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Deployment of Six Sigma Methodology to Reduce Complications in Intravitreal Injections

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ABSTRACT: The purpose of this study is to show how a private eye care center in Turkey initiated Six Sigma principles to reduce the number of complications encountered during and after intravitreal injections. Data were collected for 30-months. To analyse the complications among 229 injections administered on 106 patients, main tools of Six Sigma's Define-Measure-Analyze-Improve-Control (DMAIC) improvement cycle such as SIPOC table, Fishbone Diagram and, Failure, Mode and Effect Analysis were implemented. Sources and root causes of seven types of complications were identified and reported. For a successful intravitreal injection, experience of the retina specialist, attention of the retina specialist and patient's ocular pathology were determined to be the "critical few" factors whereas, sterilization and hygiene, dosage of drug/agent and chemical properties of drug/agent were found to be the "trivial many"factors. The most frequently occuring and the complication with the highest hazard score was found to be subconjunctival haemorrhage. The process sigma level of the process was measured to be 3.2657. The surgical team concluded that six of the complications (out of seven) should be significantly reduced by taking the necessary preventative measures.

Keywords: Six Sigma; Ophthalmology; Intravitreal injections; Complications
JEL Classifications: I120; L15

1. Introduction

Intravitreal injections have been used since the 19th century, when transplanted rabbit vitreous and air were used to treat retinal detachment and vitreous haemorrhage (Rifkin and Schaal, 2012). However, widespread use of intravitreal injection began with intravitreal antibiotics being used for the treatment of endophthalmitis and intravitreal steroids for the treatment of intraocular inflammation (Charles and Calzada, 2011). Over the past ten years, anti–vascular endothelial growth factor (anti-VEGF) agents began to be widely used to treat diabetic macular edema, macular edema secondary to

vein occlusion, and for the treatment of neovascularization in age-related macular degeneration (Sampat and Garg, 2010). Today, intravitreal injections are used to deliver anti-infectious, anti-inflammatory, anti-cancer, anti-vascular endothelial growth factor agents, antivascular endothelial growth factor medications, and gas into the eye (Rifkin and Schaal, 2012).

Intravitreal injections play a critical role in daily ophthalmic practice (Sampat and Garg, 2010). Intravitreal delivery of anti-VEGF and corticosteroids has currently become the standard of care treatment for a variety of ocular conditions and retinal diseases (Table 2). This delivery is an important procedure that retina specialists use on a daily basis, and it is important to master the techniques of effective injections for patient safety and reduction of complications. Some of these complications include intraocular pressure (IOP) elevation, cataract formation, retinal detachment, vitreous hemorrhage, endophthalmitis, ocular pain, corneal abrasion, chemosis, lens injury, ocular inflammation, retinal pigment epithelial tear and acute vision loss. (Ozkiris and Erkilic, 2005; Wingate and Beaumont, 1999; Sampat and Garg, 2010; Roth et al., 2003; Sanabria et al., 2013; Shima et al., 2008; Martidis et al., 2002; Jonas et al., 2008).

The use of Six Sigma, as a quality improvement method, can be employed in order to eliminate complications resulted during and after many ophthalmic surgeries (Taner, 2013). Originally initiated by Motorola, Honeywell and General Electric (Mehrjerdi, 2011), Six Sigma is a powerful performance improvement tool that is changing the face of modern healthcare delivery today (Taner et al., 2007). Although it was initially introduced in manufacturing processes, it is being implemented in diagnostic imaging processes (Antony and Banuelas, 2002, Antony et al., 2007; Taner et al., 2012), emergency room (Miller et al., 2003), paramedic backup (Taner and Sezen, 2009), laboratory (Nevalainen et al., 2000), cataract surgery (Taner et al., 2013), phacoemulsification cataract surgery (Sahbaz et al., 2014), radiology (Cherry and Seshadri, 2000), surgical site infections (Pexton and Young, 2004), IntraLase surgery (Sahbaz et al., 2014), LASIK surgery (Taner et al., 2014), strabismus surgery (Taner et al., 2014), and stent insertion (Taner et al., 2013) as a cost-effective way to improve quality, performance and productivity.

A Six Sigma process produces 3.4 defective parts per million opportunities (DPMO) (Buck, 2001). As a method to eliminate errors, Six Sigma uses a structured methodology called DMAIC to find the main causes behind problems and to reach near perfect processes (Park and Anthony, 2008). DMAIC is useful to analyse and modify complicated time-sensitive healthcare processes involving multiple specialists and treatment areas by identifying and removing root causes of errors or complications and thus minimizing healthcare process variability (Buck, 2001; Taner et al., 2007).

In this study, a Six Sigma infrastructure was developed for a private Turkish eye centre in order to improve the outcomes of their intravitreal injection processes. In addition, sigma level of each type of complication are calculated and reported.

2. Method: Application of Six Sigma's DMAIC for Intravitreal Injections

The eye care center decided that Six Sigma was the best way to achieve their goals. A surgical team was assembled and trained in the methodology. Committed and consistent leadership to overcome the complications was assured by this team. The surgical team firstly generated a SIPOC (Supplier, Input, Process, Output and Customer) Table for intravitreal injection process (Table 1).

Using anti-VEGF agents or corticosteroids depend on the ocular pathology being treated, but mainly include improvement of vision or prevention of worsening of the vision, e.g. in the case of diabetic retinopathy (Lupeanu et al., 2013). To achieve either of these performance objectives, the surgical team first determined by brainstroming the Critical-to-Quality (CTQ) factors, i.e. the drivers of success in the process.

The surgical team determined the metrics to measure existing process. The metrics to be chosen for a Six Sigma study were:

1. Total number of intravitreal injections performed in the eye care center,
2. Number of complications.

Data were collected for a period of 30 months. In this period, a total of 229 intravitreal injections (Table 2) were performed on 106 patients. Then, the team related the retinal/ ocular disease with the corticosteroid drugs and anti-VEGF agents they administered (Table 3).

Complications had been noted by the team as they occurred. The surgical team identified seven types of complications and classified them as when (i.e. intraoperatively and/or

postoperatively), and how soon they occur, i.e. acute, sub-acute and/or chronic (Table 4). Sources (Table 5) and root-causes (Table 6) of these complications are tabulated by type.

Table 1. SIPOC Table for Intravitreal Injection

SUPPLIER	INPUT	PROCESS	OUTPUT	CUSTOMER
Retina specialist	Patient	Ocular examination	Improvement in vision acuity	Patient
Nurse	Syringe	Evaluation of ocular examination	Prevention of worsening of vision acuity	
Assistant surgeon	Topical anaesthetic drop	Decision on which anti-VEGF or corticosteroid to be used		
	Anti-VEGF agents	Preparation of the patient		
	Corticosteroids	Topical anaesthesia		
		Intravetrial injection		
		Discharge		

The incidence of complications depends on multiple sources (i.e. variables). Surgeon variables, nurse variables, drug/agent variables, equipment variables and patient variables must all be evaluated while attempting to assess the root-cause of a complication (Table 5 and Table 6).

Table 2. Number of intravetrial injections performed by type

Type	Count
Triamcinolone	22
Bevacizumab	101
Ranibizumab	93
Bevazicumab+Triamcinolone	13
Total	229

Table 3. Retinal/Ocular disease vs Anti-VEGF agents/Corticosteroids

Retinal/Ocular Disease	Corticosteroid drugs	Anti-VEGF agents	
	Triamcinolone	Bevacizumab	Ranibizumab
Age-related macular degeneration		X	X
Retinal vein occlusion	X	X	X
Diabetic Retinopathy	X	X	X
Cystoid macular edema	X	X	X
Vascular occlusion	X	X	X

Table 4. Complications Experienced (July 2011 – December 2013)

	Complication	Intra-Operative	Post-Operative	Acute	Sub-Acute	Chronic
Type I	Subconjunctival haemorrhage	X	X	X		
Type II	Increase in IOP	X	X	X	X	
Type III	Anterior uveitis		X	X		
Type IV	Anterior/Posterior inflammation		X	X	X	
Type V	Endophthalmitis		X	X	X	
Type VI	Retinal detachment		X		X	X
Type VII	Cataract		X		X	X

3. Analysis

The surgical team analysed the occurrence frequency of each complication (Table 7) and related them with the root-causes on Table 6. The analysis revealed that Type I, II and III were the three most frequently occurring complications in the intravitreal injections (Table 5). Then, they classified the CTQs as "vital few factors" and "trivial many factors" according to how frequent they caused the complications. The "vital few" factors, i.e. the factors that had the most impact on the success of intravitreal injection were determined to be the experience of the retina specialist, attention of the retina specialist and patient's ocular pathology. The other factors, i.e. sterilization and hygiene, dosage of drug/agent and chemical properties of drug/agent were the "trivial many".

Table 5. Sources of Complications

	Surgeon	Nurse	Patient	Drug/ Agent	Equipment
Type I	X		X		
Type II	X		X	X	
Type III				X	X
Type IV				X	X
Type V	X	X	X		X
Type VI	X		X		
Type VII	X		X		

To measure the current sigma level of a complication, surgical team calculated the current Defects per One Million Opportunities (DPMO) and sigma levels for each complication type (Table 5). For this, two distinct datasets (i.e., total number of phacoemulsification cataract surgeries performed (A) and total number of complications occurred (B) were required. Then, DPMO is calculated from the following formula:

$$DPMO = B \times 1{,}000{,}000/A$$

Normal distribution underlies Six Sigma's statistical assumptions. An empirically-based 1.5 sigma shift is introduced into the calculation. A higher sigma level indicates a lower rate of complications and a more efficient process (Taner, 2013).

Table 6. Root-causes of Complications

	Experience	Attention	Dosage of Drug/ Agent	Sterilization And Hygiene	Patient's Ocular Pathology	Chemical properties of Drug/Agent
Type I	X	X			X	
Type II	X	X	X		X	
Type III			X	X		X
Type IV			X	X		X
Type V	X			X	X	
Type VI	X	X			X	
Type VII	X	X			X	

The surgical team calculated the current Defects per One Million Opportunities (DPMO) and sigma levels for each complication type (Table 7). The process sigma level, showing the operating performance, calculated from the arithmetic average of seven complications, was found to be 3.2657.

Table 7. Cumulative frequency, DPMO and Sigma Levels

	Count	Frequency (%)	DPMO	Sigma Level
Type I	105	45.85	458515	1.60
Type II	42	18.34	183406	2.40
Type III	16	6.99	69869	2.98
Type IV	5	2.18	21834	3.52
Type V	1	0.44	4367	4.12
Type VI	1	0.44	4367	4.12
Type VII	1	0.44	4367	4.12

The highest sigma level was obtained for Type V, VI and VII. The lowest sigma level was found to belong to Type I. Having sigma levels lower than 4.00; Type I, II, III and IV needed to be significantly reduced.

Table 8. Severity Scores

Severity Score	4	3	2	1
Severity of Complication	Permanent harm	Temporary harm	Bias	No harm

4. Discussion

Risk assessment of the intravitreal injection was achieved by the Failure Mode and Effect Analysis (FMEA). Utilization of the FMEA involved break down the process into individual steps: potential failure modes (i.e. complications), severity score, probability score, hazard score, criticality and detection, so that the surgery team could look at key drivers in the process based on the past experience.

Complication trends and their consequences over a 30-month period had been monitored and recorded. Surgical team prioritized the complications according to how serious their consequences were (i.e. severity score), how frequently they occurred (i.e. probability score) and how easily they could be detected. Hazard analysis was employed in order to identify failure modes and their causes and effects. The surgery team determined the severity of each complication and assigned scores for them. The severity of each complication was scored from 1 to 4 (Table 8).

Table 9. FMEA Table

Complication Type	Hazard Analysis			Decision Tree Analysis	
	Severity Score	Probability Score	Hazard Score	Critical?	Detectable?
Type I	1	0.4585	0.4585	No	Yes
Type II	2	0.1834	0.3668	No	Yes
Type III	2	0.0699	0.1398	No	Yes
Type IV	2	0.0218	0.0436	No	Yes
Type V	4	0.0044	0.0176	Yes	Yes
Type VI	4	0.0044	0.0176	Yes	Yes
Type VII	3	0.0044	0.0132	Yes	Yes

For each complication type, the hazard score was calculated by multiplying the severity score with the probability score. Consequently, an FMEA table was drawn (Table 9). Among the complications, Type I yielded the highest hazard score. Type V, VI and VII were equally the least hazardous complications.

The surgical team developed preventative measures for each type of complication in order to bring the overall intravitreal injection process under control. They also noted that there had still been limited progress in understanding the basic mechanisms underlying the complications such as Type III and IV. Nonetheless, they implemented a corrective action plan (See the Appendix) to reduce and/or eliminate the other complications.

5. Conclusion

This study shows that the majority of intravitreal injection complications in the eye care centre had occurred postoperatively. These complications were almost always related to the experience, injection skills and attention of retina specialists. Therefore, retina specialists are in a key position to reduce and/or eliminate these complications.

The operating sigma level of intravitreal injections performed in 30 months was found to be 3.2657. To increase the sigma level and thus the overall success rate of intravitreal injections in the eye care center, four types of complications, namely Type I, II, III and IV, should be significantly reduced. This can be achieved by complying the preventative measures.

Consequently, implementing the Six Sigma philosophy in ophthalmology processes can prevent and manage complications as well as significantly eliminate and/or minimize their occurrence.

By the deployment of Six Sigma's DMAIC tools, robust visual acuity outcomes will always be achievable.

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Appendix

Corrective Action Plan	
Complication Type	**Preventative Measure(s)**
Type I	-Determine the compliance of patient's bleeding and coagulation values. -Administer the injection away from the superficial vascular area.
Type II	-Preoperatively check and if necessary lower the IOP. -Administer the intravitreal injection very slowly. -Apply the paracentesis procedure to the anterior chamber and carefully discharge the aqueous humor if the IOP during the intravitreal injection is high. -Lower the IOP if it is postoperatively high.
Type III	-Administer only the intravitreal drugs specifically produced for eye.
Type IV	-Administer only the intravitreal drugs specifically produced for eye.
Type V	-Sterilize the operating room, equipment and instruments. -Clean the patient’s eye and its sorrounding.
Type VI	-Preoperatively scan the retina of the patient. -Determine and if necessary cure the weak regions of retina. -Make sure that the injection site is away from the limbus, but within the pars plana area. –Administer the intravitreal injection very slowly.
Type VII	-Make sure that the intravitreal injection is not made very close to limbus. -Make sure that the direction of the intravitreal injection is towards the center of the eye.