orphanaesthesia

Anaesthesia recommendations for

Van der Woude syndrome

Disease name: Van der Woude syndrome

ICD 10: Q38.0

Synonyms: VWS, Cleft lip/palate with mucous cysts of lower lip, Lip-pit syndrome, van der Woude syndrome1 (VWS1), van der Woude syndrome2 (VWS2)

Disease summary: VWS is a rare congenital disorder characterized by lower lip pits or fistulae in addition to cleft lip (CL), cleft palate (CP) or both (CLP) (1–3). The association was first reported in 1954 by Anne van der Woude (2). The VWS1 (4) is inherited as an autosomal dominant pattern caused by a mutation in the interferon regulatory factor 6 gene (IRF6), which has been mapped at 1q32-p41 region of chromosome 1 and is involved in epidermal and craniofacial development (1,2,5). The VWS2 (6) is related to a mutation in the GRHL3 gene on chromosome 1p36. The syndrome shows high penetrance but variable expressivity and is considered responsible of 0.5 - 6% of all facial cleft cases (1,2,5,7,8).

Patients with VWS typically present paramedial and lower lip pits at birth (80-88% of patients), usually bilateral. They can be associated to CL or CP and dental defects, such as hypodontia in 10-80% of VWS patients (1,2,5,7,9,10). Despite several publications assign some of the clinical signs detailed below to autosomal dominant popliteal pterygium syndrome (AD-PPS) (1,11), many of them have also been associated to VWS: single unilateral lip pits, submucosal palatal cleft, bifid uvula, ankyloglossia, limb abnormalities (skin folds, syndactyly), interalveolar synechiae, sensorineural hearing loss, congenital heart defects, anomalies of genitourinary system (10,12–15). Although some authors do not associate development delay nor intellectual disability to VWS (1), mild cognitive deficits with specific deficits in language function have been reported in patients with VWS (13).

The incidence at birth varies depending on authors (1/35,000-1/100,000) with no prevalence differences between sexes (1,7,10).

The VWS diagnosis is based on at least one of the following criteria present (12):

- Lip pits and CL and/or CP,
- Lip pits alone and a first-degree relative with CL and/or CP,
- CL and/or CP and a first-degree relative with lip pits.

Although diagnosis can be suspected on the basis of clinical findings, genetic testing of IRF6 confirmation should be appropriate (1,7).

The main differential diagnosis include AD-PPS, isolated cleft lip, oro-facial-digital syndrome type I, Hirschsprung disease, and Kabuki syndrome (1,7,10).

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Typical surgery

Maxillofacial malformations may require multiple corrective surgeries (7,9,11): simple excision of lip pits and fistulae, that can recur after surgery (2), CL, CP, ankyloglossia and interalveolar synechiae.

Pediatric dentistry and orthodontics are necessary procedures for the correction of anomalies VWS patients present (16–18).

Surgeries to correct limb deformities if associated.

Anesthesia for diagnostic imaging procedures could also be required.

Type of anaesthesia

There are no definite recommendations regarding either general or regional anaesthesia for patients with VWS.

Despite a lip fistulae removal with local anaesthesia has been reported in a 4 years old girl (7), general anaesthesia would be suggested in all paediatric patients due to poor cooperation and the need to cover the face during the procedure.

CL and CP require general anaesthesia, and multimodal analgesia including local anaesthetic infiltration, nerve blocks, opioid analgesics and non-opioid analgesics are recommended in CP surgery (19,20).

CL use to be classically repaired between 3 and 6 months of age; CP between 9 and 18 months (19) and lower lip pits at 10–12 months of age (2).

Necessary additional pre-operative testing (beside standard care)

There are no general recommendations for additional diagnostic pre-operative procedures in patients with VWS.

Only Svee and Lacombe (12,21) report association with congenital heart disease; thus, an ECG and echocardiography is warranted if cardiac signs and symptoms are present.

If clinically symptomatic, a sleep study may be necessary because obstructive sleep apnoea (OSA) appears at higher rate (31%) in patients with CP (22) than in the general paediatric population (2–3 %).

Particular preparation for airway management

Although difficult airway has not been specifically reported in VWS, the CP could be associated to paediatric difficult airway, being more frequent if CL is also present. A complete airway obstruction may occur if the tongue enters the cleft (22,23). Xue (24) reported difficult laryngoscopy in 4.77 %, that was increased in 1–6 months age group (7.06 %), and difficult intubation in 1.93 % in a sample of 985 infants aged from 1 month to 3 years, that underwent CL and CP repair surgery.

Belanger (22) suggests placing a gauze in the CP so the laryngoscope blade do not drop into and obstructs the view, in patients with unilateral left or bilateral cleft palate. An oropharyngeal airway is also recommended to achieve adequate mask ventilation (22).

Patients with VWS can have associated intraoral synechiae, which may have different anatomical locations, thickness, and tissue composition (12). In extensive forms, the airway may be compromised and urgent surgical release or early tracheostomy should be required (12). Cautions to avoid bleeding into the pharynx should be undertaken during the resection procedure. Mouth opening could be compromised after surgical release due to temporomandibular joint (TMJ) ankylosis and extubation should be considered a risk scenario for difficult airway complications.

There are a report of two cases of VWS and interalveolar sinequiae (12). In both cases, a nasopharyngeal tube was passed via 1 nostril, proximal to the larynx, after inhaled anaesthesia induction with spontaneous breathing. The tube was connected to the breathing circuit and lidocaine was injected through the tube. Then fibre-optic nasal intubation was performed via the other nostril.

Fibre-optic nasal intubation while maintaining spontaneous breathing should be considered in patients with intraoral sinequiae. After inhalational anaesthesia with maintenance of spontaneous ventilation, the airway is topically anesthetized with lidocaine by a spray-as-you-go (SAYGO) technique (25,26). Lidocaine is sprayed via the fibre-optic bronchoscope (FOB) on the vocal cords to prevent laryngospasm before the FOB is inserted into the trachea. During the procedure, inhalation and oxygen supply are continued via an endoscopy mask or a nasal tube.

Cuffed tubes are recommended if reconstructive surgery is indicated (27) and suction of pharyngeal blood and secretions prior to extubation is encouraged (27). Preformed endotracheal tubes could be employed in CL and CP surgeries.

Particular preparation for transfusion or administration of blood products

No specific recommendations are given. There are no reports of typical bleeding disorders in patients with VWS.

Particular preparation for anticoagulation

There is no need for specific preparation for anticoagulation.

Particular precautions for positioning, transportation and mobilisation

After CP surgery, the patient should be transferred in lateral or prone position to prevent blood aspiration.

Interactions of chronic disease and anaesthesia medications

Not reported.

Anaesthetic procedure

Consider avoiding preoperative sedative medication in those patients with suspected difficult airway or intraoral synechiae.

Endocarditis prophylaxis should be given in indicated situations.

Particular or additional monitoring

Using particular monitoring depends on the patient's individual risk and comorbidities. Nasogastric feeding tube should be placed if the patient have difficulties with oral feeding (12).

Possible complications

Perioperative bleeding, airway obstruction, oropharyngeal infection, feeding difficulties, flap dehiscence and palatal fistula have been described as complications of CL/CP surgery (27–29). If a throat pack is used, it must be removed before anaesthesia eduction and extubation. Acute tongue enlargement after throat packing has also been reported (27). Patients with VWS are prone to develop postsurgical wound complications (29).

Post-operative care

Postoperatively, it is important to monitor for signs of airway obstruction and bleeding. OSA could be associated to CP (22).

To prevent wound breakdown and partial dehiscence after cleft palate, pacifiers and aspiration probes during postoperative care must be avoided.

Disease-related acute problems and effect on anaesthesia and recovery

Airway problems as mentioned above.

Ambulatory anaesthesia

Minor procedures (lip pits) especially in patients without comorbidities can be carried out as day case surgery. When soft palate is involved in CP surgical repair, paediatric intensive care unit admission should be considered after surgery.

Obstetrical anaesthesia

There are no reports about obstetric anaesthesia procedures in patients suffering from VWS.

References

1. Van der Woude syndrome [Internet]. Available from: https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=967&Disease_Disease_Search_diseaseGroup=Van-der-Woude-syndrome&Disease_Disease_Search_diseaseType=Pat&Disease(s)/group of diseases=Van-der-Woude-syndrome&title=Van der Woude syndrome&s
2. Peralta-Mamani M, Terrero-Pérez Á, Dalben G, Rubira CMF, Honório HM, Rubira-Bullen IF. Treatment of lower lip pits in Van der Woude syndrome: a systematic review. Int J Oral Maxillofac Surg [Internet]. 2018 Apr;47(4):421–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0901502717316417
3. Kitchin S, Grames L, Naidoo SD, Skolnick G, Schoenborn A, Snyder-Warwick A, et al. Surgical, Speech, and Audiologic Outcomes in Patients With Orofacial Cleft and Van der Woude Syndrome. J Craniofac Surg [Internet]. 2019 Jul;30(5):1484–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31299749. https://omim.org/entry/119300.
4. Lam AK, David DJ, Townsend GC, Anderson PJ. Van der Woude syndrome: dentofacial features and implications for clinical practice. Aust Dent J [Internet]. 2010 Mar;55(1):51–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20415912. https://omim.org/entry/606713.
5. Angiero F, Farronato D, Ferrante F, Paglia M, Crippa R, Rufino L, et al. Clinical, histomorphological and therapeutic features of the Van der Woude Syndrome: literature review and presentation of an unusual case. Eur J Paediatr Dent [Internet]. 2018 Mar;19(1):70–3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29569458
6. Tehranchi A, Behnia H, Nadjmi N, Yassaee VR, Ravesh Z, Mina M. Multidisciplinary management of a patient with van der Woude syndrome: A case report. Int J Surg Case Rep [Internet]. 2017;30:142–7. Available from: http://dx.doi.org/10.1016/j.ijscr.2016.11.032
7. Bozkurt M, Kulahci Y, Zor F, Kapi E, Yucetas A. Reconstruction of the lower lip in van der woude syndrome. Ann Plast Surg. 2009;62(4):451–5.
8. Rizos M. Van der Woude syndrome: a review. Cardinal signs, epidemiology, associated features, differential diagnosis, expressivity, genetic counselling and treatment. The European Journal of Orthodontics [Internet]. 2004 Feb 1;26(1):17–24. Available from: https://academic.oup.com/ejo/article-lookup/doi/10.1093/ejo/26.1.17
9. Bennun RD, Stefano E, Moggi LE. Van der Woude and Popliteal Pterygium Syndromes. Journal of Craniofacial Surgery [Internet]. 2018 Sep;29(6):1434–6. Available from: http://journals.lww.com/00001665-201809000-00018
10. Svee A, Frykholm P, Linder A, Hakelius M, Skoog V, Nowinski D. Early Release of Interalveolar Synechiae Under General Anesthesia Through Fiberscopic Nasal Intubation. Journal of Craniofacial Surgery [Internet]. 2012 Jul;23(4):e299–302. Available from: http://journals.lww.com/00001665-201207000-00099
11. Nopoulos P, Richman L, Andreasen N, Murray JC, Schutte B. Cognitive dysfunction in adults with Van der Woude syndrome. Genetics in Medicine [Internet]. 2007 Apr;9(4):213–8. Available from: http://www.nature.com/doifinder/10.1097/GIM.0b013e3180335abd
12. Ziai MN, Benson AG, Djalilian HR. Congenital Lip Pits and Van der Woude Syndrome. Journal of Craniofacial Surgery [Internet]. 2005 Sep;16(5):930–2. Available from: http://journals.lww.com/00001665-200509000-00038
13. Pingul MM, Quintos JB. Van der Woude Syndrome (Lip Pit-Cleft Lip Syndrome). J Pediatr [Internet]. 2014 May;164(5):1235. Available from: http://dx.doi.org/10.1016/j.jpeds.2013.12.039
14. Rizos M. Van der Woude syndrome: a review. Cardinal signs, epidemiology, associated features, differential diagnosis, expressivity, genetic counselling and treatment. The European Journal of Orthodontics [Internet]. 2004 Feb 1;26(1):17–24. Available from: https://academic.oup.com/ejo/article-lookup/doi/10.1093/ejo/26.1.17
15. Tehranchi A, Behnia H, Nadjmi N, Yassaee VR, Ravesh Z, Mina M. Multidisciplinary management of a patient with van der Woude syndrome: A case report. Int J Surg Case Rep

[Internet]. 2017;30:142–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2210261216305107

16. Estévez-Arroyo B, Gómez-Mendo I, Romero-Maroto M, Solano-Reina E, Iglesias-Linares A. Craniofacial characteristics in Van der Woude syndrome. Oral Dis [Internet]. 2022 Mar 22; Available from: https://onlinelibrary.wiley.com/doi/10.1111/odi.14187
17. Reena, Bandyopadhyay K, Paul A. Postoperative analgesia for cleft lip and palate repair in children. J Anaesthesiol Clin Pharmacol [Internet]. 2016;32(1):5. Available from: http://www.joacp.org/text.asp?2016/32/1/5/175649
18. Moffitt JK, Cepeda A, Ekeoduru RA, Teichgraeber JF, Nguyen PD, Greives MR. Enhanced Recovery After Surgery Protocol for Primary Cleft Palate Repair: Improving Transition of Care. Journal of Craniofacial Surgery [Internet]. 2021 Jan;32(1):e72–6. Available from: https://journals.lww.com/10.1097/SCS.0000000000006985
19. Lacombe D, Pedespan JM, Fontan D, Chateil JF, Verloes A. Phenotypic variability in van der Woude syndrome. Genet Couns [Internet]. 1995;6(3):221–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8588850
20. Belanger J, Kossick M. Methods of identifying and managing the difficult airway in the pediatric population. AANA J [Internet]. 2015 Feb;83(1):35–41. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25842632
21. Frénéa S, Richard M, Payen JF. L'intubation difficile chez l'enfant : mythe ou réalité ? Ann Fr Anesth Reanim [Internet]. 2003 Jul;22(7):653–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0750765803001771
22. Xue FS, Zhang GH, Li P, Sun HT, Li CW, Liu KP, et al. The clinical observation of difficult laryngoscopy and difficult intubation in infants with cleft lip and palate. Pediatric Anesthesia [Internet]. 2006 Mar;16(3):283–9. Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1460-9592.2005.01762.x
23. Xue FS, Liu HP, He N, Xu YC, Yang QY, Liao X, et al. Spray-as-you-go airway topical anesthesia in patients with a difficult airway: A randomized, double-blind comparison of 2% and 4% lidocaine. Anesth Analg. 2009;108(2):536–43.
24. Dhasmana S, Singh V, Pal US. Nebulisation Versus Spray-as-You-Go Airway Topical Anaesthesia in Patients with Temporomandibular Joint Ankylosis using 2 % Lignocaine. J Maxillofac Oral Surg [Internet]. 2015;14(2):398–402. Available from: http://dx.doi.org/10.1007/s12663-013-0613-5
25. Smarius BJA, Guillaume CHAL, Jonker G, van der Molen ABM, Breugem CC. The use of throat packs in pediatric cleft lip/palate surgery: a retrospective study. Clin Oral Investig [Internet]. 2018 Dec 22;22(9):3053–9. Available from: http://link.springer.com/10.1007/s00784-018-2387-0
26. Machotta A. Anästhesiologisches Management bei Korrekturen von Lippen-Kiefer-Gaumenspalten bei Kindern. Anaesthesist [Internet]. 2005 May;54(5):455–66. Available from: http://link.springer.com/10.1007/s00101-005-0823-4
27. Jones JLP, Canady JW, Brookes JT, Wehby GL, L'Heureux J, Schutte BC, et al. Wound complications after cleft repair in children with Van der Woude syndrome. J Craniofac Surg [Internet]. 2010 Sep;21(5):1350–3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20856020.

Date last modified: **November 2022**

Authors:

Cristina Del Río Peña, Pediatric Anesthesiology, 12 de Octubre Hospital, Madrid. Miembro del Grupo de Trabajo "Enfermedades Raras y Anestesia" de la Sección Pediátrica de la SEDAR
cristina.rio@salud.madrid.org

Carlos Errando Oyonarte, Head, Anesthesiology and Reanimation Department. Hospital Can Misses, Ibiza, Balearic Islands, Spain.
errando013@gmail.com

Pascual Sanabria Carretero, Pediatric Anesthesiology, La Paz Children's Hospital, Madrid. Miembro del Grupo de Trabajo "Enfermedades Raras y Anestesia" de la Sección Pediátrica de la SEDAR
psanabriacarretero@gmail.com

Disclosure: The authors have no financial or other competing interest to disclose. This recommendation was unfunded.

Reviewers:

Rosa Maria Yañez-Vico, Complutense University of Madrid (UCM). School of Dentistry, Madrid; BIOCRAN (Craniofacial Biology: Orthodontics and Dentofacial Orthopedics) Research Group, Complutense University of Madrid, Spain
rosayane@ucm.es

Nina Scheiba, Dermatologist, Skin and Laser Centre Heidelberg, Germany
Dr.n.scheiba@durani-facharzt.de

Please note that this recommendation was not reviewed by an anaesthesiologist and a disease experts but by two disease experts instead.

Disclosure The reviewers have no financial or other competing interest to disclose.