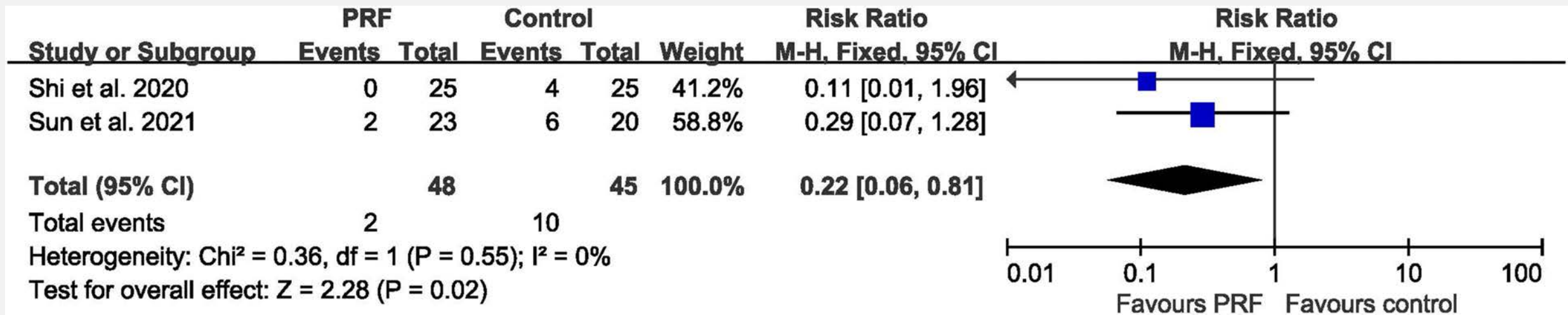


Figure 9 Comparison of PRF and control treatment: TPHN incidence.

Effective Treatment of Postherpetic Neuralgia at the First Branch of the Trigeminal Nerve by High-Voltage Pulsed Radiofrequency

*Hongxi Li, Yuanyuan Ding, Yongqiang Zhu, Zhenkai Han and Peng Yao**

Department of Pain Management, Shengjing Hospital of China Medical University, Shenyang, China

- **Role of cryotherapy in trigeminal neuralgia with certain modifications: A long-term prospective study**
- [Vishal Bansal](#)¹, [Apoorva Mowar](#)², [Prajesh Dubey](#)³, [Saloni Gupta](#)⁴
- Affiliations expand
- PMID: 32107186
- DOI: [10.1016/j.oooo.2019.10.013](https://doi.org/10.1016/j.oooo.2019.10.013)
-

- **Abstract**
- **Objective:** The aim of this study was to investigate the application of cryosurgery with certain modifications as a treatment modality for patients diagnosed with trigeminal neuralgia refractory to pharmacologic treatments.
- **Study design:** Forty-nine patients diagnosed with trigeminal neuralgia were treated with cryosurgery, involving the infraorbital nerve (13), inferior alveolar nerve (18), mental nerve (17), and supraorbital nerve (1), with closed, curved type of cryoprobe with nitrous oxide, at a temperature of -98°C , and pressure 70 kg/cm^2 or 100 psi.
- **Results:** Pain-free interval was observed to be less than 18 months in 4.08% patients, 36 to 40 months in 48.97% patients, 48 to 52 months in 32.65% patients, and greater than 52 months in 14.28% patients. All the patients experienced loss of fine and crude sensations for a period of 6 to 24 months.
- **Conclusions:** Cryotherapy could be a safe and economic modality that can be repeated, if required.