Innovations in Pharmaceuticals and Pharmacotherapy

www.innpharmacotherapy.com

eISSN: 2321–323X

Review article

A comprehensive review on antipsychotics in dentistry

Preeti Nair[1], Nisheeth Saawarn[2], Pearl Helena Chand[3]*, Sahil Kohli[4], Pulkit Sharma[5]

[1]Professor and Head, Department of Oral Medicine and Radiology, People's College of Dental Sciences, Bhopal, India.
[2]Reader, Department of Oral Medicine and Radiology, People's College of Dental Sciences, Bhopal, India.
[3]Post Graduate Student, Department of Oral Medicine and Radiology, People's College of Dental Sciences, Bhopal, India.
[4]Post Graduate Student, Department of Oral Medicine and Radiology, People's College of Dental Sciences, Bhopal, India.
[5]Post Graduate Student, Department of Oral and Maxillofacial, People's College of Dental Sciences, Bhopal, India.

Abstract

Psychiatric disorders are not uncommon; almost 10% of the population worldwide is affected. They are characterized by disorganized thought process, bizarre behavior and emotional reactions, these individuals may experience delirium, hallucinations, confusion and may interpret the surrounding events differently. Overall prevalence rate of psychic disorders in India vary from 9.5 to 370 per 1000 population. A variety of psychotropic drugs combined with psychotherapy, cognitive behavioral therapy and family support help to cope with this illness. Antipsychotics are categorized as first generation (conventional or typical) and second (atypical) generation antipsychotics. Though they are safe and have high therapeutic index, they all come with wide ranging side effects i.e. sedation, postural hypotension, extrapyramidal signs (dystonia, tardive dyskinesia), disturbed metabolism, agranulocytosis, thrombocytopenia, dyslipidemia and prolactin levels. They also lead to oral manifestations such as dry mouth, increase in cavities, sialorrhea, taste abnormalities (dysgeusia, ageusia). The drugs which are routinely prescribed by an oral physician such as NSAIDs, erythromycin and tramadol may possibly interact with antipsychotics reducing their efficacies. Over the last few decades there has been a tremendous increase in the use of antipsychotics; consequently negative impact on oral health has been increasing. Tact and skill in diagnosis of mental illnesses/use of antipsychotics is essential due to social stigma associated with these disorders. Prejudicial attitude in health care workers is another hindrance which must be overcome. Hence dental health care worker should have an assiduous approach while dealing with these patients so as to reduce morbidity or life threatening circumstances.

Keywords: Antipsychotic agents, adverse effects, classification, dental treatment.

***Corresponding author: Pearl Helena Chand,** Post Graduate Student, Department of Oral Medicine and Radiology, People's College of Dental Sciences, Bhopal, India. pearl.chand99@gmail.com

1. Introduction

Mental disorders affect about 10% of the population, out of which one percent are detected with severe illness [1]. According to the community based epidemiologic studies, the overall prevalence rate of psychiatric disorders in India vary from 9.5 to 370 per 1000 population. The prevalence rate is disproportionately low as compared to the international data. This may probably be due to a combination of reasons like lifestyle, good family

support, culture, happy and comfortable environment [2]. Visiting a psychiatrist and undergoing psychiatric counseling and treatment is erroneously considered as a social stigma due to lack of awareness and adequate facilities.

Psychosis is defined as a severe mental disorder characterized by disorganized thought process, weird behavior and inappropriate emotional reactions. These individual may also experience delirium, hallucinations, confusion or paranoid delusions resulting in interpretation of events differently, incapability of doing routine work and loss of communication with other people [3]. Psychosis may affect an individual's life in various ways. It has been witnessed that though all psychiatrically ill patients may not perceive it as distressful; some feel anguished, experiencing a significant impact in their routine lifestyle. They may feel alone, neglected, frustrated, depressed, confused or stressed.

A variety of psychotropic drugs combined with psychotherapy, cognitive behavioral therapy and family support help cope with this illness. Antipsychotic agents are useful and remain the cornerstone in the management of psychosis [1]. These help in alleviating disordered beliefs or thoughts, hallucinations and confusions, thus making these patients more acceptable to the society [3]. Like all other drugs, antipsychotics too come with their own set of shortcomings and adverse effects and hence the risk versus benefit should become the dictum for their usage [4, 5].

The various co-morbidities experienced by patients taking psychotropic drugs are orthostatic hypotension, weight gain, diabetes mellitus or low bone densities; which are of higher concern as compared to oro-dental problems [6]. Fatigue, lethargy and lack of motor control experienced by these persons can further impair good oral hygiene practice. Thus mentally sick patients are more susceptible to poor oral health because of negligence, stigma and fear [7, 8, 9]. Dental or oral health is an intrinsic part of overall health of an individual and enhances the quality of life and the morale of individual, not only by better aesthetics, but also by improving overall digestive efficiency [6, 9]. Oro-facial complications manifested in the individuals under psychiatric treatment can pose a challenge on the dental chair [6]. Till date not much has been debated on dental status of these patients or of problems associated with psychotropic drugs. This paper attempts to comprehensively describe the challenges faced by an oral physician while dealing with individuals under antipsychotic treatment.

To undertake this review an extensive Pubmed and Google search on terms/papers using words "Antipsychotics" or "Psychotropic drugs", "Dental considerations", "Mental disorders" was done. Conclusions of studies especially after 1990 were included and text books were also consulted.

How do antipsychotics work?

Antipsychotic medications are classified under two different categories: *Typical* or *First Generation Antipsychotics* and *Atypical* or *Second Generation Antipsychotics* [1, 4, 5].

Typical or *First Generation Antipsychotics,* also called as *Conventional* or *Neuroleptic Antipsychotics* are phenothiazine derivatives and were introduced in 1950s [1,10,12]. These include drugs like Chlorpromazine, Thioridazine, Perphenazine, Fluphenazine, Haloperidol etc which are prescribed till date. [4] They work by blocking Dopamine D2 receptors and their potency depends on capacity to bind to D2 receptor and may be classified as *"high-potency"* and *"low-potency"* [4, 11].

Atypical antipsychotics were introduced in 1989 and they are so called as they produce fewer extrapyramidal symptoms [4]. Clozapine, aripripazole, quetiapine, olanzapine, risperidone are a few examples; the latter three were approved in the U.S. in 1994 [12]. These are weak D2-recptor blockers as compared to the first generation drugs, but have extra 5-HT_2 or serotonin, alpha adrenergic, H_1 blocking property with relative selectivity for D4 dopaminergic receptors and are hence termed as *"serotonin-dopamine antagonists"* while the typical antipsychotics are termed as *"dopamine antagonist"* [1, 11, 12] [Table No: 1].

What are the general adverse effects?

Even though antipsychotics are usually safe drugs with high therapeutic index, [14] they may show one or more adverse effects as discussed below:

Central Nervous System: Patient may experience mental confusion, lethargy or drowsiness and it is not dose-related [11]. Low potency typical and clozapine are usually more sedative when compared to other antipsychotics [4].

Table1. List of first and second generation antipsychotic drugs

First generation or Typical Antipsychotics	Second generation or Atypical Antipsychotics
• Chlorpromazine	• Aripiprazole
• Thioridazine	• Clozapine
• Perphenazine	• Olanzapine
• Fluphenazine	• Quetiapine
• Haloperidol	• Risperidone
• Thiothixene	• Ziprasidone
• Trifluoperazine	• Paliperidone

α Adrenergic Blockade: Orthostatic hypotension and palpitation is common with low potency conventional agents and clozapine depending on the level of adrenoreceptor antagonism [4]. Caution should be exercised as the patient may experience giddiness or fall due to exaggerated venous pooling by inhibiting the reflex vasoconstriction.

Anticholinergic effects: The blockage of acetycholine action in CNS results in xerostomia, constipation, blurred vision and urinary retention in males. These effects are usually associated with clozapine and low potency first generation drugs [4, 13].

Extrapyramidal signs: These effects are seen with the usage of typical antipsychotics and are due to dopaminergic bloakade in the basal ganglia [11]. These may manifest as:

a) *Dystonia*: involves unusual spasm of linguo-facial muscles resulting in torticollis (neck), retrocollis, oculogyric crisis (eye) and grimacing. It may develop within few hours or during the first three days of therapy. It may result in locked mandible either in open or closed position with protruded tongue and may also cause airway obstruction due to laryngospasm [4, 11- 13].

b) *Akathisia*: It is manifested as feeling of discomfort or restlessness, inability to sit in one place, fidgety behaviour and agitation, occurring within 1-8 weeks of antipsychotic therapy [12, 13].

c) *Tardive dyskinesia*: It is a neurological syndrome that appears late with the usage of these drugs [14]. It has been reported in about 25% of the patients, within seven years of therapy. This manifests as involuntary movements that are either choreatic or slow like puffing of cheek, smacking of lip, tongue protrusion. It would be a robust task for a dental care worker to efficiently perform dental treatment procedures in these patients [12, 13, 15].

d) *Pseudoparkinsonism*: It means Parkinson's- like symptoms like tremor, rigidity of extremities, mask-like facies, drooling of saliva, stiff gait which usually develop within 2-3 months of drug therapy [12, 13]. Perioral tremors is a rarity that occurs after a few years of therapy referred to as "Rabbit Syndrome"[11]. It is a rhythmic motion of the lips similar to the chewing movements of a rabbit. Clinician may misdiagnose patients with *rabbit syndrome* as tardive dyskinesia that involves involuntary tongue movements. The striking feature of this syndrome is the stereotyped involuntary movement of the buccal mucosa without involving tongue movements [1].

Neuroleptic malignant syndrome: It is a rare, severe form of Parkinsonism. It is an idiosyncratic reaction which manifests as crude tremors, catatonia which fluctuates in intensity, autonomic instability (increase in body temperature, blood pressure, labile pulse, unstable sweating) and elevated level of creatinine kinase, white blood cells and occasionally causes myoglobinemia [1, 14]

Metabolic effects: Psychiatric medications can increase the metabolic risk in the patients. Weight gain or obesity due to increased deposition of fat is one of the major side effects and is not dose dependant. Physical inactivity and unhealthy eating may act as catalysts [1]. Weight gain is highest with clozapine and olanzapine and minimal with other antipsychotics [17].There is also impaired glucose control which results in mild resistance to insulin and type 2 diabetes mellitus- like condition. Caucasians are more likely to develop diabetes [18]. Individuals under antipsychotics are at five times higher risk to develop hyperlipidaemia due to increased triglyceride levels than normal individuals and it is associated more frequently with low potency drugs of both generations [1]. Hence it is mandatory to advise specific laboratory tests like fasting blood glucose level, fasting lipid profile before any oral surgical procedures [4,19].

Blood Dyscrasias: Antipsychotics can alter the normal blood cell counts inducing neutropenia, agranulocytosis and thrombocytopenia. Thrombocytopenia may rarely occur with the usage of *clozapine* and *valproic acid.* Platelet adhesion and aggregation is also disturbed as these drugs alter the platelet's physiological properties by altering its membrane lipid structure. Thus, alteration in quantity and function of platelets result in altered bleeding time [20]. Clozapine sometimes causes neutropenia and agranulocytosis, resulting in increased risk of bacterial infections, albeit it occurs rarely i.e. in only 0.38% of cases [4, 10, 21]. If the neutrophil count goes below 1500 cells per mm^3 then the medication should be stopped as per the FDA guidelines [4].

Prolactin levels: Antipsychotics raise the prolactin level by blocking the normal tonic inhibition on pituitary mamotropic cells [4]. Use of typical antipsychotics and risperidone *has* been associated with "Hyperprolactinemia" [11, 22]. It may cause gynecomastia, galactorrhea, hirsutism, acne, loss of bone mineral density (osteoporosis) and infertility. These symptoms appear within a few weeks of therapy [13, 23].

Cardiac vascular system: High frequency of cardiovascular disease is a leading cause of death in these patients. Obesity, lethargy, dyslipidaemia, type 2 DM etc. are the major risk factors for cardiovascular disease in this population affecting the overall morbidity and mortality [1, 18, 19, 24]. Prolonged QT and PR interval and altered T wave in ECG is a common finding. Prolonged QT interval results in sudden death or *torsades de pointes*; incidence of which is twice in these patients [1, 4, 25, 26]. Drugs that prolong QT interval like erythromycin, clarythromycin, ketaconazole, sumatriptan must be prescribed cautiously [4, 26] (Figure 1).

What are the craniofacial manifestations of individuals taking antipsychotics?

Health and wellness of the craniofacial region is essential for overall physical appearance and health of an individual. Adverse effects of antipsychotics are not limited to only CNS dysfunction, cardiovascular abnormality or haematological disorders but ultimately affect oro-facial region too. These adverse effects involving craniofacial region are of major concern for a dental clinician too. The wide range of these side effects can be discussed as follows:

Salivary gland: Normal functioning of salivary gland depends on both sympathetic and parasympathetic innervations. Sympathetic stimulation mostly affects composition of saliva where as parasympathetic stimulation results in increased salivation. The increase in salivary flow is evoked by agonist muscarinic action i.e. on M_3 receptors. Parasympathetically, induces large volume of saliva and is not rich in protein content where as sympathetic innervations induces protein rich saliva.

"Dry mouth" or "Xerostomia" is a predominant side effect of psychotropics which is due to inhibition of

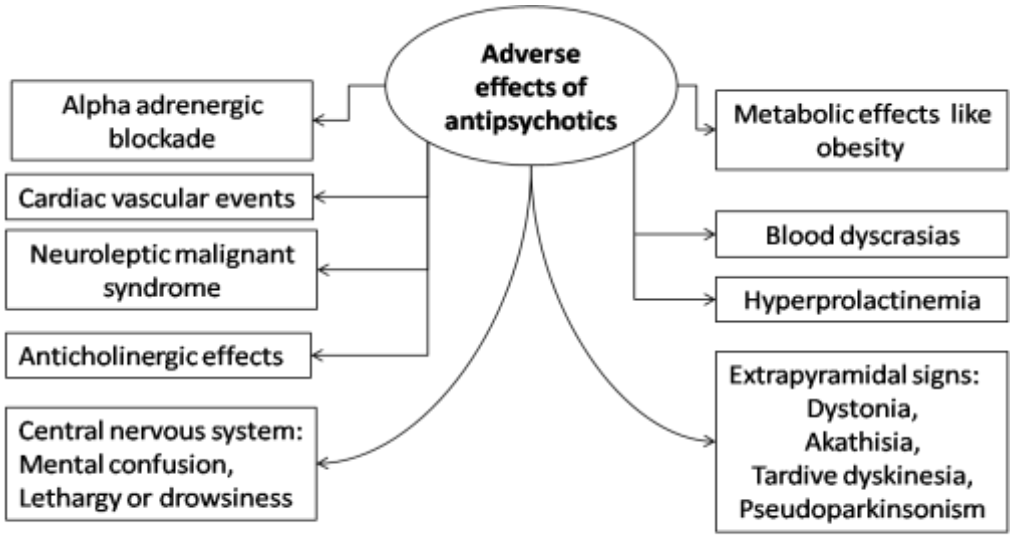

Figure No 01: General adverse effects of antipsychotics

parasympathetic stimulation. Antipsychotics not only alter the quantity of saliva but also its composition by affecting the dual (sympathetic and parasympathetic) innervations of salivary glands. Thus reduced salivary flow hampers the lubrication, buffering, digestion, antimicrobial and cleansing action and results in dental caries, difficulty in mastication, burning sensation, intolerance to hot and spicy foods, in ability to speak, cracked lips and corner of the mouth, altered taste, oral mucosal ulcerations, mucositis, gingivitis and periodontal diseases [13, 17, 27, 28].

Sialorrhea: It has been reported that antipsychotics like clozapine or haloperidol can cause increased salivation at night. Thus patients are troubled with choking sensation and aspiration of saliva during night [29-31].

Pre-clinical studies have also reported that clozapine and its chief metabolite N-desmethylclozapine decrease the flow of saliva by antagonistic actions on muscarinic M_3 receptors and α_1- adrenergic receptors. But these two drugs have an agonistic action on muscarinic M_1 receptor during sleep, maintaining a low-grade flow of saliva [32].

Sialadenitis: Salivary gland dysfunction is usually associated with siladenitis and sialorrhea. Novel antipsychotics like clozapine and clonidine may cause transient salivary gland swelling [29, 30].

Taste change: Antipsychotics may cause atrophy of tongue papillae, loss of taste acuity (hypogeusia), altered taste (dysgeusia) and sometimes even loss of taste (ageusia) [30].

Hirsutism: It is defined as excess growth of androgen dependant sexual hair (lips and chin) due to *hyperprolactinemia* [13, 33, 34]. Hirsutism is a sensitive issue especially among females taking antipsychotics. The stigmata associated with this condition may pose an additional challenge to the already existing psychological disturbance.

Skin eruptions: Acne, angioedema, urticaria, lichenoid reactions, photosensitivity are some of the reported skin eruptions with these drugs [13, 35].

Laryngeal disturbance: Detrimental extrapyramidal signs like dystonia that causes involuntary contraction of muscles along with contraction of larynx and tongue maybe a feature in users of these drugs. Laryngeal dystonia is rare and occurs coincidentally with oculogyric crisis, torticollis and retrocollis. It can be life threatening as it may obstruct the airway due to contracture of muscles. Hyperadduction or hyperabduction of vocal cords results in forced, slurred and strangled voice [13, 36].

Hair loss: Antipsychotics induce reversible hair loss which is usually localized but sometimes may also be generalized. It may be result in altered appearance due to hair loss from scalp and occasionally from eyebrows too [35,38]. The alopecia is usually premature and hair re-growth is seen if the medication is discontinued [13, 37].

Teeth: Maintaining good oral hygiene is an issue in mentally ill patients. These patients are more pre-occupied about their systemic problems i.e. obesity, glucose intolerance, postural hypotension etc. thus neglecting their oral health. Further, they are unable to practice better oral hygiene due to lack of motor control, lethargy, fatigue and poor motivation. They are prone to dental caries, gingivitis and periodontitis due to decreased salivation and poor oral hygiene [13].

Miscellaneous: Secondary *bruxism* is seen in patients taking antipsychotics (Quitinapine) [12] Occlusal splints have been effective in ameliorating the effects of bruxism [13, 39].

What are the challenges faced by a dental health care worker?

Diagnosing, managing/treating mentally disabled patients require skill and tact. Clinicians should have a thorough knowledge about the drugs and their associated side effects. Overcoming prejudicial attitude, assessing the cognitive status of the individual and obtaining a careful history on substance abuse would complement successful dental treatment.

The various dental considerations are as follows:

a) Patient should be advised to rise slowly from the dental chair to avoid injury as they may experience postural hypotension. Antipsychotics may potentiate the sedative and hypotensive effect of general anesthetic agent. Hence craniofacial

surgery, under GA, requires one to be cautious about its side effects to prevent morbidity as he/she may develop infection because of immunosuppresion and water intoxication due to hypersecretion of ADH [1,11].

b) Drugs used in psychiatric practice can cause increased bleeding during the surgical procedures. Certain drugs like valproic acid and clozapine can cause uncontrolled bleeding due to impaired platelet aggregation; thus it is mandatory for the clinician to evaluate the haematological values before any surgeries [30].

c) Neutropenia and agranulocytosis make these patients more prone to fatal bacterial infections.

d) Involuntary oro- facial movement or muscle contracture in these patients may precipitate trauma during dental instrumentation (micro motor, sharp instruments); extreme caution must be exercised.

e) Isolation in patients with *sialorrhea* may be a cumbersome task.

f) Diminished salivary flow leads to dental caries, oral mucosal ulcerations, gingivitis, periodontitis, candidal infections and also interferes with proper retention of dentures..

g) Prescribing drugs: NSAIDS and antibiotics (metranidazole, erythromycin) are an integral part of management in dentistry; pharmacokinetic interactions warrant caution in their usage in patients on antipsychotics.

- Administration of *NSAIDS* or *metranidazole* in those taking *lithium* may result in lithium toxicity due to its increased lithium concentration in the plasma and decreased excretion [40-42].
- *Tramadol* along with antipsychotics may cause elations, hallucinations, altered mood, sleep disturbances, nightmares etc. Administration of *carbamazipine* might reduce the efficacy of *tramadol* because of its increased metabolism [1].
- *Erythromycin* when co- administered with valproate or carbamazipine, may result in their toxicity due to the increased serum level of *valproic acid* and *carbamazipine* [3].

Conclusion

Nearly 20% of the adult population in India suffers from psychiatric disorder. Over the last few decades there has been a tremendous increase in the use of antipsychotics; consequently negative impact on oral health has been increasing. Multicentric studies assessing use of psychotropic drugs in dental patients and sharing these challenges with one another emboldens oral health care workers. Thorough knowledge on polypharmacy, accompanied by good patient compliance is a prudent approach in these patients. This would be handy in not only preventing litigations but also providing satisfactory dental care in them.

References

1. Bromhead H & Feeney A. (2010) Anaesthesia and Psychiatric drugs –part Mood stabilisers and antipsychotics. *Anaesthesia Tutorial of The Week,* (175), 1-6.
2. Math S.B & Srinivasaraju R. (2010) Indian Psychiatric epidemiological studies: Learning from the past. *Indian Journal Psychiatry*, 52(1), 95-103.
3. Abrams, Anne C & Goldsmith T L. 1998. Clinical Drug Therapy: Rationales for Nursing Practice. Philadelphia: Lippincott.
4. Munech J & Hamer Ann.M. (2010). Adverse Effects of Antipsychotic Medications *American Family Physician*, 81(5), 617-622.
5. Scarff J R and Casey D (2011). A. Newer Oral Atypical Antipsychotic Agents: A Review. P T, 36(12):832-838.
6. Tani et al. (2012). Dental conditions in inpatients with schizophrenia: A large-scale multi-site survey. *BMC Oral Health*, 12, 32.
7. Grewal H, Sharma H, Rajpal, Bhatia M.S. & Choudhary R (2014). Oral Health of Non-Institutionalized psychiatric patients: A Dentist Perception. *Delhi Psychiatry Journal*, 17 (1), 44-47.
8. Jyoti B, Muneeshwar P D, Srivastava R, Singh A R, Kiran M & Simlai J (2012). Oral Health Status and Treatment Needs of Psychiatric Inpatients in Ranchi, India. Journal of *Indian Academy of Oral Medicine and Radiol0gy,* 24(3), 177-181.
9. Dangore-Khasbage S, Khairkar PH, Degwekar SS, Bhowate RR, Bhake AS, Singh A & Lohe VK (2012). Prevalence of oral mucosal disorders in institutionalized and non- institutionalized psychiatric patients: a study from AVBR Hospital in central India. *Journal of Oral Science*, 54(1), 85-91.
10. Haddad PM & Sharma SG (2007). Adverse effects of atypical atipsychotics: diiferential risk and clinical implications. *CNS Drugs*, 21(11), 911-936.
11. Tripathi K.D. 2005 Essentials of Medical Pharmacology (4th ed). New Delhi: Jaypee Brothers Medical Publishers.
12. Friedlander AH & Marder SR (2002). The psychopathology, medical management and dental implications of schizophrenia. *Journal of the American Dental Association*, 133(5), 603-610.
13. Seeman MV (2011). Antipsychotics and physical attractiveness. *Clinical Shizophrenia & Related Psychoses*, 5(3), 142-146.

14. Hardman JG, Limbird LE & Gilman AG, (Eds) (2001). Goodman & Gilman's The Pharmacological Basis of Therapeutics, 10th Edition. New York: McGraw-Hill.
15. Kasantikul D &Kanchanatawan B (2007). Antipsychotic-induced tardive movement disorders: a series of twelve cases. *Journal of the Medical Association of Thailand*, 90(1), 188-194.
16. Schwartz M & Hocherman S (2004). Antipsychotic induced rabbit syndrome: epidemiology, management and pathophysiology. *CNS Drugs*, 18(4), 213-220.
17. DE Hert M, Correll CU, Bobes J, Cetkovich-Bakmas M, Cohen D, Asai I, Detraux J, Gautam S, Möller HJ, Ndetei DM, Newcomer JW, Uwakwe R & Leucht S (2011). Physical illness in patients with severe mental disorders I. Prevalence, impact of medications and disparities in health care. *World Psychiatry*, 10, 52-77
18. Lambert T (2011). Managing the metabolic adverse effects of antipsychotic drugs in patients with psychosis. *Australian Prescriber*, 34, 97–99.
19. Newcomer J W & Haupt D W (2006). The Metabolic Effects of Antipsychotic Medications. *Canadian Journal of Psychiatry*, 51(8), 480-491.
20. Semiz M, Yücel H, & Kavakçı Ö (2013). Atypical antipsychotic use is an independent predictor for the increased mean platelet volume in patients with schizophrenia: A preliminary study. *Journal of Research in Medical Sciences*, 18(7), 561-566.
21. Velayudhan R & Kakkan S (2014). Late Onset Clozapine Induced Agranulocytosis. *Indian Journal of Psychological Medicine*, 36(4), 425-427.
22. Bostwick JR, Guthrie SK & Ellingrod VL (2009). Antipsychotic-induced hyperprolactinemia. *Pharmacotherapy*, 29(1), 64-73.
23. Wieck A & Haddad PM (2003). Antipsychotic induced hyperprolactinaemia in women:pathophysiology, severity and consequence. *British Journal of Psychiatry*, 182, 199-204.
24. Newcomer JW (2007). Antipsychotic medications: metabolic and cardiovascular risk. *Journal of Clinical Psychiatry*, 68 (4), 8-13.
25. Roden DM (2004). Drug-induced prolongation of the QT interval. *The New England Journal of Medicine*, 350(10), 1013-1022.
26. Letsas KP, Efremidis M, Filippatos GS & Sideris AM **(**2007). Drug-induced long QT syndrome. *The Hellenic Journal of Cardiology*, 48(5), 296-299.
27. Swager LWM & Morgan SK (2011). Psychotropic-induced dry mouth: Don't overlook this potentially serious side effect. *Current Psychiatry*, 10(12), 54.
28. Ameida P, Johann A, Alanis L , Lima A & Grégio A (2012). Antidepressants: Side Effects in the Mouth. *Oral Health Care - Pediatric, Research, Epidemiology and Clinical Practices.* In Tech, 113-128.
29. Scully C., Bagan J V (2004). Adverse Drug Reactions In The Orofacial Region. *Critical Reviews in Oral Biology and Medicine,* 15(4), 221-240.
30. Venkataraman BK, Iyengar AR, Ganapathy KS, Mohan CV, & Nagesh KS (2013). Diagnostic Oral Medicine. New Delhi: Wolters Kluwer Health.
31. Chi L Y & Chu K Y. Oral Health of People with Psychiatric Disorders (2012). *Oral Health Care - Prosthodontics, Periodontology, Biology, Research and Systemic Conditions. In Tech*, 287-298.
32. Ekström J, Khosravani N, Castagnola M & Messana I (2012). Saliva and the control of its secretion. *Dysphagia*. *Berlin: Springer*, 19–47
33. Patel A, Malek N, Haq F, Turnbow L & Raza S (2013). Hirsutism in a Female Adolescent Induced by Long-Acting Injectable Risperidone: A Case Report. *Primary Care Companion for CNS Disorders*, 15(3), PCC.12l01454.
34. Bergemann N, Mundt C, Parzer P, Jannakos I, Nagl I & Salbach B (2005). Plasma concentrations of estradiol in women suffering from schizophrenia treated with conventional versus atypical antipsychotics. *Schizophrenia Research*,73(2-3), 357-366
35. Fernández-Torres R, Almagro M, del Pozo J, Robles O, Martínez-González C, Mazaira M & Fonseca E (2008). Lichenoid drug eruption induced by olanzapine. Actas *Dermosifiliografacias*, 99(3), 221-224.
36. Miodownik C, Lerner V & Witztum E (2011). Pisa Syndrome and Laryngeal Dystonia Induced by Novel Antipsychotics. *The Israel Journal of Psychiatry and Related Sciences*, 48 (3), 195-200.
37. Mermi O, Atmaca M, Kilic F, Gurok MG & Kuloglu M (2014). Fluoxetine Induced Hair Loss: A Case Report. Dusunen Adam: *The Journal of Psychiatry Neurological Sciences*, 27, 266-269.
38. Kuloglu M, Korkmaz S, Kilic N, Saglam S, Gurok MG & Atmaca M (2012). Olanzapine Induced Hair Loss: A Case Report. *Bulletin of Clinical Psychopharmacology*, 22(4), 362-365
39. Page M & Somerville-Brown L M (2007). Psychotropic drugs and dentistry. *Australian Prescriber*, 30, 98–101.
40. Becker DE (2008). Psychotropic Drugs: Implications for Dental Practice. *Anesthesia Progress*, 55(3), 89-99.
41. Scully C & Cawson RA (Eds) (2005). Medical Problems in Dentistry.5th ed. Edinburgh; Oxford: Elsevier Churchill Livingstone.
42. Chadwick B, Waller D G & Edwards J G (2005). Potentially hazardous drug interactions with psychotropics. *Advances in Psychiatric Treatment*, 11, 440-449.