· Original article ·

Clinical analysis of surgical treatment in patients with senile cataract and hematologic disease

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Received: 2013-09-13 Accepted: 2013-10-20

老年性白内障合并血液疾病患者手术治疗的临床疗效分析

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摘要

目的:评估白内障摘除联合人工晶体植入术对老年性白内障合并血液疾病患者的临床疗效。

方法:40 例(58 眼)老年性白内障合并血液疾病患者接受了白内障摘除联合人工晶体植入术。术前评估,包括凝血试验,白细胞分类和骨髓检查。对老年性白内障患者合并血小板减少,白细胞减少,贫血,全血细胞减少(通过血液检测确定)的患者给予适当的术前治疗。随机选择血液检查结果相似,年龄相仿的 30 例老年性白内障研究组患者的作为对照组。记录术后矫正视力,术中及术后并发症。记录研究组患者血液病的原因。采用 t 检验,对比两组的血液凝固数据。

结果:研究组和对照组的血浆凝血酶原时间和活化部分凝血活酶时间没有显著差异($P=0.379$ 和 $P=0.945$)。所有患者手术矫正视力均有一定程度的改善(>0.4, 96.55%)。术后未发生感染,出血或发烧。部分患者血液病的病因不明;大多数患者有糖尿病,高血压,肝硬化或肾脏疾病。

结论:有效的围手术期治疗,使老年性白内障合并血液疾病患者可以安全地进行白内障摘除联合人工晶体植入术,并且术后效果良好。

关键词:白内障;围手术期;血液系统疾病

引用:何敏,葛晓燕,武耀红,王万辉. 老年性白内障和血液疾病患者手术治疗的临床疗效分析. 国际眼科杂志 2013;13(11):2169-2173

Abstract

• AIM: To evaluate the clinical efficacy of cataract extraction and intraocular lens implantation in patients with senile cataract and hematologic disease.

• METHODS: Forty patients (58 eyes) with senile cataract and hematologic disease underwent cataract extraction and intraocular lens implantation. Preoperative assessment included blood coagulation testing, leukocyte classification, and bone marrow examination. Appropriate preoperative treatments were administered to patients with senile cataract and thrombocytopenia, leukopenia, anemia, and/or pancytopenia (identified through blood testing). Thirty patients with senile cataract and normal routine bloodwork findings, with ages similar to those of patients in the study group, were randomly recruited as a control group. Postoperative corrected visual acuity and intraoperative and postoperative complications were recorded. The causes of hematologic disease in patients in the study group were recorded. Blood clotting data were compared between groups using t-tests.

• RESULTS: Plasma prothrombin time and activated partial thromboplastin time did not differ significantly between the study and control groups ($P=0.379$ and $P=0.945$, respectively). Surgery improved corrected visual acuity in all patients (>0.4 in 56 [96.55%] eyes). No postoperative infection, bleeding or fever occurred. The etiology of hematological disease was unknown in some patients; most patients had diabetes mellitus, hypertension, cirrhosis, and/or kidney disease.

• CONCLUSION: With adequate perioperative treatment, patients with senile cataract and hematological disease can safely undergo cataract operation and intraocular lens implantation, with good outcomes.

• KEYWORDS: cataract; perioperative period; hematologic disease
DOI:10.3980/j. issn. 1672-5123. 2013. 11. 02

Citation: He M, Ge XY, Wu YH, Wang WH. Clinical analysis of surgical treatment in patients with senile cataract and hematologic disease. *Guoji Yanke Zazhi* (*Int Eye Sci*) 2013;13(11):2169-2173

INTRODUCTION

With ongoing improvements in ophthalmic microsurgery technology and equipment, the indications for senile cataract extraction have gradually been expanded. However, some oculists believe that thrombocytopenia is an important risk factor for bleeding during ophthalmic surgery[1] and

leukopenia is a significant risk factor for postoperative infection[2] and wound healing problems. These beliefs often prevent patients with senile cataract, many of whom have blood system abnormalities such as thrombocytopenia, leukopenia, or anemia, from receiving timely surgical treatment in the clinical setting. Most patients with senile cataract and hematological disease are elderly and have conditions that impact their quality of life, such as mature cataract, low visual acuity, and one or more systemic diseases such as diabetes, high blood pressure, and liver or kidney dysfunction.

This retrospective study was performed to evaluate the safety and effectiveness of ophthalmic surgery for senilecataract in patients with hematological disease. To our knowledge, this report of our experience with 40 such patients is the first to examine surgery for senile cataract in this patient group.

SUBJECTS AND METHODS

Subjects The study sample comprised 40 patients with senile cataract (58 eyes) and a blood system abnormality treated at the Department of Ophthalmology, Second Hospital of Shanxi Medical University, between April 2008 and June 2011. Patients with corrected visual acuity <10/30 and at least two consecutive hemograms showing an anomaly (thrombocytopenia, leukopenia, anemia, or pancytopenia) were included in the study sample. For patients with high blood pressure, systolic blood pressure <150mmHg and diastolic blood pressure <100mmHg were used as inclusion criteria. Patients with diabetes whose fasting plasma glucose level was <8.3mmol/L[3] and postprandial blood glucose level was <10mmol/L were included. Patients with any of the following conditions were excluded: fever, skin and/or mucosal bleeding, oral and/or nasal bleeding, other infection or bleeding symptom (*e.g.*, melena), uncertain perception of light or its directionality, retina or choroid detachment diagnosed by color Doppler ultrasound, intraocular pressure >25mmHg, and malignancy or tumor.

Thirty patients with senile cataract and normal routine bloodwork findings, with ages similar to those of patients in the study group, were randomly recruited as a control group. The control group was subject to the same inclusion and exclusion criteria as the study group, except for normal hemograms.

This research was performed according to the principles of the Declaration of Helsinki, and written consent was obtained from all subjects after they had been informed of the nature and possible consequences of the study. The research was approved by the institutional ethics committee of the Second Hospital of Shanxi Medical University.

Diagnosis Criteria Thrombocytopenia was defined as a platelet count $<100\times10^9$/L according to standard criteria[4]; a platelet count of 50×10^9/L was used as the threshold value distinguishing mild to moderate from severe thrombocytopenia[5]. In patients with leukocyte counts $<4\times10^9$/L, leukopenia was classified as neutropenia (absolute neutrophil count $<2.0\times10^9$/L) or agranulocytosis (absolute neutrophil count $<0.5\times10^9$/L)[6]. The diagnostic criteria for anemia were hemoglobin concentration <120g/L and hematocrit <40% in men, and hemoglobin concentration <110g/L and hematocrit <37% in women. According to hemoglobin concentration, anemia was classified as very severe (≤30g/L), severe (31-60g/L), moderate (61-90g/L), or mild (91-120g/L in men, 91-110g/L in women)[7]. Pancytopenia, which involves concomitant reductions in red and white blood cells and platelets[8], was defined as platelet count $<100\times10^9$/L, leukocyte count $<4\times10^9$/L, and hemoglobin concentration <120g/L in men or <110g/L in women.

Preoperative Examination and Treatment All patients underwent basic ophthalmic examinations, including vision testing, slit lamp and direct ophthalmoscopic fundus examinations, non-contact intraocular pressure and corneal curvature measurements, and acquisition of A- and/or B-images utilizing a sequence of stored ultrasonic time signals. Preoperative assessment included routine bloodwork, urine and blood coagulation series, measurement of fasting blood glucose level, determination of immune status, electrocardiography, and chest X-ray. Patients with plasma mean activated partial thromboplastin times (APTTs) or prothrombin times (PTs) outside of the normal ranges (23-38s and 11-15s, respectively, according to the laboratory of the Second Hospital of Shanxi Medical University) were excluded from the study.

The hematology department was consulted on abnormal findings of routine bloodwork, and the following treatments were applied. In patients with secondary thrombocytopenia caused by diabetes, cirrhosis, or spleen hyperfunction, initial treatment involved the correction of unstable fasting plasma glucose level or blood pressure. For thrombocytopenia of unknown etiology, the whole body was checked for signs of bleeding, bone marrow aspiration and rheumatism series were performed, and platelet function was checked to rule out secondary factors; in the absence of relevant findings, patients were diagnosed with primary thrombocytopenia[9,10]. Patients with mild to moderate thrombocytopenia were not treated. For patients with severe thrombocytopenia, an infusion containing 2u (1u=platelet count $>2.5\times10^{11}$) solid-phase single-donor platelets was injected intravenously on the day before surgery, and routine bloodwork findings were reviewed on the day of surgery. Surgery was performed only when the platelet count exceeded 50×10^9/L, and an additional 2u platelets was administered to patients with low counts.

Neutrophil counts were obtained for patients with leukopenia. Normal neutrophil counts were considered to indicate mild leukopenia, which was not treated. For patients with low neutrophil counts, leukocytes were classified using conventional arterial line filters to rule out malignancy, infection, and other systemic diseases. Patients with neutrophil counts $<1.5\times10^9$/L and normal white blood cells were given hypodermic injections of recombinant human granulocyte colony-stimulating factor (200 or 300μg) 3d before surgery to prevent postoperative infection[11], and

routine bloodwork was then reviewed 1d before surgery. Surgery was performed if the neutrophil count was $>1.5\times10^9$/L, and another injection was administered if it was not. All patients with anemia had mild to moderate chronic anemia and thus received no specific treatment.

Surgical Method All patients underwent manual small-incision cataract surgery (MSICS)[12]. Surface (0.4% oxybuprocaine eye drops; Santen Pharmaceutical Co., Ltd., Osaka, Japan) or retrobulbar (2% lidocaine; Shanghai Xudong Haipu Pharmaceutical Co., Ltd., Shanghai, China) anesthesia was administered. Preoperative mydriasis was obtained. The surgeon made a 5-6mm limbal incision at the 12 o'clock position and in many cases attempted continuous circular capsulotomy. If capsular calcification or other anterior segment anomaly prevented this maneuver, discontinuous anterior capsulotomy was performed using a cystitome or scissors. After nucleus extraction and removal of cortical remnants, a rigid poly (methyl methacrylate) intraocular lens (OII; Ophthalmic Innovations International, Inc., Ontario, CA, USA) was implanted in the posterior chamber. In-bag implantation was performed in all cases. The incision was closed without suturing. Surgery-related complications were recorded.

Postoperative Management Patients were instructed in postoperative eye care, including the use of tobramycin/dexamethasone (TobraDex; Alcon Cusi, El Masnou, Spain) for 1 month. Three months postoperatively, corrected distance visual acuity (CDVA) was reassessed in daylight at a distance of 6m using a Snellen tumbling E chart.

Statistical Analysis *T*-tests were used to compare blood clotting data between the study and control groups, with $P<0.05$ considered to indicate statistical significance. Pre- and post-treatment platelet counts were compared in patients with severe thrombocytopenia. An Excel (Microsoft Corporation, Redmond, WA, USA) database was established and SPSS software (ver. 13.0; SPSS Inc., Chicago, IL, USA) was used for analyses.

RESULTS

The sample included 21 men and 19 women with a mean age of 71.90±8.08 (range, 56-84) years. Twenty-two of the 40 patients had thrombocytopenia (primary, $n=12$; secondary, $n=10$), 12 had leukopenia (including 10 with thrombocytopenia), 14 had anemia (including two with thrombocytopenia), and four had pancytopenia caused by cirrhosis.

Preoperative CDVA was classified as light perception ($n=6$ eyes), hand motion ($n=22$), finger counting ($n=10$), 1/50-2/20 ($n=14$), and 2/20-10/30 ($n=6$). Preoperative CDVA was ≤0.1 in 89.66% of patients. Because the majority of patients had mature or hypermature cataracts preventing refraction, mean uncorrected distance visual acuity values were used to represent CDVA.

The mean platelet count was $67.82\pm20.43\times10^9$/L in the 22 patients with thrombocytopenia. Six (27.27%) of these patients had severe thrombocytopenia (mean pre-treatment platelet count, $43.97\pm2.00\times10^9$/L) and 16 (72.73%) had mild to moderate thrombocytopenia (mean pre-treatment platelet count, $76.76\pm4.10\times10^9$/L). This condition was caused by diabetes mellitus and hypertension ($n=2$), diabetes mellitus and cirrhosis ($n=4$), chronic lymphocytic leukemia ($n=2$), and hepatitis B combined with cirrhosis ($n=2$); the etiology was unknown in 12 cases. In patients with severe thrombocytopenia, post-treatment platelet counts (mean, $72.63\pm3.25\times10^9$/L) showed significant improvement ($P<0.01$).

In the 12 patients with leukopenia, the mean white blood cell count was $2.67\pm0.52\times10^9$/L and the mean absolute granulocyte count was $1.34\pm0.29\times10^9$/L. All patients with leukopenia also had neutropenia and 10 (83%) patients also had thrombocytopenia. Etiologies of leukopenia were diabetes mellitus and hypertension ($n=2$), diabetes mellitus and cirrhosis ($n=4$), spleen hyperfunction combined with cirrhosis ($n=2$), and unknown ($n=4$). In the nine patients with thrombocytopenia and leukopenia, leukocyte classification, rheumatism series, platelet function, and bone marrow aspiration findings were normal.

Anemia was mild in five cases and moderate in nine cases. The mean hemoglobin concentration in these patients was 95.45 (range, 76.2-117) g/L. This condition was caused by renal insufficiency ($n=8$), diabetes and cirrhosis ($n=4$), spleen hyperfunction ($n=1$), and chronic lymphocytic leukemia in combination with hemolytic anemia ($n=1$). Two of 14 patients with anemia also had thrombocytopenia. In the four patients with pancytopenia, cirrhosis caused reduction of blood cells.

Mean plasma PT and APTT did not differ significantly between the study and control groups ($P=0.379$ and $P=0.945$, respectively; Table 1).

Table 1 Mean plasma prothrombin times (PTs) and activated partial thromboplastin times (APTTs) in the study and control groups

Groups	*n*	PT (s)	APTT (s)
Study group	40	14.49±3.06	30.81±5.90
Control group	30	13.94±1.81	32.65±5.01
P		0.379	0.945

One patient experienced capsule rupture intraoperatively, and an artificial crystal was implanted in phase 2 surgery; CDVA was 0.6 in this patient at 3 months postoperatively. No other significant intraoperative or postoperative (*e. g.*, infection, bleeding, fever) complication occurred. Patients' visual acuity had improved to varying degrees at 3 months postoperatively; CDVA was >0.4 in 56 (96.55%) eyes and >0.5 in 42 (72.41%) eyes.

DISCUSSION

With aging populations, the incidence of senile cataract has increased annually, resulting in dramatic increases in cataract surgery in recent years[13]. Some elderly patients have one or more chronic diseases that contribute to hematological disorders[14], such as hypertension, diabetes, coronary heart disease, or liver or kidney disease. Due to the limited number

of specialists and some hospitals' avoidance of cataract surgery because of potential complications (*e.g.*, bleeding and/or infection), some patients with senile cataract and hematological disease do not receive timely treatment. Most of these patients have mature or hypermature cataract and poor preoperative eyesight; surgery is considered to be a high-risk procedure in such patients.

Low preoperative visual acuity in most of our patients severely compromised quality of life. Cataract extraction improved CDVA (to >0.4) in most patients, who reported high levels of satisfaction. Retina laser treatment was performed to treat retinopathy in two eyes in two patients with diabetes, and postoperative corrected visual acuity was 0.1.

We used MSICS in these patients due to the mature or hypermature status of cataracts and the technological independence of this method from the surgeon's skill. MSICS has been shown to be more favorable than extracapsular cataract extraction (ECCE) in terms of operative time, visual recovery, and minimal complications [15]. Some authors have suggested that MSICS induces less astigmatism than other modalities, resulting in better uncorrected visual acuity compared with ECCE [16,17], and lower cost compared with phacoemulsification [18]. Only one minor intraoperative complication occurred in our study: posterior capsule rupture in one eye (1/58, 1.7%). This complication rate is similar to that reported in another study (2.0%) [19], and reflects the ophthalmologists' skill and experience.

Surgical Issues in Patients with Thrombocytopenia Thrombocytopenia is classified as primary or secondary, according to its etiology [10]. In 12 patients with senile cataract and primary thrombocytopenia, general condition was good, biochemical parameters (except lower than normal platelet counts) were normal, and no other systemic disease was present. Most cases of secondary thrombocytopenia (n = 10 patients) were associated with diabetes, high blood pressure, cirrhosis, and chronic lymphocytic leukemia. Due to the low platelet counts characterizing thrombocytopenia, the clinical hemorrhage rate was about 30%. The incidence of major bleeding was found to be significantly higher in elderly than in younger patients with thrombocytopenia [20]. Abnormal platelet quality and quantity are closely related to intraoperative bleeding, which is usually slight in patients with platelet counts $<50\times10^9$/L, but may be severe in those with platelet counts $<20\times10^9$/L[21,22]. Thus, platelet counts should generally be $\geqslant50\times10^9$/L in patients undergoing minor surgery and $\geqslant80\times10^9$/L in those undergoing major surgery [23]. To avoid intraoperative and postoperative bleeding in patients with severe thrombocytopenia, we took treatment measures in consultation with the hematology department. We administered no particular treatment to patients with mild to moderate thrombocytopenia, and no intraoperative or postoperative bleeding occurred in these patients. This finding suggests that patients with cataract and mild to moderate thrombocytopenia may not require preventive treatment. Fabian *et al*[24] administered no preventive treatment to seven patients with cataract and severe factor XI deficiency, and no preoperative or postoperative complication, such as hemorrhage, occurred. Thus, the issue of whether patients with severe thrombocytopenia require preoperative medication requires further discussion.

Surgical Issues in Patients with Leukopenia Common causes of leukopenia include infection, physical and chemical factors, spleen hyperfunction, connective tissue and allergic diseases, and acquired causes. Clinical granulocytopenia is usually caused by long-term medication and is typically systemic [25]. Eight patients with granulocytopenia in our sample had received long-term drug treatment for diabetes, high blood pressure, cirrhosis, and/or other disease. Neutrophil counts <0.5–1.0×10^9/L are generally considered to indicate susceptibility to severe postoperative infection and compromised wound healing, contraindicating surgery. Neutrophil counts $>1.0\times10^9$/L are generally required for most surgeries, and counts $>1.5\times10^9$/L are required for major surgery [23]. To ensure safety, we routinely administered recombinant human granulocyte colony-stimulating factors to patients with preoperative granulocyte counts $<1.5\times10^9$/L and did not perform surgery until preoperative neutrophil counts exceeded this value. Our patients showed no sign of postoperative infection.

Surgical Issues in Patients with Anemia With population aging, the prevalence of anemia has increased annually in elderly patients[14]. In such patients, anemia is typically caused by blood loss or deficiency, chronic disease/inflammation, chronic renal insufficiency, or unknown factors [26]. The body generally adapts and compensates to chronic anemia (hemoglobin concentration ~6g/L), and surgery is typically well tolerated under these conditions[23]. We administered no particular treatment to patients with preoperative anemia.

Surgical Issues in Patients with Pancytopenia Many diseases can cause pancytopenia, but etiologies can be classified into three main categories: diseases outside of the hematopoietic system (most commonly hypersplenism), hematological diseases, and unknown factors [27]. Cirrhosis, the most common cause of hypersplenism, may result in pancytopenia [28], but its pathogenesis remains incompletely understood. Pancytopenia was caused by cirrhosis in all affected patients in our sample. According to hematological parameters, patients with pancytopenia were given preoperative treatment.

With increased understanding of cataract and improvements in diagnosis and treatment, hematological disease combined with senile cataract is no longer a contraindication for cataract surgery. Appropriate pre- and perioperative treatment and preparation enable the performance of cataract extraction to improve visual acuity in patients with these conditions.

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