Glaucoma and Sleep Apnoea: Is there a Link? A Review

Shandell Moore, BOrth&OphthalSc(Hons)
Linda Malesic, BOrth(Hons)PhD

Department of Clinical Vision Sciences, La Trobe University, Melbourne, Australia

ABSTRACT

Glaucoma is one of leading causes of vision loss in Australia. There are well documented and accepted risk factors associated with glaucoma such as family history, high myopia, diabetes and if an individual is of black decent. It is only since the turn of the 21st century that researchers have attempted to establish if there is a link between glaucoma and sleep apnoea and whether this too could be a risk factor in the pathogenesis of glaucoma. The cause of glaucoma and damage to the optic nerve head due to sleep apnoea remains unclear, however, it has been postulated that a decrease in optic nerve head blood flow occurs during the prolonged apneic episodes leading to ischemia, just as occurs in low tension glaucoma. This review will discuss key studies that have researched the prevalence of sleep apnoea in individuals who have glaucoma and discuss whether sleep apnoea should be considered a risk factor in the pathogenesis of glaucoma.

Keywords: glaucoma, sleep apnoea, low tension glaucoma, risk factor, retinal vasculature

GLAUCOMA AND ITS PATHOGENESIS

Glaucoma is a group of eye diseases which result in characteristic damage to the optic nerve and associated visual field loss that may be caused by a number of pathological processes[1]. Glaucoma is a major eye health problem throughout the world and is said to be the second leading cause of vision loss, affecting over 160,000 Australians[2].

Two potential theories into the pathogenesis of glaucoma have been described; a mechanical and a vascular theory[3]. The mechanical theory proposes that a rise in intraocular pressure (IOP) results in compression of the optic nerve and damage to the retinal cells[3]. This theory supports a number of glaucomatous conditions such as pseudoexfoliation syndrome (PXF), pigmentary dispersion syndrome (PDS), neovascular glaucoma and primary-open angle glaucoma[4]. There is resistance to aqueous outflow through the trabecular meshwork which causes a rise in intraocular pressure, it is this that leads to the development of glaucoma and damage to the optic nerve through compression[5]. However, not all elements of glaucoma can be explained through the rise in IOP. Low tension glaucoma (LTG) can be described as the glaucoma that develops despite no rise in IOP due to a decrease in the vascular supply to the optic nerve causing damage[3]. This type of glaucomatous damage can be described by the vascular theory, where there is a lack of blood supply to the optic nerve head causing death to the retinal nerve fibres due to an increase in vascular resistance which decreases blood flow to the smaller capillary fibres that supply the optic nerve[6].

GLAUCOMA RISK FACTORS

There are well documented and accepted risk factors associated with glaucoma. It is important to recognise these risk factors in individuals to promote early detection and treatment to prevent irreversible blindness, as well as to increase awareness so that individuals understand which risk factors leave them susceptible to the development of glaucoma. An individual with a family history of glaucoma increases their risk of development by up to 9 times, and up to 6 times if they are over the age of 60[7]. Other risk factors include high myopia, diabetes, hypertension, migraines and if they are of a black decent[8]. Like diabetes and hypertension, sleep apnoea also affects blood flow to and around the optic nerve[6], secondary to the apneic episodes which occur whilst an individual sleeps[9]. It is only since the turn of the twenty-first century that researchers[10-16] have tried to establish if there is a link between glaucoma and sleep apnoea and

Correspondence: **Shandell Moore**
Department of Clinical Vision Sciences, La Trobe University, VIC 3086, Australia
Email: shandellmoore@hotmail.com

whether this too could be a risk factor in the pathogenesis of glaucoma.

SLEEP APNOEA AND ITS EARLY ASSOCIATION WITH GLAUCOMA

It is estimated that 2% of women and 4% of male adults suffer sleep apnoea in America[17] and up to 80-95% of adults have undiagnosed sleep apnoea in Western countries[17]. Sleep apnoea is characterized by repeated episodes, in which a sufferer ceases breathing during sleep for periods of up to 2 minutes due to upper airway obstruction, which are terminated only after awakening from sleep[17]. An individual may not be aware of their sleep apnoea despite these apneic episodes which can occur hundreds of times throughout one night[18]. This disrupts the individual's quality of sleep which leads to excessive daytime sleepiness, insomnia and fatigue due to this non-restorative sleep[18].

The early work of Walsh and Monplaisir[19] sparked interest into sleep apnoea and the development of glaucoma. Walsh and Montplaisir conducted a study that looked at sleep apnoea combined with glaucoma in two generations of a family, and found that 5 members of this family in fact had this combination. However, it could be said the risk factor of family history may have played a more influential role in the development of glaucoma in this sample of participants than the sleep apnoea. Despite this, it was hypothesised that a change in venous pressure during apneic episodes of sleep apnoea causes intraocular pressure to rise causing the glaucoma[20]. Since this novel study Walsh & Montplaisir, it has taken almost 20 years for other researchers[10-16] to re-visit the link between glaucoma and sleep apnoea. The cause of glaucoma and damage to the optic nerve due to sleep apnoea remains unclear, however, it has been postulated[11-13] that a decrease in optic nerve head blood flow occurs during the prolonged apneic episodes leading to ischemia, just as occurs in LTG.

Recent review articles in this area[9, 21], are either written in a foreign language[21] or do not focus specifically on to the effect of sleep apnoea and the development of glaucoma but rather the effects on the eye in general[9]. This paper appears to be the first to review a number of selected key articles on sleep apnoea and whether it's a risk factor in the pathogenesis of glaucoma.

SLEEP APNOEA AS A GLAUCOMA RISK FACTOR

Marcus et al.[15] aimed to determine the prevalence of sleep breathing disorders and whether this could be a risk factor in patients with LTG. Marcus et al., recruited 23 participants with LTG, 14 were LTG suspects and 30 participants who had no ocular pathology served as the control group. All participants were over the age of 60. A series of questions based on sleeping habits were administered to all participants to ascertain sleep history, in terms of being a snorer or possibility of having sleep apnoea. A physician then graded the participants as having a positive or negative sleep history based on their answers. Those with a positive sleep history were offered an overnight polysomnography. Nine of the LTG participants and 4 of the LTG suspects chose to undergo the overnight polysomnography. The results from the polysomnography diagnosed 5 of the 9 participants with LTG and 2 of the LTG suspects with sleep apnoea. Marcus et al, concluded that sleep breathing disorders may be a risk factor in the pathogenesis of glaucoma. The researchers used the title of sleep breathing disorders, however focused on the prevalence of sleep apnoea in their participants, therefore not being clear to the reader what they were actually investigating, sleep breathing disorders or solely sleep apnoea. Throughout their conclusion they referred to their findings and higher prevalence to be attributable to the sleep breathing disorders as a group of problems; however their results appeared to concentrate on the diagnosis of sleep apnoea. In addition, not all participants who were diagnosed with a positive sleep history underwent the polysomnography which questions the validity of their findings. Nonetheless, the frequency of positive sleep histories was higher in the LTG groups (diagnosed or suspects) when compared to the control group. However, this high rate of positive sleep histories may have resulted from the interview questions used in this study. The test may not have been sensitive enough to detect sleeping problems which would lead to a positive sleep history and possibly sleep apnoea.

Sergi et al,[16] attempted to determine the prevalence of LTG in recently diagnosed sleep apnoea sufferers. The methodology of Sergi et al, built on Marcus et al,[15] by recruiting participants who had been diagnosed with sleep apnoea and which of those had undiagnosed LTG, rather than the reverse which was used in Marcus et al.'s study. This strengthened the findings of this study with respect to the relationship between sleep apnoea and its effects of developing LTG. Sergi et al, recruited 50 recently diagnosed sleep apnoea sufferers and 40 healthy controls. They all underwent an ophthalmological assessment including IOP, Humphrey visual field analysis (HVFA), cup-to-disc ratio analysis to diagnose LTG. Three of the 50 (6%) sleep apnoeic participants were diagnosed with LTG compared to none of the controls. This result when compared to the prevalence of 2% in the Caucasian population over the age of 40[2] signifies that sleep apnoea may ultimately be a risk factor in the development of LTG. In fact, based on the findings by Sergi et al. the researchers propose that there is a possibility that an individual with sleep apnoea is twice more likely to develop LTG.

Using a larger cohort of patients, Girkin, McGwin, McNeal & Owsley[14] retrospectively audited the medical histories of 667 males over the age of 50 years, to note the date they

were diagnosed with POAG and whether this correlated with the time they were diagnosed with sleep apnoea, if at all. Despite females sharing in the 5% prevalence of sleep apnoea in Western Countries[17], they were excluded from the study as the researchers stipulated that a meaningful analysis could not be achieved with the small sample number of females identified. Girkin, McGwin, McNeal & Owsley found that there was a weak correlation between sleep apnoea and the development of POAG. The correlation coefficient was 0.76, which proved borderline significance. No participant in the age and sex matched control group that had pre-diagnosed sleep apnoea developed glaucoma by the end of the observation period, however this time frame was not specified in the research paper. Therefore it is not known to the reader if this was a long enough time frame for POAG to develop. Furthermore, it is important to note that the lack of blood flow and oxygen that does not circulate throughout the body during apnoeic episodes has an effect on the eye[9] is more likely to cause LTG due to damage to the optic nerve as a result of an insufficient vascular supply over time[15] as opposed to the individual developing POAG as a result of mechanical compression[13]. It is therefore possible for a higher prevalence to occur if the same methodology was used to analyse LTG.

Mojon, et al.[10] aimed at determining the prevalence of glaucoma, both POAG and LTG in sleep apnoea sufferers. The researchers used an ophthalmological assessment in combination with an overnight polysomnography to aid in their diagnosis of both types of glaucoma and sleep apnoea. The researchers included 114 participants who were referred for polysomnographic testing with suspected sleep apnoea. A history, visual acuity, applanation tonometry, slit lamp examination evaluating the anterior segments; gonioscopy and automated perimetry were performed. Mojon et al. calculated the prevalence of those being diagnosed with some degree of sleep apnoea to be 60.5% (69 from 114 participants) based on the overnight assessment. In this cohort of patients Mojon et al., found that 3 of the 114 participants had POAG and 2 with LTG. The 5 participants with either POAG or LTG were diagnosed with moderate or severe sleep apnoea. The prevalence for those diagnosed with glaucoma and sleep apnoea was therefore reported to be 7.2% (5 of the 69 participants with sleep apnoea). However, 3 of the 5 individuals with glaucoma had already been diagnosed prior to the research; therefore it is not clear if glaucoma resulted from the apneic episodes or from other glaucoma risk factors (i.e. family history). Although a history was taken, the findings from this did not lead to the exclusion of any of the participants, in particular those with other risk factors of glaucoma, such as cardiovascular disease. This limitation would suggest that the finding may reflect a skewed impression of the association of sleep apnoea and glaucoma. Moreover, when comparing the prevalence of glaucoma in patients with sleep apnoea found in this study (7.2%) to that of the general population over the age of 40 (2%)[2], the considerably higher prevalence of glaucoma in sleep apnoea sufferers questions the reliability of the findings.

To build to their previous work, Mojon and his colleagues investigated the prevalence of POAG[11] and LTG[12] in sleep apnoea sufferers as separate target groups. Mojon et al.[11] recruited 30 participants who had POAG and were admitted for an overnight polysomnography to determine if they had sleep apnoea. The researchers found the prevalence of sleep apnoea in those diagnosed with POAG to be 20% (6 of the 30 participants) which was reasonably high when compared to that of the control group of 11% (3 out of the 30 controls). A similar methodology was employed in the study by Mojon et al.[12] who recruited 16 participants with LTG for an overnight polysomnography to diagnose sleep apnoea. Mojon et al.[12] found that the prevalence was 44% (7 out of the 16 participants had sleep apnoea). Based on these findings, the researchers concluded that there is an association between glaucoma and sleep apnoea, but with a higher prevalence in those diagnosed with LTG as compared to POAG.

The difference in prevalence of sleep apnoea in POAG and LTG reported in Mojon's and his colleagues' studies may be better explained by the vascular theory on optic nerve damage in sleep apnoea sufferers than mechanical compression. However, the chosen methodology utilised by Mojon et al.[11] and Mojon et al.[12] is susceptible to a referral bias. In addition, it is difficult to include sleep apnoea as a risk factor for developing glaucoma when Mojon et al.[11] and Mojon et al.[12] observed individuals who have already been diagnosed with glaucoma. Consequently, a direct causal relationship between sleep apnoea and glaucoma is difficult to make. It would be beneficial to recruit a cohort of participants who have clinically diagnosed sleep apnoea and no glaucoma and observe those who develop POAG or LTG and compare them to a control group of healthy participants. This would better determine if sleep apnoea is a true risk factor in developing glaucoma. In addition, if treatment was given to these individuals with sleep apnoea, it may improve their glaucoma. It may decrease the damage that can occur at the optic nerve and it is this observation that may clarify the role that sleep apnoea plays in glaucoma[22].

Geyer, Cohen, Segev, Rath, Melamud, Peled & Lavie[13] also investigated the relationship between sleep apnoea and POAG but reported different prevalence rates as compared to Mojon's group[11]. They recruited, via a contact telephone conversation, 228 participants with previously diagnosed sleep apnoea. An ocular examination was scheduled to determine the prevalence of POAG in this population. The eye examination included applanation tonometry, gonioscopy, optic disc assessment and 24-2 automated perimetry testing. An overnight polysomnography was also used to confirm sleep apnoea. Geyer et al[13] found that 5 of the 228 participants had POAG, resulting in a 2% prevalence of

glaucoma in those individuals diagnosed with sleep apnoea. This finding is more in line with the prevalence of glaucoma in the general population (2%)[2]. The larger sample size would suggest a more realistic prevalence of sleep apnoea and glaucoma in the Geyer et al[13] study, however no control group was included as it was in Mojon et al's[11] study.

CONCLUSION

There is support in the literature[10-13, 15-16] for a relationship between sleep apnoea and glaucoma (POAG and LTG). However, sleep apnoea as risk factor for developing glaucoma is yet to be firmly established. Further research needs to be conducted to explore this relationship. A prospective aged matched control clinical trial investigating recently diagnosed sleep apnoea sufferers and the number of individuals that go on to develop glaucoma, particularly LTG in a large cohort of participants, would be beneficial. It would also be valuable to look at snoring and its effect on the eye, as snorers often develop sleep apnoea. Studying the effects of treating an individual's sleep apnoea and whether this prevents glaucoma from developing or minimises the progression of glaucoma, is also of interest and could be further explored.

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