



# Anesthesia Considerations for Cataract Surgery in Patients with Schizophrenia: A Narrative Review

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## Abstract

Schizophrenia is ranked among the top 10 global burdens of disease. About 1% of people meet the diagnostic criteria for this disorder over their lifetime. Schizophrenic patients can develop cataract, particularly related to age and medications, requiring surgery and anesthesia. Many concerning factors, including cognitive function, anxiety, behavioral issues, poor cooperation and paroxysmal movements, may lead to general anesthesia as the default method. Antipsychotic agents should be continued during the perioperative period if possible. Topical/regional anesthesia is suitable in most schizophrenic patients undergoing cataract surgery. It reduces potential drug interactions and many postoperative complications; however, appropriate patient selection is paramount to its success. General anesthesia remains the primary technique for patients who are considered unsuitable for the topical/regional technique. Early involvement of a psychiatrist in the perioperative period, especially for patients requiring general anesthesia, is beneficial but often under-utilized. This narrative review summarizes the anesthetic considerations for cataract surgery in patients with schizophrenia.

**Keywords:** Cataract, Schizophrenia, General Anesthesia, Local Anesthesia, Regional Anesthesia, Perioperative Complications

## 1. Context

Schizophrenia, with the estimated incidence of 15.2 per 100,000 population (1), is a disorder characterized by profound alterations of thought, language, perception and sense of self with impairment in social and occupational functioning (2). Up to 1% of people meet the diagnostic criteria for this illness over their lifetime (2), and it is ranked among the top 10 global burdens of disease by the World Health Organization (WHO) (3). Schizophrenic patients can develop cataract, particularly related to age and medications (4, 5), requiring surgery and anesthesia.

Schizophrenia poses many challenges to anesthesiologists, including other associated physical illnesses, hazardous behaviors, potential interactions between antipsychotic and anesthetic agents, and higher risk of postoperative complications (6, 7). General anesthesia may be the preferred option particularly for physicians with limited

experience. However, there is an increase in the incidence of morbidity and mortality associated with general anesthesia when compared with regional anesthesia. Currently, there is no published data on the prevalence of schizophrenic patients presenting for cataract surgery, nor guidelines regarding the related choice of anesthesia. We have, therefore, conducted a literature review to highlight some of the anesthetic considerations for cataract surgery in patients with schizophrenia, with a view to improve patient outcomes and safety.

## 2. Search Strategy

A literature search was conducted in October 2020 using MEDLINE (Ovid), PubMed, Embase, CINAHL, Google Scholar and Cochrane with the aim of identifying English-language articles published between January 1970 and October 2020. The search keywords used included “anesthe-

sia” in various combinations and “schizophrenia”, and relevant case reports were also included. Further related key articles were retrieved from the references of the retrieved articles. The authors examined these articles in terms of quality and relevance to anesthesia for cataract surgery in patients with schizophrenia. As a result, 50 relevant articles were included in this review.

### 3. Etiology, Pathogenesis, Types, and Symptomatology of Schizophrenia

Schizophrenia is a complex, multifactorial disorder, including genetic, neurodevelopmental (e.g., maternal pregnancy complications and birth complications) and environmental (e.g., psychosocial adversity and substance abuse) factors (3). It has many clinical presentations and individuals vary in the progression of symptoms (3). There are a number of subtypes, such as paranoid, catatonic, disorganized and undifferentiated (2), with the subtype diagnosis relating to the main presenting symptoms. The symptoms can be classified into the three main categories of positive (e.g., delusion, hallucination, disordered thought and behavior), negative (e.g., apathy, social withdrawal and blunted affect) and cognitive (e.g., impairment of attention, information processing and memory) (8).

### 4. Antipsychotic Medications

The mainstays of therapy are first and second-generation antipsychotic drugs (9). The first-generation agents (e.g., chlorpromazine, thioridazine, haloperidol, fluphenazine and prochlorperazine) exert their effect primarily on dopaminergic receptors. Second-generation agents (e.g., clozapine, quetiapine, olanzapine, risperidone, aripiprazole and lurasidone) exert their effect on many sites, including histamine, serotonin, acetylcholine, alpha-adrenergic and dopaminergic receptors. Side effects are extremely common, including blurred vision, constipation, dry mouth, urinary retention, sedation, hypotension and extrapyramidal movements (9).

### 5. Cataract Development in Patients with Schizophrenia

Ophthalmic manifestations, including cataract, maculopathy, retinopathy, strabismus and other deficits, have been reported in patients with schizophrenia (4, 10). These changes may be related to the underlying illness, antipsychotic agents or comorbidities. The presence of glaucoma and retinal disease in patients with schizophrenia are strong predictors of cataract development (11). There is

a high prevalence of smoking, diabetes mellitus, poor general health (from self-neglect) and substance abuse among this population that may also contribute to cataract formation (12). Long-term exposure to chlorpromazine (at a dose of greater than 300 mg per day) and prochlorperazine are associated with an up to 8-fold increased risk for cataract development (11). Second-generation antipsychotic agents are also independently associated with an increased risk of cataract (5). In addition, benzodiazepines, tricyclic antidepressants and monoamine oxidase inhibitors are implicated in cataract development (5, 13). The exact mechanism of antipsychotic agents in cataract formation is unclear. It has been postulated that these medications may photosensitize the eye, and in combination with ultraviolet light exposure, increase the risk of cataract formation (14).

### 6. Choice of Anesthetic Modality for Cataract Surgery

Regional anesthesia (RA) and general anesthesia (GA) are both suitable options for cataract surgery (15, 16), and there is no specific anesthetic modality for patients with schizophrenia. Regional anesthesia can be used safely if the patient is cooperative. However, GA may be an appropriate choice if there is any doubt regarding patient cooperation.

### 7. Preoperative Considerations

In addition to the usual considerations of comorbidities, type and duration of surgery, and preference of surgeon and anesthesiologist, special attention should be directed to mental state, ability to communicate, ability to understand and provide informed consent, and potential adverse interactions between antipsychotic and anesthetic agents. It is important to remember that schizophrenia is associated with increased prevalence of smoking, substance abuse, poor general health, multiple comorbidities and poor compliance (3).

### 8. Medical Comorbidities

#### 8.1. Cardiovascular Diseases

Schizophrenia is associated with a high incidence of cardiovascular diseases secondary to increased body weight, diabetes mellitus, smoking and side effects of antipsychotic drugs (7). Preoperative electrocardiograph (ECG) should be considered as antipsychotic drugs may prolong QT and PR intervals, in addition to T wave changes (7, 9). Severe QT prolongation may lead to torsade de pointes, a potential lethal arrhythmia (7, 17, 18).

### 8.2. Respiratory Diseases

The incidence of chronic obstructive lung disease (COPD) was 1.66 times higher in patients with schizophrenia than the general population (19). The increased prevalence in smoking and weight gain further reduce lung capacity and exercise tolerance (19, 20), leading to an increased risk for respiratory complications, especially after GA.

### 8.3. Metabolic Diseases

Antipsychotic agents result in weight gain, glucose intolerance and dyslipidemia (7, 20).

### 8.4. Substance Abuse

Schizophrenia is associated with a higher prevalence of substance abuse, including alcohol, cannabis and stimulants (e.g., cocaine and methamphetamine) (3, 7, 20).

### 8.5. Infectious Diseases

Patients with schizophrenia are more prone to infections such as tuberculosis (7).

## 9. Preoperative Optimization and Consent

A preoperative multidisciplinary approach, involving an ophthalmologist, an anesthetist and a psychiatrist, would be beneficial to limit adverse drug interactions and withdrawal problems. Other difficulties often encountered in these patients include lack of cooperation, poor compliance, difficulties in communication, and hazardous behaviors. Physical examination may be onerous.

It is essential to assess mental capacity of the patient, in consultation with a psychiatrist and/or the legal guardian if necessary, when obtaining informed consent. If RA is planned, the patient should be informed of the potential visual phenomena during surgery, such as lights, unusual shapes, colors, and movement, so that these would not be misinterpreted as visual hallucination.

## 10. American Society of Anesthesiologists Risk Stratification

In general, patients with affective disorders are classified as American Society of Anesthesiologists (ASA) II status. However, those at risk for psychotropic-anesthesia drug interactions may warrant ASA III status (21).

## 11. Antipsychotic Drugs in the Perioperative Period (Continue Versus Temporary Suspension)

The risks and benefits of continuing versus temporary suspension of antipsychotic medications in the perioperative period should be considered carefully. Clozapine, for instance, affects cardiac conduction and causes hypotension during anesthesia (21), which may warrant temporary suspension. However, withdrawal symptoms and rapid psychotic relapse have also been reported when clozapine was suspended (21). Preoperative psychiatric consultation may be useful in these circumstances.

Withdrawal symptoms usually appear 1 to 4 days after the suspension of medications and may persist for 7 to 14 days. Haloperidol, the treatment of choice for withdrawal symptoms, carries the risk of torsade de pointes, arrhythmias and neuroleptic malignant syndrome (NMS) (21). Antipsychotic medications should be reintroduced as soon as practical after surgery.

It is preferable and ideal to continue antipsychotics during the perioperative period, if possible, to minimize withdrawal symptoms and psychiatric relapse (21). The risks of temporary suspension of the antipsychotic medications may outweigh the benefits, especially in short-term, RA-based cataract surgery with no anticipated complexity.

## 12. General Anesthesia

Many schizophrenia patients suffer from significant anxiety and may not cooperate with instructions or remain still. Sudden unexpected movements during surgery may lead to sight-threatening complications (22). General anesthesia remains the technique of choice when patient cooperation is in doubt. The airway can be secured with either an endotracheal tube or supraglottic airway devices (23). All intravenous induction agents, except ketamine (side effects include raised intraocular pressure, postoperative hallucinations and delirium), can be used safely (24, 25). All volatile agents are safe. However, enflurane, an older agent, carries a higher risk for hypotension, arrhythmia and seizure (26, 27). Anesthesia can be maintained with either volatile agents or total intravenous techniques (15). One study on schizophrenic patients presenting for orthopedic procedures, however, has shown that psychosis emergence or confusion in the first 48 hours after surgery was significantly higher in patients receiving GA with propofol, fentanyl and sevoflurane (54%), when compared with propofol and fentanyl (30%) (28).

### 13. Intraoperative Problems and Management

Special attention should be directed to the potential adverse interactions between antipsychotic and anesthetic agents. Antipsychotic medications may increase heart rate (29). Hypotension is common, especially during and after the induction of anesthesia and in patients treated with chlorpromazine (7, 30). Other risk factors for intraoperative hypotension include advanced age, increased sensitivity to volatile anesthesia and direct influences on the renin-angiotensin system (7). Therefore, anesthetics should be carefully titrated to individual response. Antipsychotic agents also potentiate the effects of opioid analgesia (7).

Ondansetron can prolong QT interval, while metoclopramide can have extra-pyramidal side effects (26, 31). These antiemetic agents should be administered with caution in schizophrenic patients as they may potentiate certain side effects of antipsychotic medications. Schizophrenic patients are prone to hypothermia secondary to impaired thermal regulation (dopaminergic blockade at the hypothalamus) (9, 32). However, most cataract operations are of short duration. Intraoperative temperature monitoring and external warming devices should be considered if complex or prolonged surgery is anticipated.

There has been a report of borderline association between the antipsychotic agent (quetiapine) and intraoperative floppy iris syndrome, in line with its antagonistic action on alpha-adrenergic receptors (33). Intracameral adrenaline and phenylephrine, often used to reduce iris floppiness (34), may cause hypertension, especially in patients taking monoamine oxidase inhibitor or tricyclic antidepressant (35).

Neuroleptic malignant syndrome, with the prevalence of 0.02% to 2.4% in patients taking antipsychotic medications, is characterized by hyperthermia, muscle rigidity and autonomic instability (7, 36), and it carries up to 20% mortality (9). Treatment includes dantrolene and supportive measures (9). It may be difficult to differentiate the cause between neuroleptic malignant syndrome and malignant hyperthermia in the early phase as both conditions share similar clinical presentations.

Long-term antipsychotic therapy may cause abnormalities of hypothalamic-pituitary-adrenal axis and autonomic nerve dysfunction (37), with diminished stress response to anesthesia and surgery (7). Chronic administration of antipsychotic can cause water intoxication secondary to the secretion of vasopressin, aldosterone and atrial natriuretic peptide (9, 36). Although the routine short-duration cataract surgery is unlikely to create a significant stress response, these potential changes should

be considered during prolonged surgery (e.g., matured cataract because of long-term health neglect, difficult and complex surgery).

Simple analgesia with paracetamol is usually sufficient as cataract surgery is associated with minimal postoperative pain (38). Perioperative analgesia with opioids and non-steroidal anti-inflammatory agents is uncommon. Concomitant administration of tramadol and antipsychotic agents may precipitate seizure or serotonin syndrome (9).

### 14. Postoperative Considerations

Schizophrenic patients suffered from significantly higher postoperative complications with the 30-day mortality risk nearly threefold, in all types of surgery including eye, when compared with patients without mental disorders (6). They have, for instance, an increased incidence of silent myocardial infarct (7). The exact reason is unclear and is most likely multifactorial (6). Poor communication and ambiguous complaints may delay the recognition of complications. Poor nutrition, self-neglect and substance abuse may further contribute to a higher incidence of adverse events. Molnar and Fava have suggested that surgical stress worsens psychotic symptoms (39). Postoperative confusion is significantly higher in schizophrenic patients and is likely related to the hypersecretion of cortisol, adrenaline and noradrenaline (40, 41). Other postoperative problems have been reported in patients with schizophrenia undergoing non-ophthalmic surgery, including (I) paralytic ileus after major surgery (7, 30), (II) pain as a risk factor for postoperative confusion (26), (III) impaired lung function, COPD and chronic bronchitis resulting in increased risk for postoperative pneumonia (42), and (IV) sudden death secondary to cardiac arrhythmias, which is five times more common in schizophrenic patients (43). We were unable to find any published reports to support that these postoperative complications also occur following GA in schizophrenic patients undergoing cataract surgery.

### 15. Regional Anesthesia

Regional ophthalmic anesthesia, including needle-based blocks, sub-Tenon's block and topical anesthesia, offers a safe alternative to GA in patients on antipsychotic medications because it avoids the need for airway manipulation, minimizes cardiovascular and other systemic adverse effects, reduces postoperative nausea and vomiting and facilitates early ambulation. Other advantages of regional anesthesia (RA) include improved alertness,

reduced recovery time, reduced postoperative confusion and reduced adverse interactions between antipsychotic and anesthetic agents.

However, other influencing factors, such as anxiety, poor cooperation and potential intraoperative patient movement, should be addressed when selecting RA. Patient's comfort during surgery can be further improved with verbal reassurance, hand holding, adjustments in operating table position and limb padding to minimize movement. Tenting of drapes over the patient and oxygen delivery via nasal cannula also reduce carbon dioxide retention and claustrophobia. Appropriate patient selection is paramount to the success of RA.

An ophthalmic block is considered superior to topical anesthesia if surgical complexity (e.g., matured cataract or intraoperative floppy iris syndrome) is anticipated. Adrenaline-containing local anesthetic agent may cause acute hypertensive crises (as explained before). However, this is not commonly encountered as adrenaline is generally avoided during an ophthalmic block because it may induce ocular ischemia (44).

## 16. Sedation with Local/Regional Anesthesia

Monitored anesthesia care during cataract surgery should be performed under the supervision of an anesthesiologist as recommended by The Royal College of Anesthesiologists and The Royal College of Ophthalmologists, United Kingdom (45). Intravenous sedation should be titrated carefully to its desirable effects. Midazolam and propofol are the commonly used agents, while a short acting opioid (e.g., alfentanil and fentanyl) is sometimes added to supplement analgesia (46). The Ramsay sedation score may be useful to assess their clinical effects (47).

Postoperative delirium is a vexing problem in patients with schizophrenia. Dexmedetomidine may be useful as it is associated with less postoperative delirium (3%) than propofol (50%) or midazolam (50%) (48, 49). Additional advantages of dexmedetomidine include preserved respiratory mechanics, lowered intraocular pressure and analgesia (48). Although the combination of dexmedetomidine and peribulbar block has been reported as advantageous in a 20-year-old patient with schizophrenia undergoing strabismus surgery (50), we are not aware of its specific use for cataract surgery of schizophrenic patients.

In an unpublished institutional audit (Miami, USA), there were 103 schizophrenic patients presenting for cataract surgery over a 4-year period. General anesthesia was administered to 7% of the cases while local anesthesia was administered to the remainder (topical anesthesia to regional anesthesia ratio was 2:1). Similar clinical experi-

ences were shared by other co-authors from their respective institutions (Australia, India, Iran and Singapore).

## 17. Conclusions

To date, published studies have not addressed the issue of optimal anesthetic techniques for cataract surgery in patients with schizophrenia. It is important to raise the awareness of anesthesiologists and surgeons regarding the potential problems associated with schizophrenic patients undergoing cataract surgery. There is an urgent need for further research in this area.

The choice of anesthetic technique depends on many factors, including cognitive function, cooperation of the patient, surgical complexity and duration, as well as physician preference. A careful preoperative evaluation should facilitate the selection of appropriate patients for different anesthetic modalities. Antipsychotic agents should be continued during the perioperative period, if possible. Many of these patients can have their cataract surgery performed safely under RA, which reduces the risks of potential drug interactions and many postoperative complications. General anesthesia remains the option for those patients considered unsuitable for RA. Early involvement of a psychiatrist in the perioperative period, especially for patients requiring general anesthesia, is beneficial but often underutilized.

## Footnotes

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