

Substance abuse and conscious sedation: theoretical and practical considerations

Aliya Hasan*¹ and Valmiki Sharma²

Key points

Educates dental professionals of the indications for conscious sedation methods.

Illustrates the practical considerations of substance abuse and conscious sedation.

Discusses the management of drug tolerance and those undergoing conscious sedation.

Provides an overview of non-pharmacological anxiety management.

Abstract

Substance abuse is an issue that has been widely recognised both in the medical and dental professions. Many different recreational drugs exist and their use can have important consequences in relation to conscious sedation. As the use of illicit drugs is growing, it is important to have an understanding of the impact of substance abuse on determining if a patient is a suitable candidate for conscious sedation. It is important to appreciate that while human studies in this area are limited, animal studies and observation of the reactions of substance abusers to sedative agents demonstrate a potential link between illicit drug use and conscious sedation through drug interaction. This paper aims to discuss the importance of understanding substance abuse, the potential effects such substances can have in relation to conscious sedation and appropriate management techniques for substance abusers in order to provide optimum safe care when undergoing conscious sedation techniques.

Introduction

Conscious sedation is defined as:

'A technique in which the use of a drug or drugs produces a state of depression of the central nervous system enabling treatment to be carried out but during which verbal contact is maintained throughout the period of sedation. The drugs and techniques used to provide conscious sedation for dental treatment should carry a margin of safety wide enough to render the loss of consciousness unlikely.'¹

Encompassing different routes of administration, including oral, inhalation and intravenous conscious sedation, can be used to aid in the provision of dental treatment to anxious patients, those with a severe gag

reflex, those with certain adverse medical conditions, and in special care dentistry.² The use of conscious sedation dates back to the 1800s, when Horace Wells sedated a patient for a tooth extraction using nitrous oxide.³ A century later, conscious sedation techniques advanced with the creation of the Jorgensen Technique, named after Professor Niels Bjorn Jorgensen, a dentist working in Los Angeles. This involved incremental doses of intravenous pentobarbital to a patient in combination with meperidine and scopolamine in saline.⁴ Since then, many improvements to conscious sedation techniques have been, and continue to be, developed.

Various challenges exist when carrying out conscious sedation for dental procedures. However, in the author's opinion, one of the increasingly prevalent issues is the risk assessment and determination of the effects of substance abuse on the use of conscious sedation.

Indications for the use of conscious sedation in dentistry

There are several indications for the use of conscious sedation in dentistry. As previously mentioned, dental anxiety is one of the most

common reasons for the use of conscious sedation. The Adult Dental Health Survey in 2009 reported that 12% of the adult population stated that they have extreme anxiety in relation to dental treatment.⁵ Therefore, dentally phobic patients may undertake conscious sedation for dental procedures. Of this subset, many are referred for specialist dental treatment under sedation in secondary care settings.

Another indication for the use of conscious sedation is for patients with a severe gag reflex. Patients who are unable to tolerate treatment secondary to this issue may be offered conscious sedation; notably, intravenous sedation can help to overcome an overactive gag reflex.⁶ Other indications for conscious sedation include patients with adverse medical conditions that may benefit from the effects of the sedative agents, such as uncontrolled epilepsy or movement disorders, both of which respond favourably to midazolam.⁷

More subjectively, conscious sedation can also be used to enable more anxiety provoking dental procedures to be completed with greater comfort. For example, with the surgical removal of a lower third molar, the use of conscious sedation can help to reduce anxiety and awareness during the procedure.⁷

¹Former Dental Core Trainee in Paediatric Dentistry, Dental and Maxillofacial Department, Great Ormond Street Hospital, Great Ormond Street, London, WC1N 3JH; ²Consultant in Oral and Maxillofacial Surgery, Royal Free London NHS Foundation Trust, Hampstead, London, NW3 2QG

*Correspondence to: Aliya Hasan
Email: aliya.hasan@nhs.net

Refereed Paper.

Accepted 22 July 2019

<https://doi.org/10.1038/s41415-019-0897-z>

The properties of sedative agents

Sedative agents have multiple properties that make conscious sedation a treatment of choice for many patients. With safe therapeutic margins, benzodiazepines have favourable anxiolytic properties. Benzodiazepines bind to GABA_A receptors (gamma amino-butyric acid) in the brain which augments the opening of chloride ion channels thereby potentiating the inhibitory effects of GABA.⁸ This allows for a patient to be maintained in a relaxed state and thus, the procedure to continue without difficulty.

Some sedative agents can also act as anti-hypertensives. For example, benzodiazepines have vasodilatory effects. In one study by Klockgether-Radke *et al.*, it was shown that midazolam has vasodilatory effects on coronary arteries.⁹ This can be useful in patients with a history of hypertension, as their blood pressure will decrease as the sedative agent is administered.

Other beneficial effects of benzodiazepines include a degree of inhibition of the gag reflex and anterograde amnesic properties.¹⁰ This can result in a patient seemingly not being able to recall the dental procedure therefore allaying their anxiety somewhat for future dental visits.

What is substance abuse?

The World Health Organisation (WHO) define substance abuse as: ‘The harmful or hazardous use of psychoactive substances including alcohol and illicit drugs.’¹¹

Substance abuse statistics

In England currently, the use of recreational drugs is growing in popularity. The term ‘Recreational Drug’ refers to any drug used socially and not for medical reasons.¹² Examples of the types of recreational drugs used in England are shown in the table below.

In 2015 in England and Wales, there were 2,479 deaths from the use of illicit drugs. This is the highest number of recreational drug-related deaths since 1993.¹³ Between 2015 and 2016, 8.4% of adults aged between 1659 years admitted to using illicit drugs and in 2014, 24% of 15-year-olds also admitted to this.¹³ The UK Drug Strategy was introduced in 2017 in a bid to reduce substance abuse in the UK and support those who are addicts into recovery.¹⁴ Currently, literature on the effect of recreational drugs in relation to conscious sedation is sparse.

This paper aims to focus on two very commonly used recreational drugs; cannabis and alcohol to highlight their potential

interactions with sedative agents and steps that may be employed to mitigate complications in dental practice.

Cannabis and alcohol

One of the most common recreational drugs used worldwide is cannabis. The United Nations published The World Drug Report in 2016 where it was evidenced that in 2014, 183 million people worldwide were using cannabis.¹⁵ This is a Class B drug with the effects of producing a ‘dream-like’ state with an altered state of mind.¹⁶ Cannabis is a hallucinogenic drug containing 66 cannabinoids which are active components of the drug that bind to cannabinoid receptors in the brain to produce the desired effect.¹⁷ In England between 2014 and 201, 6.7% of adults admitted to taking cannabis.¹⁸

Another popular recreational drug is alcohol. The Department of Health, recommends weekly consumption of alcohol should not exceed 14 units of alcohol; the equivalent of seven pints of low strength (4%) lager, beer or cider.¹⁹ Alcohol misuse is common, with 6,813 deaths in 2015 in England being due to alcohol consumption.²⁰ Patients who have increased alcohol intake may present to general dental

Table 1 Common names for popular recreational drugs²²

Drug	UK street names	UK street appearance	Effect
Cannabis	Marijuana, Weed, Skunk, Dope Resin, Bhang, Grass, Hash, Ganja, Herb, Hashish	Soft black resin, Furry green leaves, Hard brown lumps, Dark oil.	Sedated and relaxed (stoned), can feel time is slower, hallucination
Cocaine	Blow, Crack, Coke, Snow, White Lady, Charlie, Ching, Chang, Freebase, Aunt Nora	Coke: Fine white powder Crack: White rocks Freebase: Crystals	Happy, excited, confident, wide awake, increased sex drive
Phencyclidine (PCP)	PCP, Angel Dust, Hog, Peace pills	Oily yellow liquid, White to brown crystals and powders.	‘Numb’ feeling, can be euphoriant or depressant. Can lead to psychosis
Heroin	Smack, Skag, Horse, China White, Big H, Brown Sugar, Junk, Thunder, Gear, Brown, Speedball (mixed with cocaine)	Usually ‘cut’ with different substances so can be brownish white to brown powder.	Dizziness initially. Happiness, relaxed, euphoric, sleepy
Lysergic acid diethylamide (LSD)	LSD, Acid, Tab, Dot, Drops, Rainbow, Smiles, Paper Mushroom, Trip, Tripper, Lucy, Micro Dot, Blotter	Paper squares with pictures (tabs), Tiny pellets, Liquid.	World appears distorted including time, giggly, euphoric, awestruck with surrounding things
Amphetamine sulphate	Speed, Billy, Whizz, Addys, Uppers, Zing, Smart Pills, Study Buddys	Off white pinkish powder that can look like crystals, Can be a white/grey paste.	Alert, energised, excited, can lead to delusion and psychosis
Synthetic cannabinoids	Spice, Mary Joy, K2, K3, Black Mamba, Blue Cheese, X, Ecsees, Amsterdam Gold, Bombay Blue	Spice commonest in UK: sachets describing contents as incense/herbal smoking mixture.	Effects similar but more potent to cannabis but can lead to paranoia
Methylene dioxy methamphetamine (MDMA)	Ecstasy, E, Dizzle, Molly, Superman, Mandy, Dolphins, Beans, MD, Cowies, Mitsubishiis	Monographed pills: Ecstasy. White powder usually in cigarette wrapper: MDMA.	Very happy, ‘loved up’, energetic, more in tune with surroundings and music
Ketamine	Vitamin K, Special K, Wonk, K, Super K, Ket	Grainy white or brown crystalline powder. Unusually tablet.	Chilled and relaxed, dreamlike, detached, happy.
Benzodiazepines	Downers, Jellies, Eggs, Roofies, Rohypnol, Norries, Mazzies, Vallies, Blues, Benzos, Moggies	Tablets, Capsules, Injections and Suppositories	Calm and relaxed. Sometimes used to ‘come down’ off speed, cocaine, crack etc...

practitioners and may have complications such as alcohol-related liver disease, the most severe of which may require liver transplants. Complications of liver disease particularly relevant to dentistry include impaired hepatic metabolism of metabolites from conscious sedation drugs as well as local anaesthetics (amides), immunosuppression and post-operative bleeding risks.²¹ Additionally, alcohol can cause a myriad of mental health disorders (eg, anxiety, depression and anti-social behaviour) either during intoxication or withdrawal. On the more extreme end of the spectrum, it can lead to alcohol induced psychotic disorder (AIPD) that may impact on the patient's capacity and therefore consent and safeguarding issues may arise.

Pre-assessment considerations for intravenous conscious sedation in relation to drug misuse

Prior to carrying out intravenous conscious sedation in a patient using recreational drugs it is important to undertake a comprehensive pre-assessment in relation to drug use. This involves a detailed drug history ensuring that the patient fully comprehends the questions and encouraging them to be explicitly clear in their answers. Due to several recreational drugs having various names for the same drug, it is important to have a knowledge of this as patients may only know one name for a particular drug. A table of alternative common names for some popular recreational drugs is shown in Table 1 below. Points to include in the drug history are shown in Figure 1.

Being aware of the drug history of a patient allows safe management tailored to their needs. In a colonoscopy study by Patel *et al.*, it was shown that although people with a history of alcohol misuse may be difficult to sedate, chronic opioid users are certainly more difficult to sedate.²³ Understanding a patient's drug history and predicting their response to sedation, can help determine which environment is most suitable for providing care or whether or not a patient is a suitable candidate for conscious sedation at all. In turn, when assessing a patient for conscious sedation, an in-depth medical history is also important. For patients with co-morbidities related to recreational drug taking, it is important to ascertain their ASA Grade (American Society of Anaesthesiologists) and how the use of conscious sedation may affect their wellbeing. For example, patients with severe

Fig. 1 A diagrammatic representation of a detailed drug history



alcoholic liver disease are classified as ASA Grade 4. With such patients, it is important to understand how hepatic impairment relates to the metabolism and removal of sedatives.²⁴

Dental professionals should be mindful that not all patients will declare their entire medical history. If one suspects a patient may not be disclosing their full medical history, the importance and relevance of disclosing issues should be emphasised for ensuring safe treatment and prevention of harm. If there are further difficulties, permission should be sought to contact the patient's general medical practitioner (GP) to obtain a comprehensive medical and drug history, although even then the GP may be unaware of any substance misuse.

Drug tolerance and conscious sedation

For dental practitioners and anaesthetists, it is important to be aware of the possible effects of recreational drugs with different sedative agents. It has been hypothesised that some drugs (for example alcohol, amphetamines and opioids) can lead to a tolerance to certain sedative agents. This suggests that sedating groups of patients taking said drugs may be difficult.²⁵

There are two important implications of drug tolerance. Firstly, a standard dose of sedative agent is not always enough to sedate a patient who is drug dependant and this could result

in inadvertent over-sedation, where a sedation practitioner pursues a suitable level of sedation to allow treatment to continue. Secondly, some drug dependant patients will develop cross tolerance. Essentially this means that tolerance to one drug may result in tolerance to another that acts in a similar way. It has been shown that cross tolerance can exist between benzodiazepines and alcohol. The consequence of this is that a patient becomes very difficult to sedate as normal doses of sedative do not work.²⁶ For the dental practitioner or anaesthetist, this can be very challenging in terms of maintaining safe sedation practice while achieving adequate patient response.

Management of recreational drug use and sedation

It is important to appreciate the potential relationship between substance abuse and conscious sedation in order to correctly manage these patients. For cannabis users, few studies exist regarding the interaction between cannabis and sedative agents. However, a study by Flisberg *et al.*²⁷ suggested an interaction between cannabis and a sedative agent (propofol). Cannabis users in this study needed a significantly higher dose of propofol before a laryngeal mask could be inserted compared to the non-cannabis group.²⁷ This does suggest that there may be a correlation between the use and cannabis and difficulty in sedating such patients.

Table 2 Recreational drugs and oral manifestations^{33,34,35,36,37,38}

Drug	Oral manifestation
Cocaine	Xerostomia
Ecstasy	Xerostomia, Tooth surface loss
Tobacco	Periodontal disease, Oral squamous cell carcinoma
Alcohol	Xerostomia, Dental trauma

The cannabinoids contained in cannabis are fat soluble and therefore accumulate in fatty tissues. The average half-life of cannabis is estimated to be between 28 and 56 hours in regular users of the drug; however, once cannabinoids enter adipose tissue it has been estimated that there is a prolonged half-life of approximately 7 days.^{28,29}

Kuczkowski discussed that cannabis use can induce tachycardia and myocardial depression. It is suggested that due to this, cannabis may compound the effects of anaesthetic agents and thus affect arterial pressure and heart rate.³⁰ Some practitioners request that patients who use cannabis refrain from doing so for a period of time (up to 72 hours) before having conscious sedation for a dental procedure to reduce the likelihood of drug interactions.³¹

Alcohol dependence may affect the provision of conscious sedation due to the damaging long-term effects of alcohol on the body. In England the current mortality rate from alcoholic liver disease in people under 75 years of age is 8.8 per 100,000 population.³² Patients with a diagnosis of alcoholic liver disease usually require a higher level of management not commonly found in primary care environments, and this may in part explain why these individuals are referred for management in secondary care and hospital settings.

When assessing patients with alcoholic liver disease for conscious sedation, hepatic function must be considered. For milder impairments, liver function tests via the patient's GP or hospital practitioner may be sufficient and treatment can proceed with caution. Patients with severe hepatic impairment should be under the care of a local hepatology team and advice from them should be sought regarding appropriate drug administration and modifications to standard sedation protocols.

As an aside, liver function is also important to surgeons for surgical procedures. Coagulation studies and thrombocytopenia assessment (FBC) need to be undertaken to ensure adequate precautions are made for individuals at risk of post-operative haemorrhage.

It would seem sensible to reduce doses of sedative in order to prevent drug toxicity. In dental sedation with midazolam, for those with hepatic impairment, the standard protocol is modified to half the dose of midazolam increments and double the time between administering increments. This allows a greater understanding of the effect of each increment before administering further doses, enabling a safe level of sedative agent to be given, in order to reduce the risk of drug toxicity. Metabolism and elimination of the sedative may additionally be impaired, increasing recovery times and this should also be considered when treatment planning.

Oral manifestations of substance abuse

The effects of recreational drugs on the orodental tissues must be appreciated. Not only can recreational drugs affect conscious sedation techniques, but one must also consider the oral side effects of recreational drug use. An example of the oral manifestations of substance abuse can be seen in cannabis users. Individuals who frequently use cannabis and ecstasy can develop xerostomia.^{33,34} This can cause multiple oral side effects including an increase in halitosis, difficulties in swallowing and tasting foods and an increased caries risk. The management for these particular patients should include prescription of saliva substitutes and preventative methods such as fluoride varnish application, along with regular review appointments.

Another oral manifestation includes the development of tooth surface loss. Many recreational drugs (ecstasy in particular) can cause individuals to grind teeth excessively. This was demonstrated by Milosevic *et al.* In this study, 18 participants who were ecstasy users demonstrated tooth surface loss into dentine, while only three non-users had signs of this. The study also described jaw clenching as being potential factor in causing tooth surface loss; notably of the occlusal surfaces of teeth.³⁴

In turn, it is important to remember that other commonly used drugs such as tobacco, can have serious oral manifestations. It has been widely evidenced that tobacco smoking can have an adverse effect on periodontal health and lead to an increased incidence of oral squamous cell carcinoma formation. With regards to periodontal health, tobacco smoking is known to cause vasoconstriction of blood vessels supplying the periodontium. This in turn can produce a false positive effect of a stable periodontium due to the absence of bleeding on probing.³⁵ Moreover, as a lifestyle factor, those who smoke tobacco are at a 47 times increased risk of oral cell squamous carcinoma formation compared to non-smokers.³⁶ This risk is increased when alcohol and chewed tobacco are included (relative risk \times 35).

Many recreational drugs lower inhibitions and can alter the cognitive ability of individuals. Dental trauma can be as a result of fights, falls or other accidents as a result of recreational drug use. In alcohol abusers, one of the most common dental side effects is trauma.³⁷ This trauma can include luxation and avulsion injuries, leading to the need for urgent dental care. It has been stated by Bullock, that substance abuse should be considered in all patients that present with dental trauma.³⁸ Table 2 demonstrates different recreational drugs and their oral effects.

Non pharmacological anxiety management

In anxious patients who have experienced substance abuse, the likelihood of conscious sedation working effectively is not entirely predictable. In turn, opting for a general anaesthetic for these patients is often undesirable; especially when the risk/benefit ratio is unfavourable. Therefore, consideration must be given to other, non-pharmacological methods of anxiety management.

Prior to understanding which method of anxiety management is suitable, it is important to consider the severity of anxiety that a patient may have. The Modified Dental Anxiety Scale (MDAS) is a measure of anxiety that uses five questions. This scale is simple to use and can be used for adults, with an amended version created for children; the Modified Child Dental Anxiety Scale (MCDAS). As a simple screening tool, MDAS provides an accurate measure of anxiety and is widely accepted by dentists in the UK.³⁹

For patients with differing levels of anxiety, techniques for anxiety management commonly include the use of distraction. As a non-invasive

technique, the use of audio or visual distraction methods have proved to work well for anxious patients.⁴⁰ Relaxing background music or watching a video can aid in distracting a patient's mind away from the immediate situation of a dental procedure. More recently, the use of virtual reality goggles has been tested in order to aid with dental anxiety. Atzori *et al.* in 2018 described the use of virtual reality as a distraction method for children and teenagers undergoing unpleasant dental procedures. Those children using the virtual reality goggles reported to have more fun during the dental procedure than those without virtual reality goggles.⁴¹ Therefore, while this new technology is in the early stages of development, there is some evidence to show that the effects of using virtual reality as a method of distraction, is a positive step forward in anxiety management.

In turn, another non-pharmacological method of anxiety management is memory reconstruction. This technique involves reconstructing the memory of dental treatment and creating positive memories to make a dental visit more pleasant and calming for a patient. This was described in a study by Pickrell *et al.* in 2007.⁴² When comparing the control group to the intervention group, it was shown that by reconstructing a memory of a previous dental visit (whereby a child experienced fear), the child developed a sense of positivity and decreased fear about future dental treatment.

Other forms of non-pharmacological anxiety management include cognitive behavioural therapy, the use of hypnosis and rapport building. Each type of anxiety management has its merits. It is of the opinion of the author that each patient should have a comprehensive assessment of anxiety, before understanding which form of anxiety management should be undertaken.

Conclusion

Conscious sedation is widely recognised as a successful adjunct for treatment in dentistry for a variety of different indications. Due to the continued trends regarding illicit drugs, many patients can present as substance abusers. It is important to ascertain a detailed medical and drug history from a patient, detailing the degree of substance misuse, past and present, as well as any long-standing effects this may have had on the patient. As discussed in this paper, certain recreational drugs may have adverse effects on different sedative agents. Moreover,

the systemic consequences of substance abuse must also be taken into account in order to be able to manage such a patient correctly.

Even though it can be argued that the risks associated with substance abuse and sedative agents are not well understood, it is important to appreciate the potential effects of illicit drugs when planning to use conscious sedation.

References

- Farnfield G. Conscious sedation. In The Provision of Dental Care Report of an Expert Group on Sedation for Dentistry. Commissioned by the Department of Health 2003. Available online at <https://www.rqia.org.uk/RQIA/files/bcb0650d-8660-4d5f-940f-ea3b60ecf5f6.pdf> (accessed 7 November 2019).
- Conscious Sedation in Dentistry Dental Clinical Guidance. 2017. Available online at <http://www.sdcep.org.uk/wp-content/uploads/2018/07/SDCEP-Conscious-Sedation-Guidance.pdf> (accessed 7 November 2019).
- Haridas R P. Horace Wells' demonstration of nitrous oxide in boston. *Anaesthesiology* 2013; **119**: 1014–1022.
- Hayden J. The Jorgensen Philosophy of Intravenous Sedation. Available online at <http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC2516413&blobtype=pdf> (accessed 9 February 2019).
- NHS Digital. Adult Dental Health Survey. Available online at <http://content.digital.nhs.uk/article/3894/Adult-DentalHealth-Survey> (accessed 14 January 2019).
- Yoshida H, Ayuse T, Ishizaka S, Ishitobi S, Nogami T, Oi K. Management of exaggerated gag reflex using intravenous sedation in prosthodontic treatment. *Tohoku J Exp Med* 2007; **212**: 373–378.
- Conscious sedation. Available online at http://www.baos.org.uk/resources/BDAGuidanceconscious_sedation_-_nov_11.pdf (accessed 12 January 2018).
- Mennini T, Caccia S, Garattini S. Mechanism of action of anxiolytic drugs. In *Progress in drug research/Fortschritte der Arzneimittelforschung/Progrès des recherches pharmaceutiques*. pp 315–347. Basel: Birkhäuser Basel, 1987.
- Klockgether-Radke A P, Pawlowski P, Neumann P, Hellige G. Mechanisms involved in the relaxing effect of midazolam on coronary arteries. *Eur J Anaesthesiol* 2018; **22**: 135–139.
- Nadin G, Coulthard P. Memory and midazolam conscious sedation. *Br Dent J* 1997; **183**: 399–407.
- World Health Organisation. Substance abuse. WHO 2017. Available online at http://www.who.int/topics/substance_abuse/en/ (accessed 24 January 2018).
- Recreational drug definition and meaning. Collins English Dictionary. Available online at <https://www.collinsdictionary.com/dictionary/english/recreational-drug> (accessed 14 January 2019).
- Statistics on Drugs Misuse: England, 2017 – NHS Digital. 2017. Available online at <http://digital.nhs.uk/catalogue/PUB23442> (accessed 12 January 2019).
- Ho. 2017 Drug Strategy. Available online at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/628148/Drug_strategy_2017.PDF (accessed 12 January 2019).
- World Drug Report 2016. Available online at <http://www.unodc.org/wdr2016/> (accessed 9 March 2019).
- Versteeg P, Slot D, Van Der Velden U *et al.* Effect of cannabis usage on the oral environment: a review. *Int J Dent Hyg* 2008; **6**: 315–320.
- Joshi S, Ashley M. Cannabis: A joint problem for patients and the dental profession. *Br Dent J* 2016; **220**: 597–601.
- Drug Misuse: Findings from the 2014/15 Crime Survey for England and Wales Second edition. 2015. Available online at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/462885/drug-misuse-1415.pdf (accessed 12 Jan 2019).
- Choices N. Alcohol units – Live Well – NHS Choices. Available online at <https://www.nhs.uk/Livewell/alcohol/Pages/alcohol-units.aspx> (accessed 12 January 2019).
- NHS Digital (Great Britain). *Statistics on alcohol: England, 2017*. Available online at <https://www.gov.uk/government/statistics/statistics-on-alcohol-england-2017> (accessed 12 January 2018).
- Cruz-Pamplona M, Margaix-Muñoz M, Sarrión-Pérez M G. Dental considerations in patients with liver disease. *J Clin Exp Dent* 2011; **3**: 127–134.
- FRANK. Honest information about drugs. Available online at <https://www.talktofrank.com/> (accessed 8 July 2019).
- Patel R, Clayton S, Quintero E, Gill J. Chronic opioid users are more difficult to sedate than alcoholics and controls. *South Med J* 2015; **108**: 744–747.
- Coulthard P. The indicator of sedation need (IOSN). *Dent Update*; **40**: 466–468, 470–471.
- Greenwood M, Meechan J G. General medicine and surgery for dental practitioners Part 5: Liver disease. *Br Dent J* 2003; **195**: 71–73.
- Lu D P, Lu G P, Hersh E V. Augmenting sedation with hypnosis in drug-dependent patients. *Anesth Prog* 1995; **42**: 139–143.
- Flisberg P, Paech M, Shah T, Ledowski T, Kurowski I, Parsons R. Induction dose of propofol in patients using cannabis. *Eur J Anaesthesiol* 2009; **26**: 192–195.
- Hernandez M, Birnbach D J, Van Zundert AA, to Professor AAJ van Zundert C. Anaesthetic management of the illicit substance using patient. *Curr Opin Anaesthesiol Curr Opin Anaesthesiol* 2005; **18**. Available online at <https://pdfs.semanticscholar.org/8e60/770e0556ac3d2bd385823127a7d80b99346b.pdf> (accessed 7 November 2019).
- Ashton C H. Adverse effects of cannabis and cannabinoids. *Br J Anaesth* 1999; **83**: 637–649.
- Kuczowski K. Marijuana in pregnancy. Available online at <https://pdfs.semanticscholar.org/cb57/83436af1ba9bb9514cb3ae19368d6ced3991.pdf> (accessed 17 January 2019).
- Dickerson S J, Flint B. Cannabis and its effect on anaesthesia. Available online at <https://pdfs.semanticscholar.org/da3e/6bf11bcca7530c9a1d88f3a932627d4938c.pdf> (accessed 26 June 2019).
- Public Health Profiles. Liver disease. Available online at <https://fingertips.phe.org.uk/profile/liver-disease/data#page/0/gid/8000063/pat/6/par/E12000004/ati/102/are/E06000015/iid/90861/age/163/sex/4> (accessed 17 January 2019).
- Grotenhermen F. Die Wirkungen von Cannabis und THC. *Complement Med Res* 1999; **6**: 7–11.
- Milosevic A, Agrawal N, Redfearn P, Mair L. The occurrence of toothwear in users of Ecstasy (3, 4-methylenedioxyamphetamine). *Community Dent Oral Epidemiol* 1999; **27**: 283–287.
- Chapple I L C, Mealey B L, Van Dyke T E *et al.* Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Clin Periodontol* 2018; **45**: S68–S77.
- Nozad-Mojaver Y, Mirzaee M, Jafarzadeh A. Synergistic effects of cigarette smoke and saliva. *Med Oral Patol Oral Cir Bucal* 2009; **14**: E217–E221. Available online at <http://www.medicinaoral.com/medoralfree01/v14i5/medoralv14i5p217.pdf> (accessed 28 May 2019).
- Robinson P G, Acquah S, Gibson B. Drug users: oral health-related attitudes and behaviours. *Br Dent J* 2005; **198**: 219–224.
- Bullock K. Dental care of patients with substance abuse. *Dent Clin North Am* 1999; **43**: 513–526.
- Newton T, Asimakopoulou K, Daly B, Scambler S, Scott S. The management of dental anxiety: time for a sense of proportion? *Br Dent J* 2012; **213**: 271–274. DOI: 10.1038/sj.bdj.2012.830.
- Appukkuttan D P. Strategies to manage patients with dental anxiety and dental phobia: literature review. *Clin Cosmet Investig Dent* 2016; **8**: 35.
- Atzori B, Lauro Grotto R, Giugni A, Calabrò M, Alhalabi W, Hoffman H G. Virtual reality analgesia for paediatric dental patients. *Front Psychol* 2018; **9**: 2265.
- Pickrell J E, Heima M, Weinstein P *et al.* Using memory restructuring strategy to enhance dental behaviour. *Int J Paediatr Dent* 2007; **17**: 439–448.