Adrenal insufficiency due to etomidate inhalation via electronic cigarettes: three local cases

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Case presentations

Etomidate is a non-barbiturate intravenous anaesthetic agent commonly used in emergency and critical care settings, due to its rapid onset, short duration of action, and minimal cardiorespiratory suppression. Adrenal suppression is a known side-effect. From April to May 2024, three adolescents presented to the paediatric departments of local hospitals with adrenal insufficiency due to etomidate inhalation via electronic cigarette (e-cigarette) vaping, a novel form of drug misuse emerging in Hong Kong.

In Case 1, a 17-year-old male with attention deficit hyperactivity disorder was admitted with ketamine cystitis. He had mild hypokalaemia, hypertension (137/84 mmHg), and a positive urine toxicology screen by liquid chromatography–tandem mass spectrometry for cocaine, ketamine, and etomidate (Table). He reported daily vaping of 'space oil' via e-cigarettes for 4 months. Adrenal insufficiency was diagnosed based on elevated adrenocorticotropic hormone (ACTH) and a suboptimal response in a low-dose short Synacthen test. In Case 2, a 16-year-old male with autistic spectrum disorder presented with confusion, insomnia, and unsteady gait after vaping 'space oil' weekly for one month. Blood pressure and electrolytes were normal. Urine toxicology revealed etomidate and its analogue propoxate. Adrenal insufficiency was confirmed. In Case 3, a 15-year-old male with substance abuse–induced psychosis presented with emotional instability under drug effects. He reported vaping 'space oil' via e-cigarettes weekly for several months. Blood pressure and electrolytes were normal. Partial adrenal insufficiency was diagnosed with borderline results in the low-dose short Synacthen test. Two patients (Cases 1 and 2) required regular hydrocortisone replacement. In Case 1, repeated testing 5 months after cessation of etomidate revealed persistent adrenal insufficiency, likely due to second-hand smoke exposure from peers who used etomidate. For Cases 2 and 3, follow-up tests were planned after etomidate cessation. All patients received psychiatric follow-up.

Discussion

This is the first local paediatric report of adrenal insufficiency associated with etomidate misuse via e-cigarettes. Since its clinical introduction 40 years ago, recreational use via the intravenous route has been rare.[1] Nonetheless, its misuse as 'space oil' via e-cigarette vaping has surged in Hong Kong and Mainland China since 2023. e-Cigarette use is relatively common among adolescents, with a local survey reporting that 5.3% of secondary school students have had experience with e-cigarettes.[2] From May to December 2024, the Hong Kong Poison Control Centre recorded 45 cases of 'space oil' misuse presenting to Hospital Authority emergency departments, with a median patient age of 17 years.[3] Our cases also illustrate that psychiatric co-morbidities and polysubstance misuse are not uncommon among adolescent etomidate users.

Knowledge about the pharmacology of inhaled etomidate is limited since historical studies have focused on its properties in the context of a single intravenous bolus or short-duration infusion,[4] while inhalation may involve higher doses and prolonged use. Known toxicities include decreased consciousness, nausea, vomiting, myoclonus, and adrenal insufficiency. Respiratory suppression or bradycardia may develop in overdose. Long-term neurological and psychological effects, particularly dependence and withdrawal, remain poorly characterised.

Etomidate and its analogues, propoxate/isopropoxate, inhibit 11β-hydroxylase, causing adrenal insufficiency with consequent decreased cortisol and aldosterone production, and elevated precursors such as 11-deoxycorticosterone,

TABLE. Initial and follow-up investigations and treatment of the three cases

	Case 1	Case 2	Case 3	Reference ranges
Initial investigations				
Urine toxicology screen by LC-MS/MS	Cocaine metabolites, ketamine metabolites, etomidate metabolites, and other over-the-counter drugs and their metabolites including famotidine, meloxicam ofloxacin/levofloxacin, omeprazole/esomeprazole and paracetamol	Etomidate metabolites, propoxate or its chain isomer metabolites, diphenhydramine metabolites	Etomidate metabolites, cocaine metabolites	NA
Plasma sodium, mmol/L	143	140	142	136-145
Plasma potassium, mmol/L	3.2	3.6	3.5	3.4-5.0
Plasma ACTH, pmol/L	58	5.3	5.5	1.6-13.9
Morning serum cortisol, nmol/L	68	ND	43	133-537
Serum 17-OHP, nmol/L	29	1.0	1.9	<5
Serum 11-deoxycortisol, nmol/L	539	2.5	18.5	≤4.3
Serum 21-deoxycortisol, nmol/L	<2.5	<2.5	<2.5	≤2.5
Serum androstenedione, nmol/L	73.2	3	5.1	1.4-5.2
Plasma renin activity, ng/mL/hr	ND	<0.07	ND	0.08-3.84
Plasma aldosterone, pmol/L	ND	<50	ND	<972
LDSST (peak serum cortisol), nmol/L	113	238	319	≥376
Urine steroid profile	ND	ND	Abnormal*	NA
Medical treatment				
Oral hydrocortisone replacement	Regular	Regular	Stress dose when necessary	
Follow-up investigations				
Plasma ACTH, pmol/L	26	Pending	Pending	1.6-13.9
LDSST (peak serum cortisol), nmol/L	272	Pending	Pending	≥376

Abbreviations: 17-OHP = 17-hydroxyprogesterone; ACTH = adrenocorticotropic hormone; LC-MS/MS = liquid chromatography–tandem mass spectrometry; LDSST = low-dose short Synacthen test; NA = not applicable; ND = not done

* Urine steroid profile showed marked elevation in tetrahydro-deoxycortisol (THS), tetrahydro-deoxycorticosterone, and the THS to total cortisol metabolites ratio, suggestive of 11β-hydroxylase deficiency. Androgen metabolites were mildly increased

11-deoxycortisol, and 17-hydroxyprogesterone (Fig). Accumulation of deoxycorticosterone, the precursor to aldosterone, leads to mineralocorticoid excess. Marked elevation of androstenedione in Case 1 and urinary androgen metabolites in Case 3 suggested androgen excess, consistent with a recently reported local female adult case of hyperandrogenism from etomidate misuse.[5]

Adrenal suppression from etomidate is dose-dependent and reversible, lasting 6 to 8 hours after a single dose and up to 24 to 48 hours with continuous infusion.[4,6] Effects after chronic inhalation are less clear due to the variable drug content of e-cigarettes and inconsistent inhalation routes. Adrenal hyperplasia has been observed on computed tomography examinations among chronic users,[5,7] suggesting possible prolonged ACTH stimulation due to ongoing adrenal suppression beyond typical durations in clinical settings.

Etomidate-induced 11β-hydroxylase inhibition can resemble congenital adrenal hyperplasia due to 11β-hydroxylase deficiency. In addition to adrenal insufficiency, features of mineralocorticoid excess include hypertension, hypokalaemia, and suppression of endogenous renin and aldosterone, as seen in Case 2. Although mild hypokalaemia was observed in Case 1, severe hypokalaemia has been reported.[7] Cases 1 and 3 demonstrated significantly elevated 11-deoxycortisol, while 17-hydroxyprogesterone was normal to mildly elevated, suggesting the former is a more sensitive marker of enzyme inhibition, as it is immediately upstream of the inhibited enzyme (Fig). Urinary steroid profiling can identify abnormal precursor-to-product ratios. A short Synacthen test should be performed to confirm adrenal insufficiency. Cases 2 and 3 demonstrated that ACTH may be normal and cortisol response may be relatively preserved despite circumstantial evidence of 11β-hydroxylase inhibition, possibly reflecting less drug exposure or compensation between periods of drug use.

Given the uncertainty of the duration of

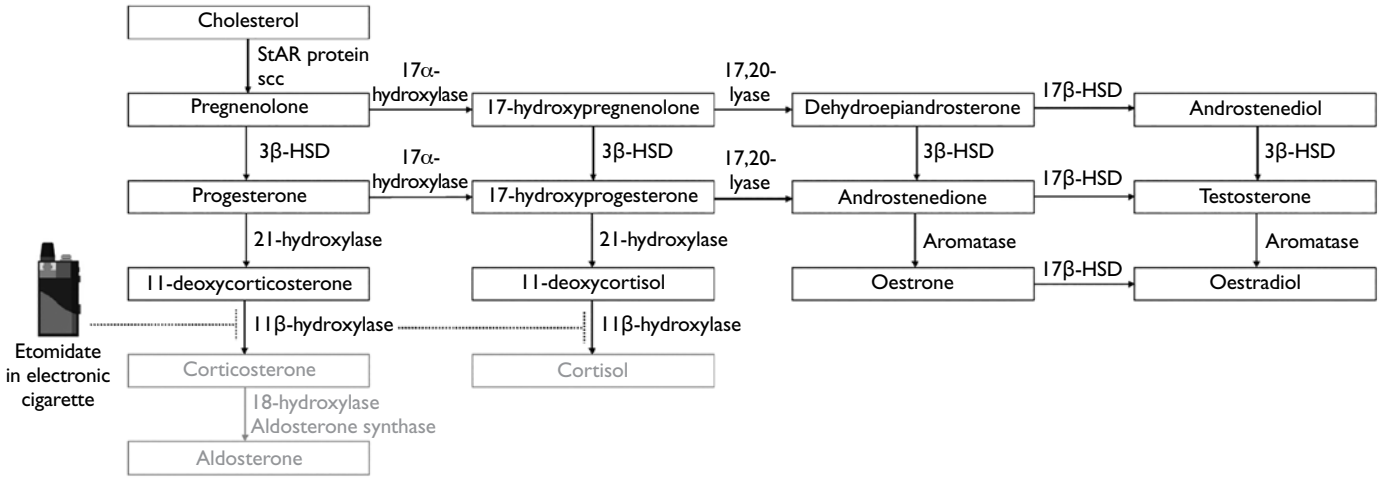

FIG. Pathway of steroidogenesis in 11β-hydroxylase suppression associated with etomidate use. Etomidate inhibits 11β-hydroxylase, blocking the conversion of 11-deoxycorticosterone (DOC) to corticosterone and 11-deoxycortisol to cortisol, and leading to elevation in adrenal precursor hormones, including DOC, 11-deoxycortisol and 17-hydroxyprogesterone

Abbreviations: 3β-HSD = 3β-hydroxysteroid dehydrogenase; 17β-HSD = 17β-hydroxysteroid dehydrogenase; scc = side-chain cleavage enzyme; StAR protein = steroidogenic acute regulatory protein

adrenal suppression, hydrocortisone replacement and/or stress dose precautions should be given for confirmed adrenal insufficiency. Etomidate users should receive counselling on hydrocortisone's role, as it does not mitigate the full spectrum of etomidate toxicities. After cessation of etomidate, follow-up testing is recommended to document adrenal recovery. Persistently abnormal results should prompt suspicion of ongoing drug use, with non-classic congenital adrenal hyperplasia due to 11β-hydroxylase deficiency being a rare differential diagnosis. Our cases highlight the challenges of achieving complete cessation of drug misuse due to peer influence and potential dependence. A multidisciplinary approach should be adopted to address the complex medical and psychosocial issues in adolescent etomidate users.

Etomidate and its three analogues—metomidate, propoxate, and isopropoxate—have been listed as dangerous drugs in Hong Kong since February 2025.[8] It is expected that more stringent regulations, along with continued law enforcement on illegal drug production and distribution, may help deter etomidate misuse. Public education should also be strengthened to emphasise that substances in e-cigarettes are not harmless, even if they are not traditionally classified as drugs.

Etomidate misuse via e-cigarettes is an emerging public health issue. Clinicians should be alert to the risk of adrenal insufficiency among e-cigarette users, particularly those who present with unexplained hypertension or hypokalaemia. Additional testing, such as toxicology screening, 11-deoxycortisol measurement, and urinary steroid profiling may provide supportive evidence. Further research is warranted to understand the pharmacological properties and long-term effects of etomidate misuse.

Author contributions

Concept or design: All authors.
Acquisition of data: YK Chung, YT Cheung, CSY Chan, CC Wong.
Analysis or interpretation of data: All authors.
Drafting of the manuscript: YK Chung.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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Ethics approval

The patients were managed in accordance with the Declaration of Helsinki and provided informed consent for all treatments, procedures, and publication.

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