Effect of Medical Therapy on Glaucoma Filtration Surgery Rates in Ontario

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Objective: To analyze trends of glaucoma filtration surgery in Ontario.

Methods: From April 1, 1992, through March 31, 2004, correlations were examined between the annual rates of trabeculectomies in Ontario, the use of glaucoma medications, and the numbers of practicing ophthalmologists and optometrists.

Results: The number of trabeculectomies per 1000 persons at risk for primary open-angle glaucoma increased from 33.5 in 1992 to 46.2 in 1996 (37.7% increase; 6.6% increase per year) and then steadily decreased to 38.2 in 2004 (17.0% decrease; 2.7% decrease per year). The number of glaucoma medications dispensed in Ontario increased from 766,000 in 1992 to 1,466,543 in 2004 (91.5% increase; 10.5% annual increase). The increase in dispensed prostaglandin analogues strongly correlated (P < .001; 95% confidence interval, −0.87 to −0.41) with the decreasing number of trabeculectomies. The decreasing number of ophthalmologists positively correlated (r = 0.87) with the filtration surgery rate after 1997.

Conclusions: The number of trabeculectomies has decreased substantially in Ontario coinciding with the introduction of medications for the treatment of glaucoma in December 1996. This decrease in trabeculectomies highly correlated with the introduction of prostaglandin analogues (P < .001) and the decreasing number of ophthalmologists from 1997 through 2004.

Arch Ophthalmol. 2006;124:1472-1477

INTRAOCULAR PRESSURE IS THE ONLY modifiable risk factor for the treatment of glaucoma. Treatment consists of medical therapy followed by surgical therapy including laser trabeculoplasty and incisional surgery. Trabeculectomy is the most frequently performed incisional surgery for glaucoma.1 Since December 1996, 3 new classes of drugs for the treatment of glaucoma have been introduced: topical carbonic anhydrase inhibitors (CAIs), prostaglandin analogues, and α2-agonists. These fairly recent advances in glaucoma therapy have improved the ability to achieve sustained reduction of intraocular pressure, which may delay the need for surgery.2-5

The purpose of the current study was to evaluate the trends in trabeculectomy rates in Ontario from 1992 through 2004 and to explore whether the introduction of new medical therapies for glaucoma influenced the number of surgical procedures performed and if this trend was maintained. Factors that may affect the numbers related to resources such as the number of ophthalmologists and optometrists licensed in Ontario during this period also were evaluated.

Methods: The numbers of filtration surgeries performed in Ontario from April 1992 through March 2004 were obtained from the Ontario Health Insurance Program. These data showed all trabeculectomies performed in Ontario in residents of Ontario with a health card during that period. Virtually all residents in Ontario have a health card that is used when obtaining medical services.

Annual estimates of the Ontario population in 5-year age groups were obtained from Statistics Canada for the same period.7 A composite primary open-angle glaucoma (POAG) prevalence curve developed and updated by Tuck and Crick7,9 was used to estimate the prevalence of POAG in Ontario each year. This prevalence curve averages the results of the major prevalence surveys in the literature and permits analysis with respect to narrowly defined age groups.10-19

The introduction dates of new medications for the treatment of glaucoma in Ontario were obtained from the pharmaceutical companies. The numbers of glaucoma medications dispensed in Ontario during the study period were obtained from the International Medical Services database. The glaucoma medications were divided into groups according to the mechanism of action and presented as the

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After 1996, the number of bottles dispensed in each category per year. The combination therapies were classified as follows: Combigan (0.2% brimonidine tartrate and 0.3% timolol maleate) as an \( \alpha_2 \)-agonist, Cosopt (dorzolamide hydrochloride and 0.3% timolol maleate) as a topical CAI, Timpilo (2% or 4% pilocarpine hydrochloride and 0.5% timolol maleate) as a parasympathomimetic, and Xalacom (0.003% latanoprost and 0.5% timolol maleate) as a prostaglandin analogue. The number of ophthalmologists and optometrists in Ontario per year from 1992 through 2004 was obtained from the Ontario Medical Association and the Ontario Association of Optometrists.

Statistical analyses included regression analysis, with filtration surgery rate as the outcome variable, and Pearson correlation matrix between pairs of variables. The variables considered were filtration surgery rate, time in years, and total number of glaucoma medications dispensed overall and within each new medication group. One bottle of any of the medications was 1 month's supply. Other variables considered were number of ophthalmologists and optometrists. The filtration surgery rates were used as the outcome variable.

The \( t \) statistic used to calculate confidence intervals (CIs) is based on 12 years of data, but the percentage of drugs dispensed for each of the new drugs is zero before 1996. This fact will distort the estimated regression coefficients for year and percentage of total drugs because the regression assumed a straight-line relationship.

**RESULTS**

The total number of trabeculectomies increased from 1735 in 1992 to 2647 in 1997 (52.6% increase) and then remained stable for the remainder of the study (Figure 1). During this time, the population in Ontario increased from 10 257 047 in 1992 to 12 246 600 in 2004 (19.4% increase; 1.5% increase per year). For those aged 40 years and older, the population increased from 4 136 704 in 1992 to 5 556 600 in 2004 (34.3% increase; 2.7% increase per year). The estimated prevalence of POAG increased from 51 727 (0.5% of the total population and 1.25% of the population older than 40 years) in 1992 to 69 154 (0.57% of total population and 1.25% of the population older than 40 years) in 2004 (33.7% increase; 2.4% increase per year). The number of trabeculectomies per 1000 individuals at risk for POAG increased from 33.5 in 1992 to 46.2 in 1996 (37.7% increase; 6.6% increase per year) and then steadily decreased to 38.2 in 2004 (17.0% decrease; 2.7% decrease per year) (Figure 2).

New medications for the treatment of glaucoma were introduced in Ontario as follows: dorzolamide hydrochloride, May 1996; 0.005% latanoprost, June 1997; 0.2% brimonidine tartrate, November 1997; Cosopt, May 1999; travaprost, November 2001; bimatoprost, May 2002; Xalacom, October 2002; and Combigan, December 2003. The total number of prescriptions for glaucoma medications dispensed in Ontario increased from 766 000 in 1992 to 1 466 543 in 2004 (91.5% increase; 10.5% increase per year) (Figure 3). For 1992 and 1996, \( \beta \)-blockers represented the greatest market share (59.5% and 52.7%, respectively) followed by parasympathomimetics (24.8% and 28.2%, respectively) and, to a lesser extent, sympathomimetics and oral CAIs. In 1997, the new glaucoma medications, topical CAIs and prostaglandins, represented 16.2% of dispensed glaucoma medications. In 1998, with the introduction of \( \alpha_2 \)-agonists, the new antiglaucoma medications accounted for 26.9% of dispensed glaucoma therapy. In 2004, \( \alpha_2 \)-agonists accounted for 64.3% of the dispensed glaucoma medications in Ontario.

The highest increase occurred in the prostaglandin analogue category, and specifically with latanoprost, which increased from 12 000 bottles when introduced in 1997 to 529 600 bottles in 2004, a 44-fold increase (Figure 4). In 1998, latanoprost accounted for 5.7% of the total number of glaucoma medications dispensed and increased to 36.1% in 2004.
The data were analyzed for correlations between time in years, filtration surgery rates, cataract surgery rates, total medications dispensed, and each new medication group (Table 1). There was a high positive correlation between time in years and both the increasing number of total medications dispensed and each new medication group. There was a nonsignificant \((P=.88)\) negative correlation between filtration surgery rates and total medications dispensed \((r=−0.05)\). However, when each group was evaluated separately, there was a stronger, although not significant, negative correlation between filtration surgery rates and dispensed prostaglandins \((r=−0.35; P=.27)\). The correlation for \(\alpha_2\)-agonists was \(-0.23\) and for topical CAIs, 0.06, which were also not significant. The total glaucoma medications dispensed rate had a high positive correlation with every new medication group.

Regression analysis (Table 2) indicated no evidence of an association between the filtration surgery rate and the number of glaucoma medications dispensed before 1997 \((P=.23; 95\% \text{ CI}, −0.002 to −0.006)\). There was a slight trend between filtration rate and time in years \((P=.07; 95\% \text{ CI}, −0.74 to 10.37)\). There was no evidence of an association between filtration surgery rate and time in years, nor was there for filtration surgery rate and the number of glaucoma medications dispensed after 1997 \((P=.25; 95\% \text{ CI}, −3.25 to 1.12 \text{ and } P=.87; 95\% \text{ CI}, −0.001 to 0.0031, \text{ respectively})\).

Regression models were used to examine the association of specific drug classes as a percentage of total medications dispensed, controlling for overall drug dispensed rate and year (Table 3). We found a strong relationship between the decreasing number of trabeculectomies and the increasing dispensed rate of prostaglandin analogues \((b=−0.63; P<.001; 95\% \text{ CI}, −0.87 \text{ to } −0.40)\). There was no evidence of association between the decreasing number of trabeculectomies and the rates for CAI \((b=0.41; P=.31; 95\% \text{ CI}, −0.47 \text{ to } 1.31)\) and for \(\alpha_2\)-agonists \((b=−0.87; P=.19; 95\% \text{ CI}, −2.28 \text{ to } 0.53)\).

The number of ophthalmologists in Ontario varied little during this time, increasing from 409 in 1992 to 431 in 1997 (5.4% increase) and then decreasing to 419 in 2004 (2.9% decrease). Despite this increase and decrease, the number of ophthalmologists per million population per year is strongly associated \((r=0.87)\) with the filtration surgery rate and strongly negatively associated with the total number of medications dispensed \((r=−0.99)\) after 1997 (Table 1).

The number of optometrists practicing in Ontario has varied more, increasing from 857 in 1992 to 1365 in 2004 (59.3% increase; 4.0% increase per year). The number of optometrists per million population per year is negatively associated \((r=−0.93)\) with the filtration surgery rate and associated with the total number of medications dispensed \((r=0.94)\) after 1997 (Table 1).

**Table 1. Correlations (r Values) Between Different Variables Related to Filtration Surgery Rate, Antiglaucoma Medications, and Cataract Surgery Rate**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Year</th>
<th>Filtration Surgery Rate</th>
<th>Medications Dispensed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>1.0</td>
<td>-0.01</td>
<td>1.0</td>
</tr>
<tr>
<td>Filtration surgery rate</td>
<td>0.01</td>
<td>-0.98</td>
<td>0.96</td>
</tr>
<tr>
<td>Medications dispensed</td>
<td>0.99</td>
<td>0.91</td>
<td>0.90</td>
</tr>
<tr>
<td>Prostaglandin analogue per 100</td>
<td>0.91</td>
<td>0.90</td>
<td>0.90</td>
</tr>
<tr>
<td>Carbonic anhydrase inhibitor per 100</td>
<td>0.90</td>
<td>0.89</td>
<td>0.89</td>
</tr>
<tr>
<td>(\alpha_2)-Agonist per 100</td>
<td>0.89</td>
<td>0.89</td>
<td>0.89</td>
</tr>
<tr>
<td>Ophthalmologists rate*</td>
<td>-0.95</td>
<td>0.90</td>
<td>0.90</td>
</tr>
<tr>
<td>Optometrists rate*</td>
<td>0.998</td>
<td>-0.93</td>
<td>0.94</td>
</tr>
</tbody>
</table>

*Indicates rate during 1997 and thereafter.

There has been a substantial decrease in the number of trabeculectomies in Ontario coinciding with the introduction of medications for the treatment of glaucoma in December 1996. This change highly correlated with the introduction of prostaglandin analogues and the decreasing number of trabeculectomies from 1997 through 2004.

Previous publications of the trends in glaucoma surgery showed a 15% to 73% decrease in the number of glaucoma surgical procedures across various periods from 1994 through 2003. The medical system in Canada is government funded and managed provincially. Virtually all residents have a provincial health card that must be presented to receive medical services funded by the provinces; therefore, there is an accurate registry of all surgical procedures performed on Canadian residents.
We found that the total number of trabeculectomies in Ontario increased by 52.6% from 1992 through 1997 and then remained stable for the remainder of the study (Figure 1). We calculated the estimated population at risk of having glaucoma in Ontario by using a composite POAG prevalence curve. When we corrected for changes in the population, we found that the number of trabeculectomies per 1000 individuals at risk for POAG increased by 37.7% from 1992 to 1996 and then steadily decreased by 17.0% to 2004 (2.7% decrease per year), similar to the trends indicated in other studies.2,4,5,20-23

When changes are observed in the volume of a given surgical procedure, multiple factors are potentially responsible, including changes in disease management, accessibility to operating room time, reimbursement rates, incidence and prevalence of a disease, and changes in patient and physician perceptions regarding treatment options. Paikal et al4 proposed that the introduction of brimonidine and latanoprost could affect the rate of trabeculectomies and trabeculoplasties performed. In Scotland, Bateman et al2 found an increase of 24.9% in prescribed glaucoma medications per 1000 population estimated to have glaucoma from 1994 through 1999. By 1999, only the beginning of the effect of these medications would be realized. In a recent study published in Australia, the number of prescriptions issued to treat glaucoma increased by 73.2% from 1992 to 2003.7 In the Netherlands, van der Valk et al21 found a decrease of 45% in the number of glaucoma surgical procedures from 1997 (the introduction year of topical CAIs) until 2000. From 2000 on, the number of surgical procedures stabilized. The total number of prescriptions increased by 20% in 1999 compared with 1998 in the Dutch study.

We found an increase of 91.5% in the number of glaucoma medications prescribed in Ontario from 1992 through 2004. During this time, the estimated prevalence of glaucoma in the population of Ontario increased 33.7%. From 1992 through 1996, the total number of glaucoma medications dispensed in Ontario increased 22.3%. After the introduction of several new glaucoma medications since December 1996, the number of medications dispensed increased by 56.6% until 2004. Explanations for the increase in the total number of glaucoma medications dispensed include the improved and maintained ocular hypotensive efficiency of the newer glaucoma medications, improved compliance, and more patients being treated with lower target pressures.2

Walland5 presented a decrease of 57.6% in rates of trabeculectomy surgery during the studied period and a 61.7% decrease if measured from the peak rate in 1996. He assumed that increased medical treatment mirrored the decrease in surgical procedures but was unable to correlate this trend statistically. Our findings that prescribing changes have been accompanied by a reduction in the number of trabeculectomies in the same period suggest an association with the effectiveness of the new glaucoma medications that has been sustained across the period.

Our data were analyzed statistically for correlations between time in years, filtration surgery rates, total medications dispensed, and specific drug groups. The results are presented in Tables 2 and 3.

### Table 2. Regression Analyses for Filtration Surgery Rates, Year, and Total Prescriptions Dispensed of Glaucoma Medications

<table>
<thead>
<tr>
<th>Regression Model</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>t Statistic</th>
<th>P Value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>4.82</td>
<td>1.74</td>
<td>2.76</td>
<td>.07</td>
<td>−0.74 to 10.37</td>
</tr>
<tr>
<td>Drugs per million</td>
<td>−0.005</td>
<td>0.003</td>
<td>−1.50</td>
<td>.23</td>
<td>−0.005 to 0.01</td>
</tr>
</tbody>
</table>

### Table 3. Regression Analyses for the Association Between Specific Drug Groups and Filtrations Surgery Rate, Controlling for Year and Total Drugs Dispensed

<table>
<thead>
<tr>
<th>Regression Model</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>t Statistic</th>
<th>P Value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostaglandin analogues</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year</td>
<td>3.87</td>
<td>0.83</td>
<td>4.65</td>
<td>.002</td>
<td>1.95 to 5.80</td>
</tr>
<tr>
<td>Drugs per million</td>
<td>−0.003</td>
<td>0.001</td>
<td>−2.36</td>
<td>.03</td>
<td>−0.005 to −0.001</td>
</tr>
</tbody>
</table>

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cations dispensed, and each new medication group (Table 1). The correlations among the percentages of different drugs were high, which may be because the values of each are zero before 1996 before they were introduced. The filtration surgery rates were not strongly associated with any one of the other variables, r<0.35 in all cases. Our statistical analysis across the 12 years of the study revealed that the filtration rate was not strongly associated with drug use, controlling for year. Analysing the data separately for 1992 to 1996 and from 1997 to 2004 showed a trend of increased filtration surgery rate before 1997 and decreased filtration surgery rate after 1997. This analysis, however, is limited by the small number of observations.

We used regression models to examine the association of specific medication classes as a percentage of total medications dispensed, controlling for overall medications dispensed and year (Table 3). We found a strong correlation between the decreasing number of trabeculectomies and the increase in medications dispensed. These analyses look at the role of the changing percentage of the total medications dispensed attributable to each of the 3 classes of new glaucoma medications, controlling for year and total medications dispensed. Only the model including prostaglandins was strongly significant (P<.001; 95% CI, −0.87 to −0.40). However, because the increase in prostaglandins was large (44 times), this result, although statistically significant, may not have been due to a cause-and-effect relationship.

In contrast to the number of trabeculectomies, the annual number of cataract surgical procedures per 1000 population with cataract in Ontario increased from 64.6 in 1992 to 109.4 in 2003 (69.3% increase; 6.0% increase per year).24 These data suggest that economic influences or changes in disease management (other than those related to the new medications) as factors that may influence the glaucoma surgery trend. They showed that the changes in reimbursement rates in the US Medicare population were not responsible for the decrease in glaucoma surgical procedures in this population.

In Ontario, the reimbursement rates for cataract and filtration surgery did not dramatically change from 1992 to 2004. Filtration procedures in Ontario are reimbursed at approximately 70% of the rate for cataract surgery. The surgical time is longer than that of cataract surgery and has a more demanding postoperative schedule, which may have some influence on the rates, although this is hard to prove.

Strutton and WALT included economic influences or changes in disease management (other than those related to the new medications) as factors that may influence the glaucoma surgery trend. They showed that the changes in reimbursement rates in the US Medicare population were not responsible for the decrease in glaucoma surgical procedures in this population.

Another factor that may affect the filtration surgery rates is the number of ophthalmologists and optometrists. We found a strong correlation between the number of ophthalmologists in Ontario and the decreasing filtration surgery rates after 1997. These data were more complicated when we used regression analysis to see if the supply of ophthalmologists was associated with the relation between trabeculectomies and the proportion of prostaglandin analogues among the drugs used after 1997. The growing number of optometrists probably has some influence on the referral of patients with glaucoma. We found a negative association between the number of optometrists and the decreasing number of trabeculectomies.

There are some limitations to this study. The filtration surgery numbers include all filtration procedures such as trabeculectomies, combined cataract and trabeculectomy, and seton surgical procedures. In addition, we are not able to discriminate on the basis of glaucoma diagnosis. To understand these rates, one must consider population data and changes in age distribution. Because POAG represents a significant proportion of glaucoma cases and prevalence estimates have been defined previously for this group, we thought this would be a reasonable denominator to consider, understanding the limitations. We found a 17.0% decrease in the number of trabeculectomies since the introduction of new medications for the treatment of glaucoma in December 1996. This decrease was sustained until March 2004, the most recent data available. We found a strong statistical correlation (P<.001) between the increasing number of new medications dispensed (with the prostaglandin medications representing the majority of newly dispensed treatments) and the decreasing number of trabeculectomies. The most likely explanation for this change is the improved effectiveness of ocular hypotensive therapy. It remains to be seen if this trend will be maintained across time.

Submitted for Publication: October 17, 2005; final revision received January 30, 2006; accepted March 14, 2006.

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Financial Disclosure: The authors do not have any commercial or proprietary interest in any of the products mentioned in the article.

REFERENCES

4. Paikal D, Yu F, Coleman AL. Trends in glaucoma surgery incidence and reim-

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