

Investigating the effect of Habolzahab (Iranian medicinal products based on Sabr, Hallila and rose flower) on the intraocular pressure of patients with open-angle glaucoma: A randomized, double-blind clinical trial

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Abstract:

Introduction: Glaucoma is the name of a group of diseases that is characterized by irreversible optic neuropathy, which is in the form of depression and analysis of the connective and nerve tissue elements of the optic disc, which ultimately causes a specific pattern of visual impairment, in the form of loss of the visual field and blindness becomes. Scholars of traditional medicine had opinions and opinions in the field of recognition, description and treatment of eye diseases and definitions of functional terms, and almost all traditional medicine books deal with the diagnosis and treatment of eye diseases. The purpose of this research was to explain the glaucoma disease in Iranian medicine and compare the medicine of Hab-al Zahab with routine drugs on the intraocular pressure and symptoms of patients with glaucoma. In order to have a positive effect, this medicine can be recommended as a natural product made in Iran, for auxiliary treatment in patients.

materials and methods: This study was done in two stages, in the first stage of this study, there was a library of text analysis type And in the second step of this study, it was a double-blind clinical trial research. All patients aged 18-75 who referred to the eye clinic of Bo Ali Hospital were included in the study according to the inclusion and exclusion criteria. Data collected from patients who had a confirmed diagnosis by an optometrist and had chronic glaucoma under routine treatment. They were entered into spss21 software and analyzed.

Results: The results of data analysis showed that the average weight of the studied patients was 71.6 ± 10.3 and the average height was 166.1 ± 7.4 and their average age was 47.6 ± 13.6 years. 67.6% were women, 50% had a diploma or lower education level. 88.2% had no history of eye surgery. 51.5% had House keeping, 82.4% did not consume alcohol. The simultaneous effect of time in the studied groups and based on the Greenhouse test shows that there is no significant difference between the left eye pressure in the intervention and control groups ($p < 0.222$), The right eye pressure simultaneously in the study groups. And in the passage of time, they have a statistically significant difference ($p < 0.042$), There is a significant difference in the frequency of Shedding tears in the intervention and control groups ($p < 0.031$), There is no significant difference in the frequency of blurred vision in both groups ($p < 0.374$), The simultaneous effect of group and time shows a significant difference between the two groups of abdominal pain ($p = 0.019$), There is a significant difference in the rate of constipation reduction in both groups ($p < 0.014$).

If additional studies are confirmed, the use of habolzahab drug can reduce intraocular pressure in the long term as an adjunctive treatment along with routine drugs.

Conclusion : Medicinal plants along with latanoprost, timolol and dorzolamide drugs reduce intraocular pressure in people suffering from this disease.

Key words : Glaucoma, open-angle glaucoma, rose flower, Hallila, Sabr, Intraocular Pressure, Persian medicine

Introduction:

Glaucoma is the name of a group of diseases that is characterized by irreversible optic neuropathy, which is in the form of depression and analysis of the connective and nerve tissue elements of the optic disc, which ultimately causes a specific pattern of visual impairment, in the form of loss of the visual field and blindness becomes(1). Glaucoma is divided into two types, open-angle and closed-angle, each of which can be primary or secondary. Glaucoma is the second cause of blindness in the world and the cause of 12.3% of blindness in the world (2). The number of people with glaucoma will increase to 111.8 million by 2040 (3, 4). Nowadays, various Medicinal and surgical methods are used to treat glaucoma. Surgical treatments usually do not have long-term effectiveness and may lead to failure after some time and the need for subsequent surgeries is always there (5). drugs of choice to lower IOP, 1- There are beta-adrenergic Obstructive drugs, that Timolol can be mentioned from this category. 2- The category of carbonic anhydrase inhibitors, that Dorzolamide is a topical drug of this category. 3- Latanoprost, which is a prostaglandin analog which is very effective as the first choice of treatment or as an auxiliary drug together with another drug (6). Scholars of traditional medicine had opinions and opinions in the field of recognition, description and treatment of eye diseases and definitions of functional terms, and almost all traditional medicine books deal with the diagnosis and treatment of eye diseases. In addition to this, many specialized books on ophthalmology, such as Tazkire Al-Kahalin, Al-Kahala, Noor Al-Ayoun, and Jame Al-Funun, have been written in this field. In the study of eye diseases in Iranian medical books, It seems that the disease of glaucoma is consistent with the disease of increased Testis humidity. The increase of this moisture, which is located in front of the eye lens, A factor to protect the lens, and its disturbance is considered to cause blindness (7); And filling the nose (brain) and dropping the excrement from the nose (brain) into the eyes is considered the cause of most eye diseases. and diarrhea as long as it is not too much, useful for the eyes and for draining the nose (brain), Medicines containing Sabr and Hallila have been suggested (8). In the PDR book, sabr plant is mentioned as a laxative with antimicrobial, antiviral and anti-neoplasti properties (9). The results of the study by Khalil Banihabib and colleagues showed that the use of sabr yellow, which is the main composition of Habshabyar as a traditional Iranian medicine product, along with timolol Compared to the use of timolol alone, causes a significant decrease over time in the intraocular pressure of patients with primary open-angle glaucoma; As it was observed in the present study that the reduction of eye pressure in the first and second months was significant in the group consuming Habshabyar. while it was not significant in the control group (10). Laxatives in Iranian medicine have a special

place in the treatment of eye diseases, which is written in Iranian medicine books. The mechanism of action of Sabr and Halileh is based on the sources of Iranian medicine with the method of emptying excrement from the head, digestive system and other organs and It also relieves constipation and diarrhea, And it is prescribed in the treatment of most eye diseases in the sources of Iranian medicine And so far, there has been no study of the effect of medicine containing Sabr or Halila or both on glaucoma in modern medicine, which may have Good effectiveness in the treatment of glaucoma. The purpose of this research was to explain the glaucoma disease in Iranian medicine and compare the medicine of Hab-al Zahab with routine drugs on the intraocular pressure and symptoms of patients with glaucoma. In order to have a positive effect, this medicine can be recommended as a natural product made in Iran, for auxiliary treatment in patients.

materials and methods:

This study was done in two stages, in the first stage of this study, there was a library of text analysis type And based on the reliable sources of traditional Iranian medicine, it has been done in different periods such as Akbari tibbe(7), Zakhireye Kharazm Shahi(24), Elixir Azam(11), kholase al-Hikma and qanon(20). And in the second step of this study, it was a double-blind clinical trial research. which was done in the eye clinic of Bo Ali Hospital. The research population of this study is all patients aged 18-75 who referred to the eye clinic of Bo Ali Hospital, who had a confirmed diagnosis by an ophthalmologist and have chronic glaucoma under routine treatment (only drug (latanoprost, timolol and dorzolamide) were taken). The number of the research sample was considered by considering the total number of the statistical population and taking into account the sample loss of 68 people (34 patients who took medicine and 34 people who took placebo). The criteria for entering the study included being able to cooperate and answer our questions, informed consent to enter, not being allergic to patience medicine, not having acute glaucoma, not being pregnant and breastfeeding, and not taking Corticosteroid, thiazide, and diuretic drugs. The exclusion criteria include not meeting the inclusion criteria and cases that were want out from the study during the study and after randomization of the samples. The samples were randomly assigned to two drug intervention groups A= (N=34) and the placebo group P= (N=34). Demographic forms of patients were used to collect data. which included such things as headache, blurred vision, conjunctival congestion, shedding tears, dilated pupils, digestive disorders and It was measured and recorded according to observation, file and ask from the patient. To measure intraocular pressure, Goldman's tenometer was used, which is connected to a slate lamp device and is the most reliable among the instruments for measuring intraocular pressure. To analyze the results of

this research, T-Test statistical test was used for quantitative variables and if they did not have normal distribution, Mann-U-Whitney test was used. We measured the difference between the two groups for the variable of eye pressure and P-Value less than 5% was considered significant And to generalize to the society, the 95% CI of the Average pressure was group given in two reports and Also, the difference in the average variable of intraocular pressure in two groups was reported. According to repeated measurements, Analysis of variance with repeated measurements was used to analyze

quantitative variables. To analyze qualitative variables in two groups, we used chi-square test. SPSS 21 statistical software was used. The analysis method was ITT. Ethical standards of research Compliance in this study include; Informed consent from the participants and reminding the participants of this issue, The freedom of the participants to enter the study And was a refusal to continue cooperation at any stage of the study And The 31 codes of ethics were completely studied in scientific researches in medical sciences.

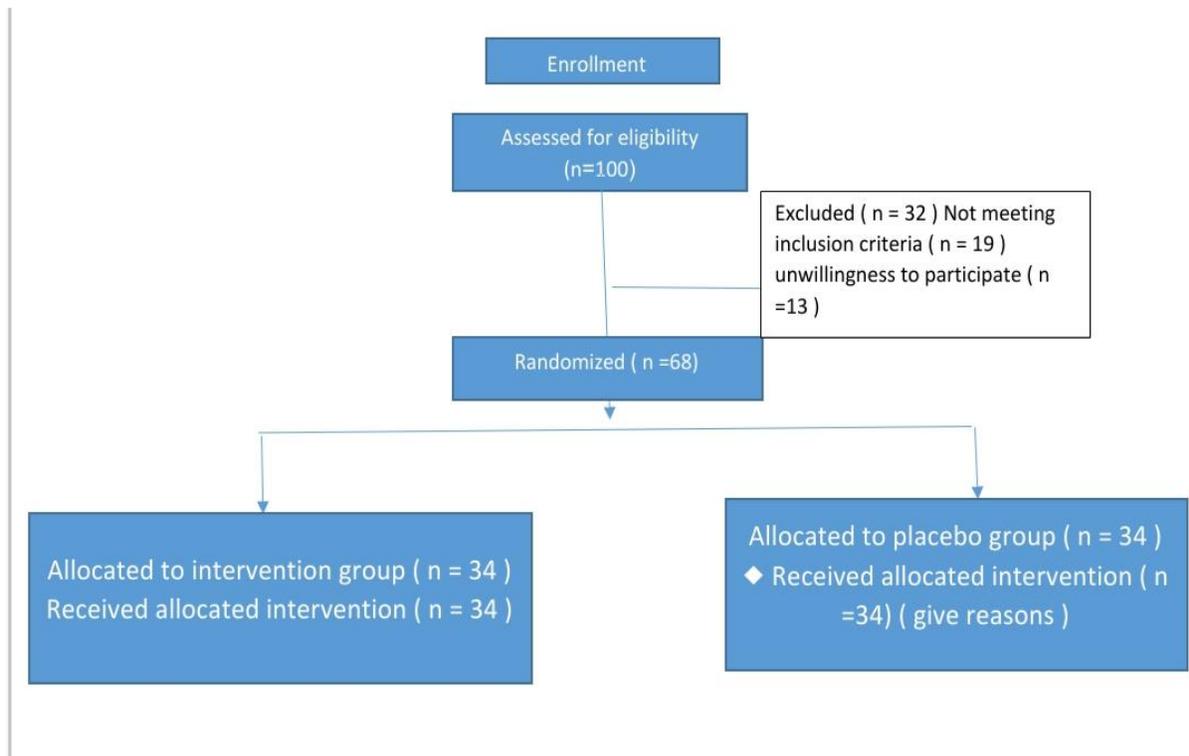


FIGURE 1 CONSORT

Findings:

68 questionnaires were completely completed. The results of data analysis showed that the average weight of the studied patients was 71.6 ± 10.3 and the average height was 166.1 ± 7.4 and their average age was 47.6 ± 13.6 years. 67.6% were women, 50% had a diploma or lower education level. 88.2% had no history of eye surgery. 51.5% had House keeping, 82.4% did not consume alcohol. The research shows that there is no significant difference in the presence of some systemic diseases between the two studied groups ($p < 0.126$). One-way repeated measure ANOVA test showed that assumed sphericity is rejected by Mauchly's test, left eye pressure ($p < 0.028$). Therefore, the Greenhouse-Geiser test shows that both the intervention and control groups experienced IOP a statistically significant decrease in IOP over time

($p < 0.001$). Also, the simultaneous effect of time in the studied groups and based on the Greenhouse test shows that there is no significant difference between the left eye pressure in the intervention and control groups ($p < 0.222$). Mauchly's test showed that the hypothesized sphericity of right eye pressure is less than 0.05% and equal to ($p < 0.001$). And in fact, the Greenhouse test shows that the average pressure of the right eye in the intervention and control groups separately at different times of the study has a statistically significant difference ($p < 0.001$). Also, there is a statistically significant difference in the right eye pressure simultaneously in the study groups and over time ($p < 0.042$). One-way repeated measure ANOVA test shows that according to Mauchly's test status, is ($p > 0.001$). The test of the second level of the greenhous shows that both the intervention and control groups have

decreased the level of shedding tears. Also, the simultaneous effect of time in the studied groups based on the Green house test, the frequency of shedding tears in the intervention and control groups has a significant difference ($p < 0.031$). The one-way repeated measure ANOVA test shows that according to the status of Mauchly's test, is ($p > 0.001$). The second level Green house test shows that both the intervention and control groups have experienced a decrease in blurred vision over time. Also, the simultaneous effect of time in both groups based on the Green house test, the frequency of blurred vision in both groups is not significantly different ($p < 0.374$). The one-way repeated measure ANOVA test shows that the assumed sphericity of the headache rate is rejected by Mauchly's test and is equal to 0.001. Therefore, the second level test of Green house shows that both the intervention and control groups have experienced a decrease in headaches over time. Also, the simultaneous effect of time in the studied groups based on the Green house test, the frequency of headache in the intervention

and control groups is different ($p < 0.058$). The one-way repeated measure ANOVA test shows that the sphericity assumed conjunctival inflammation rate with Mauchly's test is $p < 0.001$ and in the second level Green house test it is $p = 0.388$. And there is no significant difference. Also, the simultaneous effect of time in both groups has a significant difference based on the Green House test in both groups ($p = 0.052$). The one-way repeated measure ANOVA test shows that according to the status of Mauchly's test, is ($p > 0.09$). Therefore, the results show that both groups have different abdominal pain over time. Also, the simultaneous effect of group and time shows a significant difference between the two groups of abdominal pain ($p = 0.019$). According to Mauchly's test, is ($p > 0.017$). Green house second level test shows that both intervention and control groups have experienced a decrease in constipation in time ($p < 0.001$). Also, the simultaneous effect of time in the intervention and placebo groups has a significant difference based on the test of the rate of constipation reduction in both groups ($p < 0.014$).

Chart 1 :Comparison chart of headache in "group time" simultaneously in two control and intervention groups

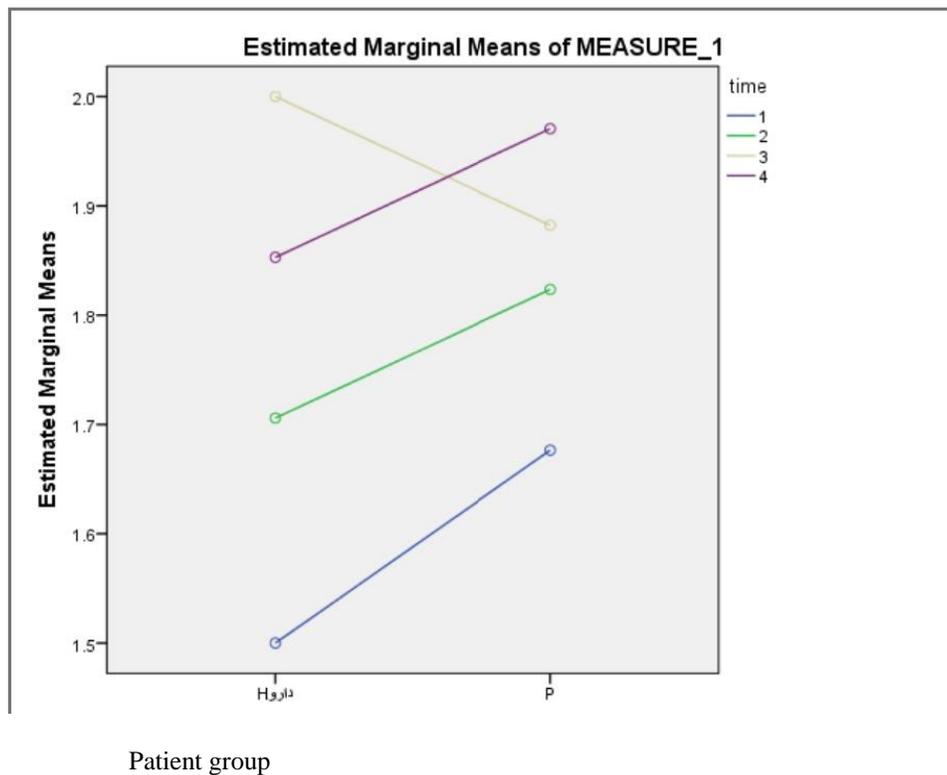


Chart 2: Comparative chart of blurring of vision in "group time" simultaneously in two control and intervention groups

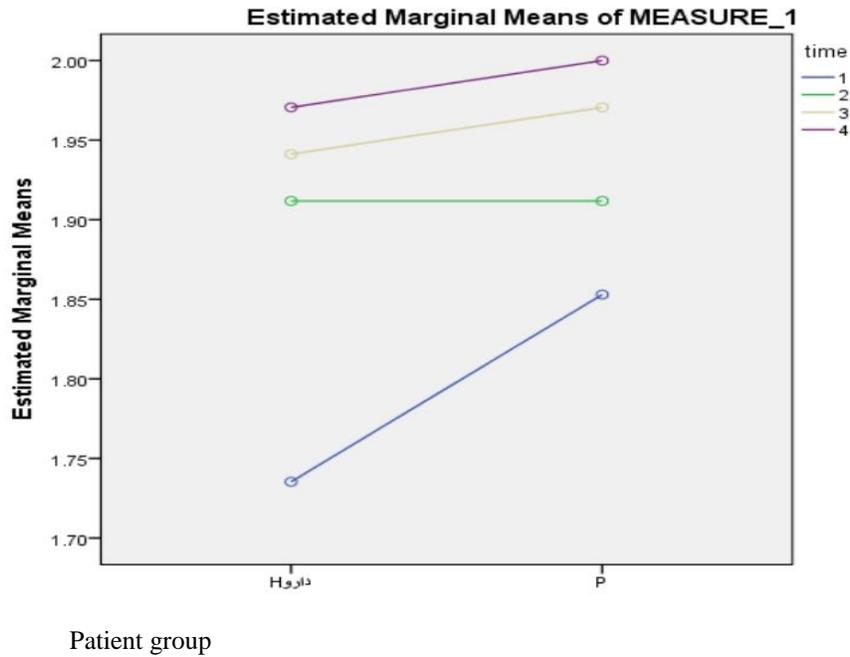


Chart 3: Comparative chart of tears in "group time" simultaneously in two control and intervention groups

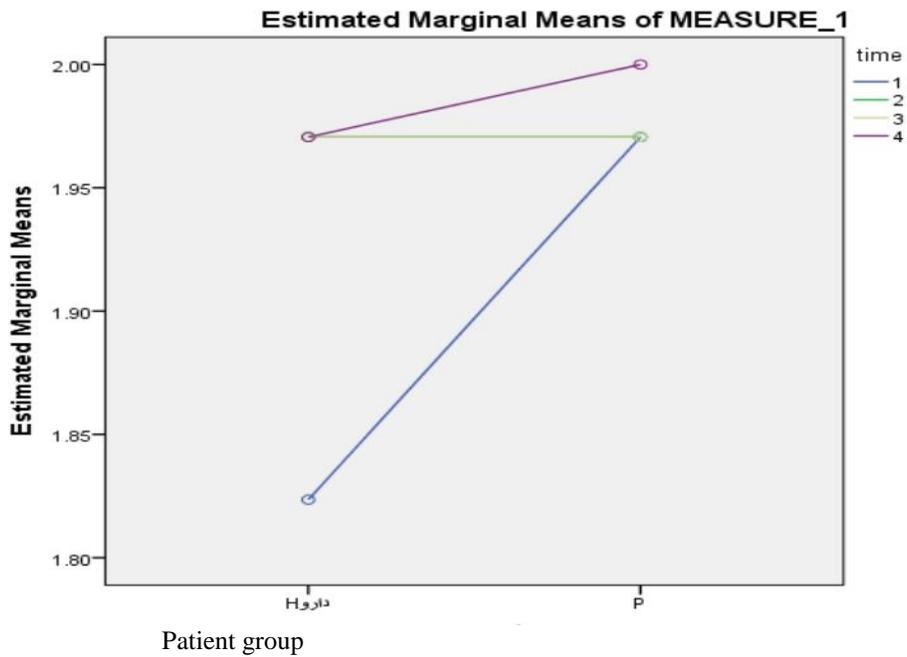
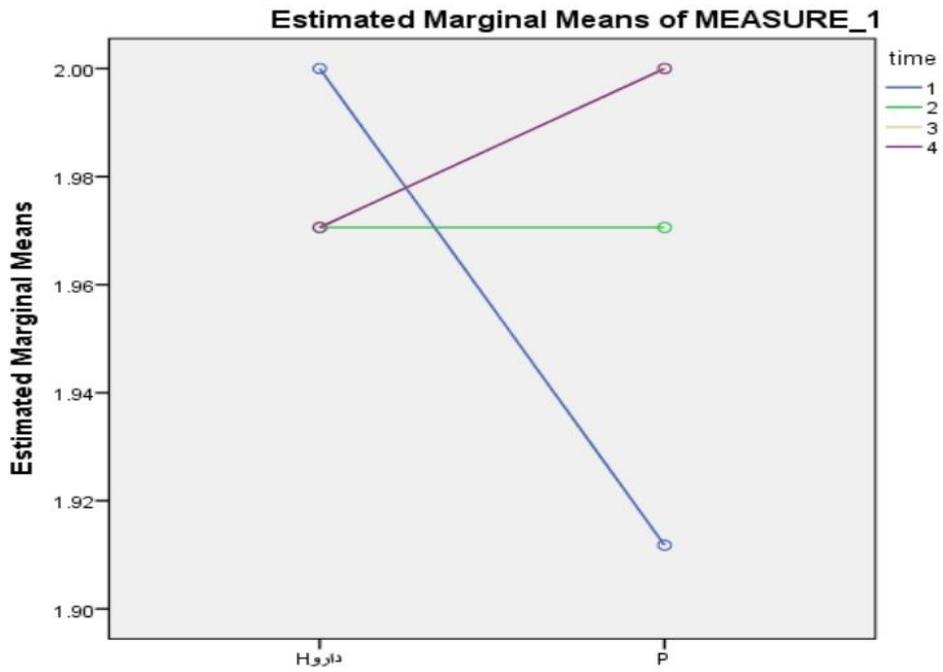
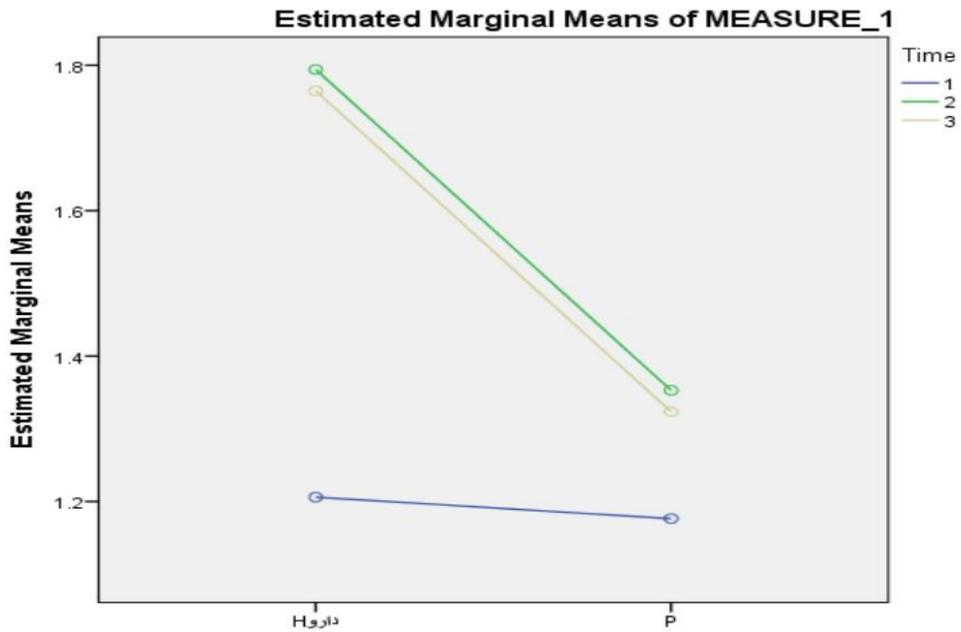


Chart 4: Comparative chart of conjunctivitis in "group time" simultaneously in two control and intervention groups



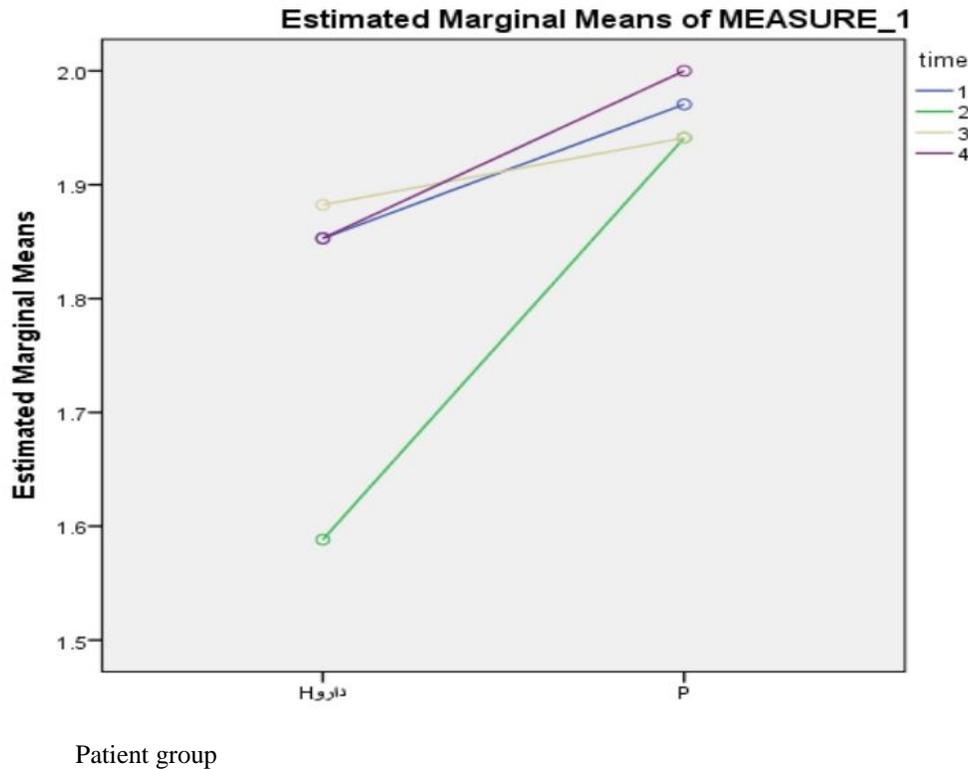
Patient group

Chart 5: Comparative chart of defecation in "group time" simultaneously in two control and intervention groups



Patient group

Chart 6: Comparative chart of abdominal pain in "group time" simultaneously in two control and intervention groups



Discussion:

Glaucoma is the name of a group of diseases that is characterized by irreversible optic neuropathy, which is in the form of depression and analysis of the connective tissue and nerve elements of the optic disc, which ultimately causes a specific pattern of visual impairment, in the form of visual field loss and blindness (1). Although increased intraocular pressure is one of its primary risk factors, its presence or absence does not play a role in defining glaucoma. Increased intraocular pressure causes pressure on the optic nerve and prevents blood supply, and the resulting damage causes blindness (2). Today, various medical and surgical methods are used to treat glaucoma. Surgical treatments usually do not have long-term effectiveness and after some time may lead to failure and there is always a need for subsequent surgeries (12). Iranian medical scholars had opinions and opinions in the field of recognition, description and treatment of eye diseases and definitions of functional terms, and almost all Iranian medical books deal with the diagnosis and treatment of eye diseases. In addition to these numerous specialized books on ophthalmology Like Tazkira Al-Kahalin, Al-Kahalah, Noor Al-Ayoun and Jami Al-Funun have been written in this context. In the study of eye diseases in Iranian medical books, it seems that glaucoma is consistent with the disease of increased testicular moisture. The increase of this moisture, which is located

in front of the lens of the eye (glacial moisture), is a factor in the degree of protection of the lens, and its disturbance is considered to cause blindness (13); And he considered stuffiness of the nose (brain) and dropping of waste from the nose (brain) into the eyes as the cause of most eye diseases, and diarrhea, provided it is not excessive, is beneficial for the eyes, and for enema (emptying) of the nose (brain), he suggested medicines containing patience and hallelujah. have done (14). In the PDR book, patience plant is mentioned as a laxative with antimicrobial, antiviral and anti-neoplastic properties (15).

Various studies have been done in this field. In the study of Sionkel et al. in 2008, it was shown that the usefulness of the combined treatment of timolol-latanoprost versus timolol-dorzolamide in patients with open-angle glaucoma was investigated, in which patients were randomly treated with the combined treatment of timolol-latanoprost and Timolol-dorzolamide for a period of six weeks; that the average IOP during the day was tested in 32 patients examined in two groups. According to statistical studies, there was no obvious difference. The average IOP did not differ in the combined treatment of timolol-latanoprost and in the combined treatment of timolol-dorzolamide (16). In their 2018 paper, Pinheiro et al(17) and Curto et al. in their 2014 report on the results of their animal research on dogs (18)And also Woźniak and

her colleagues in the 2012 report of their laboratory research on corneal cells (19) They expressed, that aloe vera, which is one of the main components of Habshabyar, it has been effective in treating eye diseases, especially inflammatory eye diseases And it can cause recovery of epithelium tissue or re-epithelialization of the cornea and It also reduces corneal fibrosis in superficial corneal wounds. In a study conducted by Fechtner et al. in 2005, they stated, that the combination of timolol-dorzolamide in reducing intraocular pressure in patients with increased intraocular pressure and glaucoma has the same effect as latanoprost alone (20). The findings of the study by Sleath et al., in order to investigate the effect of two drugs, latanoprost and timolol, on 170 patients with high intraocular pressure, showed that Both the drugs used reduced intraocular pressure in the same way and their speed of action was also the same. It was also determined that the speed of action of latanoprost was higher in males But the decrease in intraocular pressure was the same as in females And with increasing age, the effect of both drugs in reducing eye pressure decreases (21). In a 2018 study conducted by Wagilla on New Zealand white rabbits, The results showed that the use of 12% aloe vera gel together with 0.5% timolol is more effective in reducing intraocular pressure in experimental glaucoma compared to the use of 0.5% timolol alone (22). Also, Foster and colleagues have stated the use of aloe vera in the treatment of glaucoma (23). The findings of the present study are consistent with all the studies presented in terms of the effect of medicinal plants on glaucoma.

Conclusion:

There have been several studies on the effect of different types of medicinal compounds on intraocular pressure, which have produced different results. Examining and comparing the effectiveness of the two-drug combination brimonidine-timolol, dorzolamide-timolol and latanoprost-timolol showed that the combination of another drug with timolol such as brimonidine-timolol combination or dorzolamide-timolol combination or latanoprost-timolol combination in reducing intraocular pressure in Patients with primary open-angle glaucoma have similar effects and there is no significant difference between them. The study of the effectiveness of the therapeutic method of Iranian traditional medicine (Habshabyar) in the treatment of glaucoma (open angle glaucoma) showed that the use of sabzard, which is the main composition of Habshabyar as a product of Iranian traditional medicine, together with timolol, compared to the use of timolol alone, caused a significant decrease in Time in the intraocular pressure of patients with primary open-angle glaucoma. Advances in the drug treatment of glaucoma have created many choices for doctors and patients. Since glaucoma patients use several drugs, it is necessary for doctors to have sufficient information about the drugs available in the market, their mechanism of

action, side effects and adding one to another. According to this study, medicinal plants along with latanoprost, timolol and dorzolamide drugs reduce intraocular pressure in people suffering from this disease. If additional studies are confirmed, the use of habolzahb drug can reduce intraocular pressure in the long term as an adjunctive treatment along with routine drugs.

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