orphanaesthesia

Anaesthesia recommendations for patients suffering from

Liddle's Syndrome

Disease name: Liddle's Syndrome

ICD 10: I15.1

Synonyms: Pseudohyperaldosteronism

In 1963 Dr Grant Liddle, an endocrinologist in the United States described this syndrome. It is a rare inherited disorder of sodium channels resulting in excessive salt reabsorption from the distal nephron [1]. Initial presentation has been described from infancy through to late adulthood and in some circumstances first presentation of genetically prone patients has been evident with pregnancy induced hypertension [2,3]. This renal tubular defect causes severe hypertension, hypokalemia, metabolic alkalosis, decreased renin and angiotensin [2]. It is inherited as an autosomal dominant trait with variable penetrance. Complete linkage of the disorder is localized to gene 16p13-p12 or 16p12.2 [4].

These genetic defects either delete the C-terminus of β or γ ENaC or mutate a proline or a tyrosine within a short sequence, called the PY (Pro-Pro-x-Tyr) motif. This deletion/mutation of the PY motif in βENaC or γENaC impairs the ability of Nedd4-2 to bind (and thus ubiquitylate) ENaC, leading to accumulation of ENaC channels at the plasma membrane and increased channel activity. These alterations of the beta or gamma subunits of the epithelial sodium channel of the aldosterone sensitive distal nephron lead to increased sodium and water reabsorption owing to the resulting increase in transepithelial voltage [6]. Potassium and Hydrogen ions are secreted into the collecting duct, resulting in hypokalemic metabolic alkalosis. There have been only 30 cases of Liddle's Syndrome reported in English literature [2].

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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

Disease summary

The clinical phenotype resembles primary hyperaldosteronism and the presenting feature is typically hypertension in teenage years. Patients are often asymptomatic. Renal impairment may occur due to hypertension. Muscle weakness in combination with severe hypertension has been reported in elderly population with the syndrome [2]. The defining factor in the diagnosis is evidence of suppressed aldosterone levels and the lack of response to treatment with the mineralocorticoid receptor blocker spironolactone [6,7]. Metabolic abnormalities can be corrected by dietary salt restriction and administration of antagonists of the epithelial sodium channelsuch as amiloride or triamterene [8]. Renal transplantation has been used as treatment [9].

Typical surgery

- Renal Transplantation [2]
- Caesarean Section [3]

Type of anaesthesia

There are no definite recommendations for either general anaesthesia or regional anaesthesia for Liddle's syndrome. Anaesthetic considerations must include an assessment of end organ damage as untreated patients with the syndrome can develop renovascular, cardiovascular and cerebrovascular disease [4].

Use of regional anaesthesia with or without general anaesthesia can be used for intraoperative care and postoperative analgesia and can subsequently reduce the stress response and intraoperative hypertensive episodes.

The major risks of anaesthesia are related to hypokalaemia and hypertension. Pre-operative optimization therefore should include blood pressure control and normalization of the plasma potassium concentration. As triamterene and amiloride are direct antagonists of the offending channel, these drugs help lower blood pressure and reverse the biochemical abnormalities. Treatment of volume deficits during intercurrent illness help correct and minimize the biochemical abnormalities [4].

Drugs dependent on renal excretion should be used with caution if renal dysfunction is present. Many drugs are excreted by the kidneys either unchanged or as metabolites. Loading doses of drugs are unchanged but maintenance doses should be reduced or dosing interval prolonged. Hypoalbuminaemia increase the free drug availability of highly protein bound drugs e.g. induction agents [10].

Muscle weakness may also be present which could have implication for the use of muscle relaxants.Suxamethonium may increase K+ levels. Non-depolarising muscle relaxants may have prolonged effect due to hypokalaemia and alkalosis [10].

Necessary additional diagnostic procedures (preoperative)

ECG abnormalities may be present and include ST and T wave depression, prolonged QT interval, prominent U waves and ventricular ectopy [3].

Chest x-ray to rule out cardiomegaly.

Echocardiogram – assessment of left ventricular function, left ventricular hypertrophy and assessment of ejection fraction would be important with history of severe hypertension [10].

Hematological investigations: full blood count, urea, creatinine, electrolytes, coagulation profile.

Arterial Blood Gas preoperatively to assess for the extent of metabolic alkalosis [3].

If a regional anaesthetic technique is planned and the patient has reported muscle weakness, a full neurological examination should be performed and documented.

Particular preparation for airway management

No particular airway concerns have been described.

Particular preparation for transfusion or administration of blood products

No particular concerns have been described.

Particular preparation for anticoagulation

Adjust drug dosing if significant renal impairment is present.

Particular precautions for positioning, transport or mobilisation

No unique concerns have been described.

Probable interaction between anaesthetic agents and patient's long-term medication

Hypokalaemia may be present and can interfere with recovery from muscle relaxant and should be corrected pre-operatively if present. However, if patients with LS develop chronic kidney disease from severe hypertension, they may develop an adaptive hyperkalaemic response [10]. Anaesthetic drugs dependent on renal excretion and those that cause hyperkalaemia should be used with caution [10].

Particular or additional monitoring

The presence of renovascular, cardiovascular and cerebrovascular disease may require invasive monitoring with arterial and central venous pressures [4].

Possible complications

Hypokalaemia/hyperkalaemia can be associated with cardiac arrhythmias [10].

Postoperative care

Postoperative care should depend on the type of surgery and the clinical situation of the patient postoperatively.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

The main differential diagnosis is primary hyperaldosteronism (Conn's Syndrome) [6].

Ambulatory anaesthesia

Day case anaesthesias have not reported on however given the potential for hypokalaemia, metabolic alkalosis and hypertensive episodes, admission would be preferable.

Obstetrical anaesthesia

Association of Liddle's and pre-eclampsia would not be unexpected given the association between pre-existing hypertension and the development of pre-eclampsia in pregnancy. Regular monitoring of blood pressure is advised [11]. Amiloride is a pregnancy Category B drug. It has been reported in pregnancy for the treatment of Bartter's Syndrome with no adverse affect on the fetus [12].

Literature and internet links

1. Liddle GQ, Bledsoe R, Coppage WS Jr. A familial renal disorder simulating primary aldoesteronism with negligible aldosterone secretion. Trans Assoc Am Physicians 1963;76: 199-213
2. Matsushita, T. Miyahara, Y. Kohno, S. et al, Liddle's Syndrome in an Elderly Woman. Internal Medicine 37:4:391-395 April 1998PMID:9630200
3. Hayes N E, Aslani A, McCaul C L, Anaesthetic Management of a patient with Liddle's Syndromes for emergency Caesarean Hysterectomy. Internation Journal of Obstetric Anaesthesia, 178-180, 2011PMID:21183332doi: 10.1016/j.ijoa.2010.10.007. Epub 2010 Dec 22.
4. Syndromes: Rapid Recognition and Perioperative Implications, Bruno B, Igor Luginbuehl, Bruno Marcinak, Bernard Dalens (Book)
5. Rotin D. Role of UPS in Liddle syndrome. BMC Biochemistry 2008, 9 (Suppl 1):S5)
6. Palmer BF, Alpern RJ: Liddle's Syndrome. Am J Med 104:301, 1998 PMID:9552093
7. Wang C, Chan TK, Yeung RTT, Coghlan JP, Scoggins Ba, Stockigt JR. The effect of triamterene and sodium intake on renin, aldosterone and erythrocyte sodium transport in Liddles Syndrome. Journal Clinical Endocrinology Metab 52:1027-1032. 1981. PMID: 6262354
8. Inoue, T. Okauchi, Y, Matsuzake, Y. Saito, S. et al Identification of a single cytosine base insertion mutation at Arg-597 of the Beta Subunit of the human epithelial sodium channel in a family with Liddle's Syndrome. Eur J Endocrinol. 1998 Jun;138(6):691-7. PMID: 9678538
9. Botero-Velex M, Curtis JJ, Warnock DG, Liddle's Syndrome revisted – a disorder of sodium reabsorption in the distal tubule, New England Journal of Medicine; 330:187-181 PMID: 8264740
10. Allman KG, Wilson I H, Oxford Handbook of Anaesthesia, 3rd Edition, Oxford University Press 2012
11. Sibai BM, Lindheimer M, Hauth J, et al. Risk factors for pre-eclampsia, abruption placentae and adverse neonatal outcomes among women with chronic hypertension. National Institute of Child Health and Human Development Network of Maternal Fetal Medicine Units New England Journal of Medicine 1998;339:667-71 PMID: 9725924
12. O'Sullivan E, Monga M, Graves W, Bartter's syndrome in pregnancy: a case report and review. Am J Perinatol, 1997 Jan; 14(1):55-7 PMID: 10870297

Last date of modification: April 2015

These guidelines have been prepared by:

Author
Conan McCaul, Anaesthesiologist, The Rotunda Hospital, Dublin, Ireland
cmccaul@ROTUNDA.ie

Co-Author
Kim Caulfield, Anaesthesiologist, The Rotunda Hospital, Dublin, Ireland
kimcaulfield86@gmail.com

Peer revision 1
Rajiv Sinha, Paediatric Nephrologist, Christian Medical College, Vellore, India
rajivsinha_in@yahoo.com

Peer revision 2
David Ellison, Division of Nephrology and Hypertension, Oregon Health and Science University, Portland, Oregon, USA
ellisond@ohsu.edu

Please note that this guideline has not been peer-reviewed by an anaesthesiologist but by two disease experts.