



An Interesting Case: Timolol, Drug Complication in the Form of Major Depressive Disorder with Psychotic Features

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Abstract

Investigating the side effects of timolol eye drops in glaucoma patients is not a new issue, but it has been discussed for years, especially the psychological side effects of this drug on patients have been a proven issue. The case that I am reporting was a patient who had no psychological problems at all until the age of 62, and all the issues, he was free of open-angle glaucoma after one year of starting treatment with timolol drops. But despite the fact that he has undergone glaucoma surgery for two years and his disease has improved, so that he does not use any medication for glaucoma anymore, the question is why the patient's depression does not improve and he continues to go up and down. I am faced with zigzagging his clinical condition and the patient is still being treated with antipsychotic drugs and this question is still unanswered?

Keywords: Glaucoma; Side Effects; Timolol; Psychological Problems

Introduction

When I noticed in 2022 that one of my old patients had symptoms such as depression and isolation, it was very hard for me to believe that I have worked in this field for more than four decades and have known this patient for more than thirty years. But when I talked with his family and talked with the patient himself about the emergence of his new problems, which was the first that the patient was facing, I finally accepted that he also suffered from depression. The patient is basically educated, high level, close relationships With friends and family, expert in computer and information affairs, hardworking, with very good relationships with people around him, innovative and innovative, he suddenly finds himself in a situation where he is unable to even do his daily work, he did not talk to anyone. Someone who used to be able to run an office with all the employees, today would not even be willing to talk to the people around him. He remains in the same position for a long time in absolute silence while staring at the distance. He didn't want to eat, despite the fact that sometimes he only had one meal a day, not that he wanted to, but he didn't want to eat at all. The sleep situation was much, much worse, despite the fact that he was lying in bed for hours and staring at the ceiling of the room, but he didn't even blink, even if he slept, he would wake up again with the slightest sound or movement. His family asked me to fol-

low the issue seriously and help in this way. I was looking to see how I can interpret the cause of his depression and self-absorption. While he was an experienced manager in his work, he could not establish a friendly or professional relationship even with his old colleagues.

In fact, my motivation to investigate this issue came from the fact that I wanted to know why this patient faced this problem and how I can help him to get out of this situation.

About glaucoma

This term refers to a group of eye diseases that cause damage to the optic nerve due to increased intraocular pressure. Glaucoma can cause serious vision problems, including astigmatism.

Although there are many diseases that can cause glaucoma, most of the glaucoma is caused by the lack of fluid drainage from the eye.

Known risk factors of glaucoma

All people over the age of 60 and diabetic patients are exposed to this disease. It is said that this disease is twice as common in diabetic patients and six to eight times in African Americans over 40 than in whites.

Types of glaucoma

Open angle glaucoma

Almost all cases of glaucoma are open - angle glaucoma. At least 9 out of 10 glaucoma patients suffer from this disease. Sometimes it is known as chronic glaucoma or primary glaucoma. About 3 million Americans suffer from open - angle glaucoma.

Closed angle glaucoma

Sometimes the angle between the iris and the cornea is blocked by the iris. This causes angle closure glaucoma. When the angle is blocked, fluid cannot leave the eye as it normally would, leading to eye pressure problems and possible blindness as with all types of glaucoma. Angle - closure glaucoma tends to be inherited.

About half a million people in the United States have this condition. People of Asian descent and people with close ties are more affected.

Normal tension glaucoma

In Japanese, those with a family history of the disease, and those with an irregular heartbeat or a history of systemic heart disease, are more likely to be affected.

Congenital glaucoma

Some children are born with glaucoma.

Most children with this disease are diagnosed in the first year of their lives. Treatment of glaucoma apart from the use of local or oral treatments, if the patient is not controlled, surgical methods should be used.

Laser surgery for glaucoma

Laser surgery is often the first step in glaucoma treatment before using traditional surgery.

Using a very focused beam of light, a small hole is created in the tissue of the eye so that the fluid can drain more freely.

There are different types of laser surgery for glaucoma patients depending on the cause of the disease and its severity

- Selective Laser Trabeculoplasty
- Argon Laser Trabeculoplasty
- Laser Peripheral Iridectomy
- Cyclophotocoagulation and Laser Cyclophotocoagulation.

In some cases, these facilities are not available to ophthalmologists or they cannot solve their patient's problem with these methods. Then they turn to traditional glaucoma surgery. This type of surgery reduces eye pressure in about 60 to 80 percent of the time, and depending on the effectiveness, it may be more expensive than surgery.

Background

Timolol is a commonly-used topical antiglaucoma medication and has proven to be highly efficacious for most recipients. Among the reported adverse events, the neuropsychiatric spectrum has been cited, albeit for a small proportion of those treated.

My patient is a 66-year-old man with a history of long-term hypertension and hyperlipidemia under the supervision of different doctors. In terms of risk factors, he was a perfect person and he used to walk for one hour every day. In 2019, it was determined in the annual check-up exams that his eye pressure is close to 42. Numerous visits to ophthalmologists finally determined that he, has been diagnosed with open-angle glaucoma, and like other patients whom I know closely, under the supervision of ophthalmologists, treatment with timolol drops begins. Until 2022, the patient did not have any problems in terms of nerves and mental health. But suddenly, his friends notice that he avoids showing himself in limited friendly gatherings secretly and refuses to be in these gatherings. His sleep, rest, work, and even eating status are out of order and are meaningless. Lives Whenever someone asks him, he says it is not like that. I want to rest for a while or I have worked too much and I am tired. He does not want to relate to his employees who have worked with them for years. Despite the patient's wishes, his family brought him to me and I realized very well in the very first visit that his personality has completely changed and that social personality he had for years is gone.

Ohati didn't tell me, who knew him for years, what his main complaint was? And he only talked to me about his sleep problems, so I took him to my colleague Dr. Ogen Sotiri and consulted with him in person. The diagnosis was confirmed that he has Major Depressive Disorder with Psychotic features.

And according to the probable condition of the patient and his relations, which have not changed seriously, it was a question for us, what is the cause of this problem? And this was a big challenge for us and.

Psychological effects

We want to rule out the psychological side effects of Timolol. These complications have been proven, and this does not mean that this problem may occur in all patients. In some studies and researches, this problem has been emphasized when patients stay in the hospital for a long time or are at risk of becoming blind due to the disease. Glaucoma is placed automatically in their mood, complications and fear remain, and then it becomes psychological symptoms.

Psychological stress has been shown to have a minor but statistically significant effect on intraocular pressure (IOP). Stress can alter the IOP in people with closed angle glaucoma, which is also affected by their emotional state. Because IOP is a key indicator of closed angle glaucoma, it is possible that lowering stress can help patients manage their symptoms [1].

Several studies showed a higher prevalence of depressive symptoms among glaucoma patients, while Wilson., *et al.* did not confirm this finding [2].

Of course, in this case, on the issue of the side effects of timolol in a patient whose issues and problems we have comprehensively examined, we were also faced with these symptoms, even

to solve the metabolic diseases, we had to first roll out all kinds of endocrine diseases so that we can treat the disease later. The main thing to focus on is that the patient first mentioned the problems of headache, weakness and excessive anorexia, light-headedness, sleep disorders, dizziness and imbalance, so we had to first investigate the metabolic issues that may cause these symptoms in this patient. To be evaluated, and when all these investigations were done and we could not reach a definite diagnosis, I discussed the issue of timolol drug complication with the involved ophthalmologists, and they raised this issue that.

It could be a complication of using timolol, otherwise we had no experience in this regard. We have had more than 300 glaucoma patients in my colony, and all these patients have been treated with common treatments and their problems have been controlled for years with this condition, and we had no experience with this issue, which is one of the side effects of using timolol drops. It can be bipolar diseases. Later, when I introduced him to my friend, Dr. Ogen Sotiri, a psychologist, he agreed with us that the cause of the patient’s appearance in this case was a Glaucoma has been associated with a greater risk of developing major depressive disorder, bipolar disorder, and schizophrenia in the future [3]. A neurodegenerative pathway was postulated to be a common link between glaucoma and psychiatric illnesses [4].

Age	Gender	Event	Topical therapy	Resolution	Complicating features	Past psychiatric history	Year	Reference
71	M	Worsening myasthenia gravis	Timolol	1 day	Chronic myasthenia gravis	No	1979	29
<1	?	Apnea	Timolol	1 day	Bilateral ocular anomalies	No	1979	30
78	F	Syncope, visual hallucinations	Timolol	2 hours	None	No	1980	31
65	F	Depression	Multiple	2 days	Suicidal ideation	No	1982	32
65	M	Impaired response to hypoglycemia, diabetic Amaurosis fugax, transient ischemic attacks	Timolol	After cessation	Frequent hypoglycemic episodes	No	1983	33
78	M		Timolol	5 days	Arrhythmia	No	1985	34
74	F	Depression	Timolol, Pilocarpine	3 weeks	Bradycardia, taking antipsychotic meds	Yes	1993	35
65	M	Depression, insomnia	Timolol, Acetazolamide	Several days	None	No	1993	36
87	F	Lethargy, insomnia	Timolol	Several days	Bradycardia	No	1997	37
70	M	Depression	Timolol, Travaprost	1 month	Past depression also worsened with other beta-blockers	Yes	2008	38
<1	F	Apnea, hypotonia	Multiple	1 day	Congenital glaucoma, cardiogenic shock, bronchoconstriction	No	2013	39
Four patients (ages 66-93)	All F	Visual hallucinations	Variable	Several hours to days	Some existing neurologic impairment, all had retrial of medication to confirm	No	2017	40

Table 1: Case reporting of neuropsychiatric adverse events from topical timolol.

Table of prevalence of psychological diseases in patients who were treated with timolol eye drops [3].

I can't be sure that our case and his psychological problem were not caused by glaucoma. Considering the experiences of more than 300 male and female patients who suffered from this disease for years, I further emphasized that this patient did not have any pre-

vious psychological complications and our patients did not face this problem, the reason was clear to us because this The patients have lived in very excellent relationships with each other and the challenges that existed in another social environment were generally far from them, but in other studies and the fact that glaucoma can cause psychological complications in patients has been significant for us, including [2].

	Model 1				Model 2			
	OR	CI	P-Value	n	OR	CI	P-Value	n
Depression (PHQ-9 ≥ 10)	1.08	0.69–1.62	0.72	14,359	1.10	0.50–2.38	0.80	14,061
Anxiety (GAD-2 ≥ 3)	1.15	0.70–1.78	0.55	14,288	1.48	0.63–3.30	0.35	13,991

PHQ-9 Patient Health Questionnaire, GAD-2 Generalized Anxiety Disorder Scale, OR Odds ratio, CI 95% confidence Interval
 Model 1: logistic regression analysis adjusted for age, sex, socio-economic status; Model 2 additionally adjusted for systemic comorbidities (arterial hypertension, myocardial infarction, stroke, diabetes mellitus, chronic obstructive pulmonary disease, cancer), ocular diseases (cataract, macular degeneration, corneal diseases, diabetic retinopathy), visual acuity of the worse eye, IOP, antiglaucoma eye medications (Sympathomimetics, Parasympathomimetics, Carbonic anhydrase inhibitors, Beta-blockers, Prostaglandins) and general health status

Table 2: Associations of self-reported glaucoma with depression and anxiety in the Gutenberg health study (GHS), 2007-2012.

Challenges

- In view of the fact that the patient underwent classic glaucoma surgery at the end of 2022 and both eyes were operated on, and he did not use any eye medication after the beginning of 2023. I mean timolol so why still It has been almost two years and the patient's psychological condition has not changed and he is still undergoing regular psychological treatments.
- How should we evaluate the role of the patient in the continuation of his illness? Shouldn't we review the theory of the 21st century psychologist Professor William Glasser, who believes that patients who have psychological problems at any stage of their lives go through the discussion of a choice in this case and similar cases?

And William Glasser says

These patients are selected to remain in a psychological state. Because they pay a lower cost themselves and transfer all the bugs and pathogenic factors outside themselves. They reject their role. In fact, they pretend that they are innocent and that these issues have been created for them outside of them. In our case, he focuses on timolol eye drops.

The backgrounds and backgrounds of these patients cannot be completely rejected or accepted. While the patient's psychological condition is almost stabilized, the question is:

- Can we lead the patient to accept William Glaser's theory or not?
- If this is done, will the patient's condition be better or worse?

No one can answer these questions and it is very difficult for me to enter into this issue. Because I am worried that I will make his condition worse and worse. For this reason, it is a huge challenge in front of us.

In this case, we may accept that the cause of the psychological symptoms of this patient was not primarily caused by the use of the drug Timolol, but as an independent factor, i.e. without the glaucoma patient and the use of Timolol drops, it coincided, which caused the secondary occurrence of these psychological symptoms.

It means that patients with glaucoma find real threats in relation to this disease, they may be affected by it and finally be drawn to depression, which in our case considering that he has been away from this for more than two years. Medicine does not use, maybe it can be interpreted

Conclusion

- Considering that he underwent glaucoma surgery at the end of 2022 and both eyes were operated on and he did not use any medicine for his eyes after the beginning of 2023 (I mean timolol), so why is it still almost two years and The patient's psychological condition has not changed and he is still undergoing regular psychological treatments

- How should we evaluate the role of the patient in the continuation of his illness? Shouldn't we review the theory of Professor William Glaser who believes that patients who develop psychological problems at any stage go through the discussion of a choice in this case and similar cases ?
 - And William Glaser says that these patients choose to remain in a psychological state because they pay a lower cost themselves and transfer all the problems and pathogenic factors outside themselves and reject their own role and in fact pretend that they are innocent and outside of them this it has created problems for them. In our case, the problem is completely focused on the drug Timolol.
 - The backgrounds and backgrounds of these patients cannot be completely rejected or accepted, while the patient's psychological condition is almost stabilized. The question is, can we lead the patient to accept William Glaser's theory or not? If this is done, will the patient's condition be better or worse? No one can answer this question and it is very difficult for me to go into this because I am worried that I will make his situation worse and worse, so it is a huge challenge in front of us.
 - In this case, we may accept that the cause of the psychological symptoms of this patient was not primarily caused by the use of the drug Timolol, but as an independent factor; i.e., the glaucoma patient, caused the secondary occurrence of these psychological symptoms and had nothing to do with the drug. This means that patients with glaucoma may be affected by the real threats that this patient finds and eventually lead to depression, which in our case, considering that he has been away for more than a year and a half. This drug does not help, but why the psychological symptoms still remain may be interpretable.
 - Finally, will we one day be able to easily put Professor Glaser's theory in front of psychological patients and help them solve their complicated problems, beyond drug or psychological treatments or not? This question remains unanswered.
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