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Surveillance of Glaucoma Medical Therapy in a Glasgow Teaching Hospital: 26 Years Experience

M.Q. Rahman[1], D.M.I. Montgomery[2], M.N. Lazaridou[1]

Corresponding author:

D.M.I. Montgomery,
Department of Ophthalmology,
Glasgow Royal Infirmary,
Glasgow,
U.K.

Email: Donald.Montgomery@ggc.scot.nhs.uk
Telephone: 0141 211 5537
Fax: 0141 211 1220

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1. Tennent Institute of Ophthalmology, Gartnavel General Hospital, Glasgow, U.K..
2. Department of Ophthalmology, Glasgow Royal Infirmary, Glasgow, U.K.

Surveillance of Glaucoma Medical Therapy in a Glasgow Teaching Hospital: 26 Years Experience

Abstract

Aims

To report the initial findings of a unique database of 956 patients with ocular hypertension (OHT), normal tension glaucoma (NTG), and primary open angle glaucoma (POAG) attending the Glaucoma Clinic of Glasgow Royal Infirmary.

Method

The database contains retrospective data from 1981, and prospective data from 1999. Analyses have been carried out using specially written queries to generate reports relating to prescription trends and reasons for treatment discontinuation.

Results

Numbers of patients: POAG: 580, OHT: 242, NTG: 134. Of 2928 treatment change episodes recorded, failure to reach or maintain a target IOP accounted for 51.9%, while adverse effects accounted for 22.1%. Latanoprost use increased sharply since 1996, and brimonidine, betaxolol and dorzolamide, use has declined significantly. Bimatoprost had a higher rate of discontinuation due to adverse effects (25%) than travoprost (16.3%), or latanoprost (12.4%), but this was only statistically significant between latanoprost and bimatoprost (p=0.0038). In 2000 the database informed the introduction of a new treatment protocol that resulted in a fall in discontinuations due to adverse effects by almost two thirds.

Conclusion

A large and unique treatment database has been established at the Glaucoma Clinic of Glasgow Royal Infirmary. Containing data spanning a 26 year period, it promises to be an invaluable resource for audit and research and has already demonstrated its worth by informing changes in prescribing practice that have resulted in direct patient benefit.

Key words: Glaucoma, Database, Treatment Change

Introduction

Glaucoma is a group of insidiously progressive diseases affecting the optic nerve. Many patients are unaware they have glaucoma until adverse effects on vision, including reduced visual fields and contrast sensitivity, are noticed. At this point irreversible damage to the optic nerve has occurred.(1) For many years medical therapy has been the mainstay of treatment of glaucoma, and in the mid 1990s several novel topical intraocular pressure (IOP) lowering agents were introduced. A large and unique computerised database was established in 1999 at a single consultant`s (DMIM) glaucoma clinic at Glasgow Royal Infirmary, with the main aim of investigating the tolerability of these drugs. This paper presents an overview of the database, and reports its initial clinical observations with regard to trends in glaucoma medical therapy over a 26 year period, analysis of the reasons for changing medications, and an initial comparison of the newer prostaglandin analogues. We also discuss the potential of the database as a tool for audit and research.

Subjects and methods

The database was designed using Microsoft Access with the intention of collecting information on all patients who had undergone, or were undergoing, medical treatment for ocular hypertension (OHT), normal tension glaucoma (NTG), or primary open angle glaucoma (POAG). In 1999 the database was populated with retrospective data abstracted from medical records dating from as early as 1981, according to the algorithm in Figure 1. Information collected for each patient at start of treatment included the following: patient identification number; date of birth; sex; diagnosis; starting treatment and date commenced. If a subsequent visit resulted in no alteration of treatment, the date of the visit was simply logged. If an alteration did occur, this was documented in the database along with detailed reasons for the change. Since 1999, the database has been updated prospectively for all new and existing patients at every clinic visit. It currently contains complete treatment histories on 956 patients, representing over 7000 patient treatment years. Data are saved securely on a central server and may be accessed simultaneously from multiple clinic based computers. Analyses have been carried out using specially written queries to

generate reports relating to prescription trends and reasons for treatment discontinuation.

Results

The database population has a mean age of 73.7 years and comprises 58% females and 42% males. The number of patients with each diagnosis is POAG: 580, OHT: 242, NTG: 134. Using the database, the trends in glaucoma medication use were investigated from 1988 onwards and these are shown in figure 2a. As can be seen, a number of new drugs introduced in the mid 1990s were rapidly adopted. The use of latanoprost increased particularly sharply following its introduction in 1996, and for many years it has been the most commonly used topical glaucoma medication in our clinic. Other drugs, such as brimonidine, betaxolol and dorzolamide, are notable for their decline in use since the late 1990s.

The trend in the number of drugs used per patient has also been determined from the database (figure 3a). There was an initial sharp increase between 1995 and 1998, coinciding with the introduction of dorzolamide, latanoprost and brimonidine, followed by a more steady increase in the number of drugs per patient. Fortunately this trend has been offset by the subsequent introduction of combination therapies, resulting in a decrease in the average number of preparations used per patient.

A total of 2928 treatment change episodes were recorded and the reasons for these are displayed in Figure 3b. Failure to reach or maintain a target IOP level were the biggest factors in determining a change of medication accounting for more than half the total (51.9%). In almost a quarter of patients (22.1%) adverse effects of the drug used prompted a change in medication. Ten percent of changes were as a result of treatment being discontinued following drainage surgery, while 5% were accounted for by treatment subsequently being reinstated following relative failure of surgery. Perceived disease progression, either on the basis of visual field or optic disc change, was recorded as the reason for change in only 6%.

Individual medications were also investigated to determine their discontinuation rates due to all adverse effects (Table 1a).

DRUG	Patients discontinuing due to all adverse effects	Patients discontinuing due to allergy
Brimonidine	46.9%(170/362)	32.3%(117/362)
Levobunalol	45.4% (10/22)	31.8% (7/22)
Cosopt	38.5%(47/167)	12.5%(21/167)
Trusopt	31.4%(68/216)	15.7%(35/216)
Pilocarpine	27.2%(12/44)	6.8%(3/44)
Bimatoprost	25%(21/84)	5.9%(5/84)
Dipivefrine	23%(12/52)	11.5%(6/52)
Dorzolamide	22.7%(67/295)	11.5%(34/295)
Betaxolol	19.2%(61/318)	5.9%(19/318)
Timoptol	17.4%(62/356)	3.1%(14/356)
Travoprost	16.3%(17/104)	5.7%(6/104)
Brinzolamide	13.5%(49/362)	4.4%(16/362)
Latanoprost	12.4%(91/729)	4.5%(33/729)
Xalacom	12%(23/192)	3.1%(6/192)
Acetazolamide	8.5%(3/35)	0%(0/35)
Combigan	0%(0/3)	0%(0/3)
Duotrav	0%(0/5)	0%(0/5)
Ganfort	0%(0/4)	0%(0/4)
Iopidine	0%(0/1)	0%(0/1)

Table 1a: Drug discontinuations

Levobunolol and brimonidine had the highest proportion of discontinuations due to adverse effects, whilst latanoprost and xalacom were the topical medications having the lowest. Brimonidine also had the highest proportion of patients discontinuing due to allergy.

The treatment protocol that was implemented in our clinic in 1997 is shown in figure 4a. This attempted to arrange the newer agents in a hierarchy, with brimonidine selected as the favoured second line agent following beta blockers. Initial audit using the database, however, quickly revealed an unacceptable increase in the discontinuation rate due to adverse effects in the years that followed. It was clear that brimonidine and dorzolamide were particularly implicated and these findings

informed the introduction of a new protocol in 2000 (figure 4a). This also recognized the growing body of evidence for the efficacy, safety and tolerability of latanoprost as a first line agent. The effect of this change in the treatment protocol can be seen in figure 4b. From 1997 to 2000, there was a two fold increase in the number of discontinuations per treatment year ($p<0.0001$, two-sided Chi squared test). However, in the 4 year period following the introduction of the treatment protocol, the rate of discontinuations fell to almost a third of the level previously seen ($p<0.0001$, two-sided Chi squared test). This downward trend has since continued.

Discussion

Although there have been several studies looking at trends in the use of topical glaucoma medications, these have been exclusively retrospective analyses(2, 3). The database described in this report was designed to allow continuous prospective surveillance of medical therapy and contains 9 years of prospective data (1999 to present day) as well as retrospective data (from 1981-1999). Containing complete treatment histories of 956 patients, this database is, to our knowledge, unique. By facilitating audit of medical management, it has led to evidence based modifications to treatment protocols that have directly benefited patients in our patient population.

Our study shows that there has been an inexorable increase in drug prescription rates over the past 2 decades. In particular, since their introduction in the mid 1990s, there has been a sharp rise in the use of prostaglandin analogues, as has been described in previous studies.(2, 4) This probably reflects their ease of use, their tolerability, and their effectiveness at lowering IOP. Latanoprost has been the most prescribed drug in our clinic (Table 1b); it was used by more than twice as many patients as the next most prescribed drug brinzolamide.

DRUG	Number of patients taking drug
Xalatan	729
Alphagan	362
Brinzolamide	362
Timoptol	356
Betaxolol	318
Azopt	295
Trusopt	216
Xalacom	192
Cosopt	167
Travoprost	104
Bimatoprost	84
Dipivefrine	52
Pilocarpine	44
Levobunalol	22
Acetazolamide	35
Duotrav	5
Ganfort	4
Combigan	3
Iopidine	1

Table 1b: The number of patients ever on a drug

Latanoprost was the first prostaglandin analogue to be introduced in the U.K., and this undoubtedly has helped it secure a dominant market share: 46.1% of the UK glaucoma cash market, and 30.9% globally.(5) Our experience with other prostaglandin analogues is more limited and we should perhaps be wary of making direct comparisons. Nevertheless, according to our study, bimatoprost had a higher rate of discontinuation due to adverse effects (25%) than either travoprost (16.3%), or latanoprost (12.4%). A statistically significant difference could, however, only be seen when comparing latanoprost with bimatoprost (p=0.0038, two-sided Fisher's exact test). No statistically significant difference could be seen between travoprost and latanoprost (p=0.275, two-sided Fisher's exact test). Moreover, no significant difference could be seen between any of the prostaglandin derivatives studied when comparing discontinuations due to allergy.

A number of studies have examined persistency rates of glaucoma medications, but these have been retrospective analyses of administrative claims data (6, 7). Although such studies are able to broadly identify individual drugs and assess persistence and

discontinuation, they are unable to elucidate reasons why medications may have been stopped or changed. Such reasons may include patient specific factors, such as drug allergy or other side effects, but may also be due to physician specific factors, such as failure to reach or maintain a target pressure. Our database was specifically designed to allow evaluation of these factors, and hence this is a strength of our study. Our finding that over half of treatment changes were related to inadequate efficacy, with almost a quarter due to adverse effects, is a reminder that the ideal glaucoma medication has yet to be produced.

The short term nature of many previous studies assessing glaucoma medications may render extrapolation of results to long term clinical outcomes difficult (8). Our database, however, has enabled the study of patient responses to medication over extended periods of time and has the potential to reveal long term problems with specific drugs. Hypersensitivity reactions, for example, may take several years to manifest and the incidence of allergy to brimonidine was significantly underestimated by early short term studies (9, 10). A detailed long term study of the timing of episodes of allergy using our database not only helped to highlight the true extent of this issue with brimonidine but also provided evidence that brimonidine allergy may potentiate hypersensitivity to subsequently prescribed agents(11).

By adapting treatment protocols in the light of audit findings, we have been able to greatly reduce the frequency of treatment discontinuations triggered by adverse effects (figure 4b). Clearly this reflects a reduction in morbidity that is of immediate benefit to patients. We might also speculate that better tolerated treatment regimens are likely to result in improved patient compliance. Adverse effects of medication often result in additional clinic visits being necessary to implement alternative treatment and to assess its effectiveness. Consequently adverse effects are detrimental not only to the individual patient; they are also costly in terms of the additional drain they impose on healthcare resources. Such potential hidden costs should not be neglected by policymakers and clinicians, when considering the cost-effectiveness of medical therapies and when drawing up guidelines for their use.

Our database does not document intraocular pressure readings. It was felt at the outset that necessitating the recording of IOP would render the database too cumbersome,

and too time consuming to maintain in the routine clinical setting. Though this might be perceived as a weakness of the system, the view taken was that detailed documentation of switches in treatment would provide a global indicator of physician and patient satisfaction that would encompass both clinical efficacy and tolerability. The database can, however, be used to identify patients for further investigation of IOP responses to medications; previous work based on our database demonstrated a 2.6 mmHg drop in IOP when switching from latanoprost to latanoprost/timolol fixed-combination therapy.(12) It should also be noted that this study has been limited to one centre, so some of the findings may not be applicable to other practices and other patient populations.

In conclusion, a large and unique treatment database has been established at the Glaucoma Clinic of Glasgow Royal Infirmary. Containing data spanning a 26 year period, it promises to be an invaluable resource for audit and research, and has already demonstrated its worth by informing changes in prescribing practice that have resulted in direct patient benefit.

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Competing Interest: None declared.

Figure 1: Glasgow Royal Infirmary glaucoma database patient information algorithm.

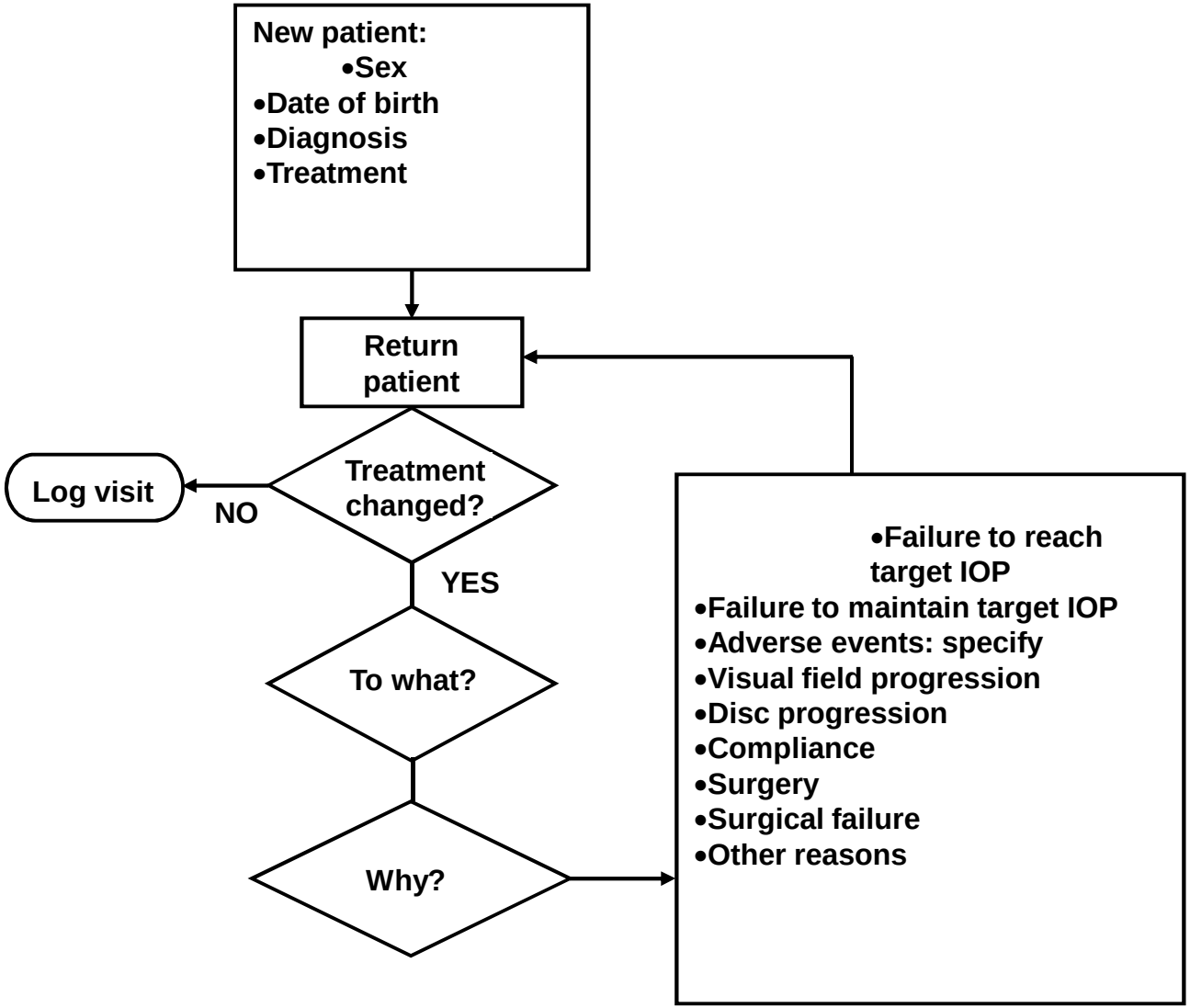

Figure 2: Trends in Drug use

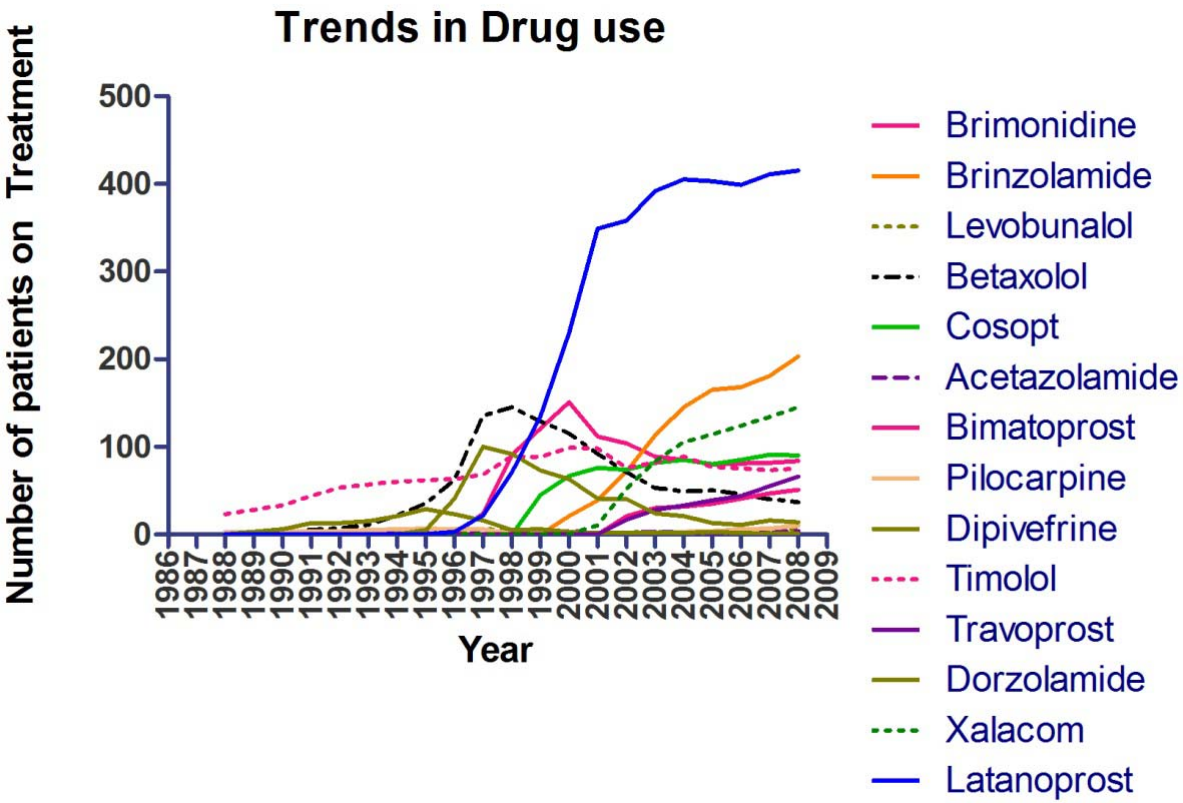

Figure 3a: The trend in the number of drugs used per patient

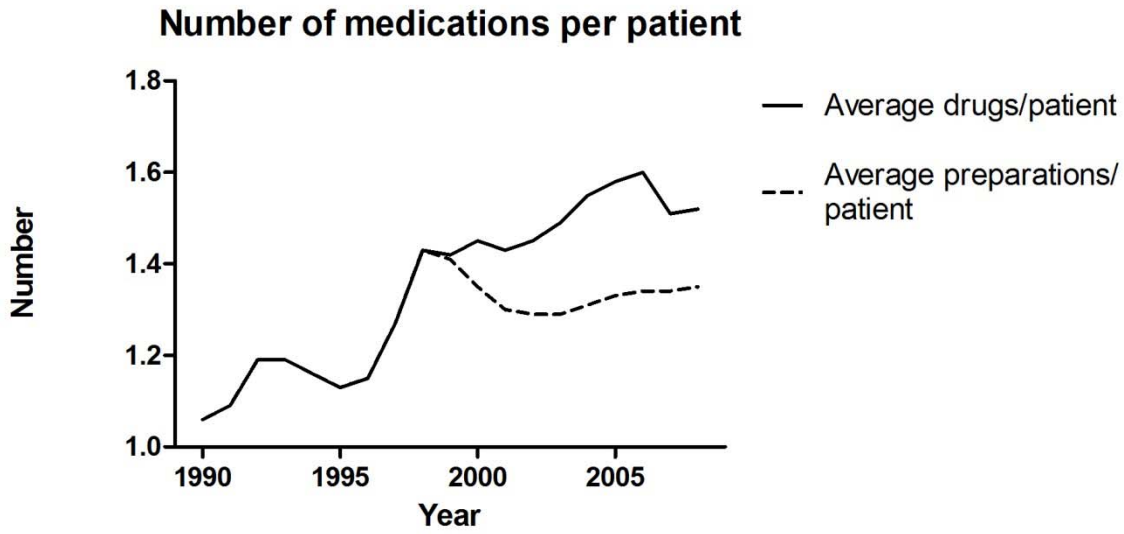

Figure 3b: The reasons for treatment change

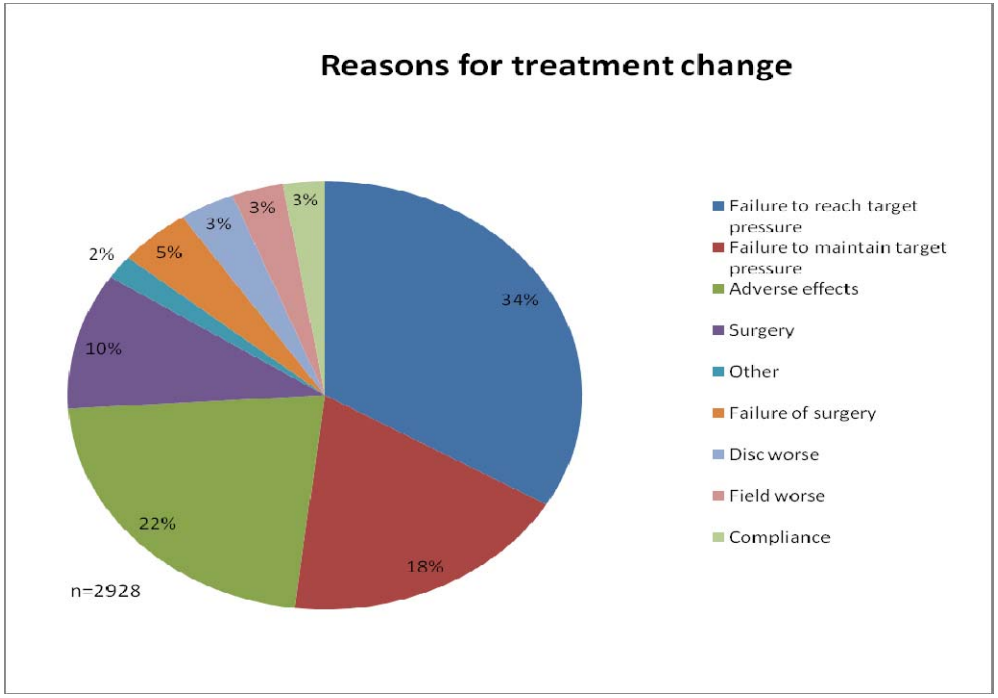

Figure 4a: Treatment Protocols in 1997 and 2000

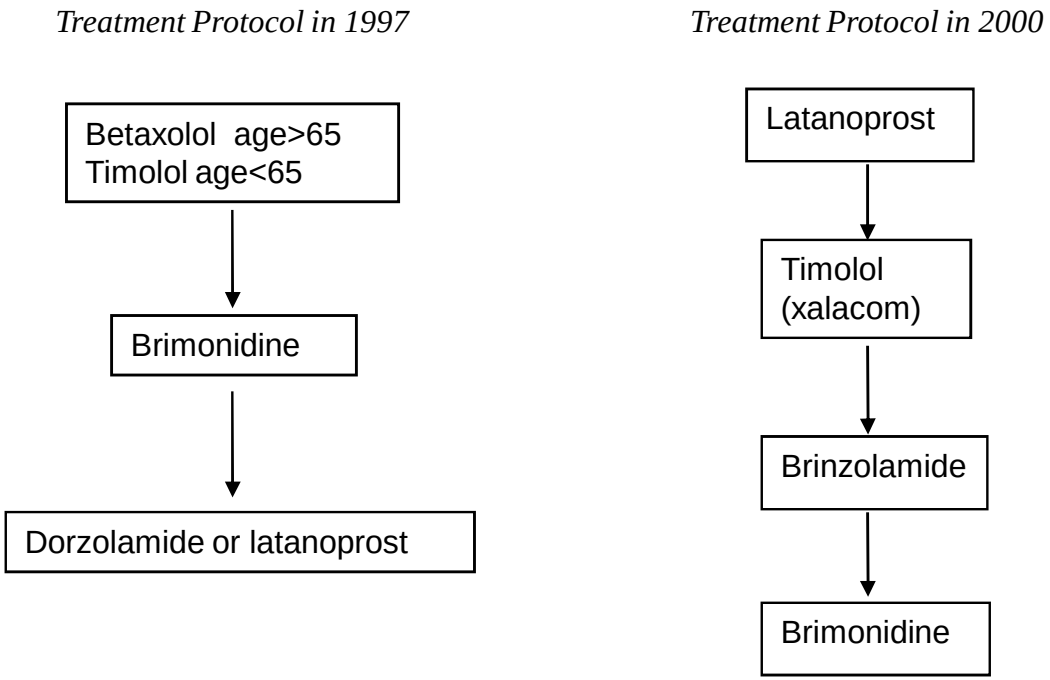
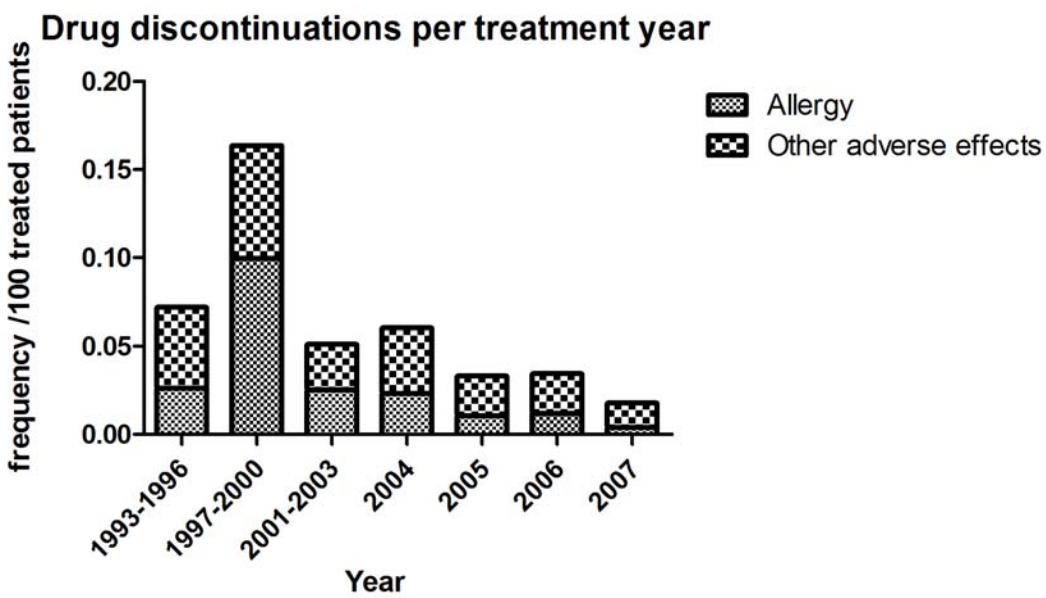
Figure 4b: Drug Discontinuations per treatment year