

Original Article: Investigating the effects of ephedrine infusion on changes in blood pressure and the need for inotropic drugs in the elderly under spinal anesthesia

Samad Eslam Jamal Golzari¹, Hamzeh Hosseinzadeh^{2*}, Parichehr Mazuji³

¹Associate Professor of Anesthesiology, Department of Anesthesiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. (ORCID: 0000-0003-3815-8770/ Email: Golzaris@Tbzmed.ac.ir)

²Professor of Anesthesiology, Department of Anesthesiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. (ORCID: 0000-0001-9384-420X)

³Anesthesiologist, Department of Anesthesiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. (ORCID: 0000-0009-8563-0023/ Email: Mazuji_pr@yahoo.com)

Use your device to scan and read the article online



Citation S. Eslam Jamal Golzari, H. Hosseinzadeh, P. Mazuji, **Investigating the effects of ephedrine infusion on changes in blood pressure and the need for inotropic drugs in the elderly under spinal anesthesia**, *EJCMPR*. 2023; 2(5):167-176.



<https://doi.org/10.5281/zenodo.8214301>

ABSTRACT

Introduction: The purpose of the current study was to test the theory that elderly patients undergoing laparoscopic rectal cancer surgery have impaired microvascular perfusion, which recovers following the administration of phenylephrine and ephedrine. **Material and Methods:** Patients were divided into one of the two groups using a random number sheet produced by computer software. Anesthetist sealed the opaque envelope with the random number sheet before starting the clinical trial. Ephedrine and N/S were infused into the patients in two different groups. **Results:** At the time of the phenylephrine injection, the microvascular flow index in the phenylephrine group decreased from 2.89 ± 0.16 at baseline to 1.85 ± 0.36 . At the same time, the number of perfused vessels decreased from 99.16 ± 1.74 percent to 64.02 ± 16.05 percent, and the density of perfused vessels decreased from 16.33 ± 4.24 mm/mm² to 10 point videos of the sublingual microcirculation's sidestream dark field images. Three images of the patients' baseline states, 10 min after anesthesia induction, and 5 min after ephedrine administration have been provided. Images for the phenylephrine group at the same time points have also been provided. **Conclusion:** MAP decline and sublingual microcirculation changes were observed in elderly patients undergoing laparoscopic surgery for rectal cancer. With the help of phenylephrine and ephedrine, sublingual microcirculation was successfully recovered.

Article info:

Received: 07 May 2023

Accepted: 04 August 2023

Available Online:

ID: EJCMPR-2308-1081

Checked for Plagiarism: Yes

Peer Reviewers Approved by:

Dr. Frank Rebout

Editor who Approved Publication:

Dr. Frank Rebout

Keywords: Ephedrine, Infusion, Blood Pressure, Spinal Anesthesia

Introduction

The percentage of elderly patients undergoing surgical treatment gradually increased along with the acceleration of the social aging process and the growth of the elderly population [1-3]. Due to the functional

decline of their organs, elderly patients frequently experience various complications during surgery, and their postoperative mortality rate is four times higher than that of middle-aged and young patients [4-6].

As a result, it is important to carefully examine the risk factors linked to postoperative mortality

*Corresponding Author: Hamzeh Hosseinzadeh (hamzeh1338@yahoo.com)

in elderly patients [7]. Hypotension and blood pressure swings are more common in elderly patients with impaired vascular self-regulation. Furthermore, because they can no longer tolerate hypotension as well, vital organs become more susceptible. The management of intraoperative anesthesia is extremely difficult due to numerous risk factors [8].

One of the main objectives of intraoperative hemodynamic management is to maintain a stable blood pressure. Although intraoperative hypotension is thought to be linked to postoperative mortality, the blood pressure cutoff value is still unknown, particularly in the geriatric population [9-11]. Determining the safe intraoperative blood pressure range in elderly patients and considering it one of the management goals of hemodynamics are therefore important clinical values [12-14].

One of the most frequent side effects from non-cardiac surgery is intraoperative hypotension. The majority of patients experience at least one episode in which the mean arterial pressure (MAP) drops below 65 mmHg, and this usually takes place soon after inducing anesthesia. In a recent randomized controlled trial, Hamilton et al found that intraoperative hypotension can result in extremely unfavorable postoperative outcomes, including acute kidney injury, death, and myocardial infarction. reported that preventing intraoperative hypotension reduces the risk of postoperative organ dysfunction by about 25%.

In particular, elderly patients having surgery for rectal cancer frequently experience poor vascular compliance [15-17], high blood pressure, and low blood volume during surgery. Perioperative hemodynamic optimization is said to improve postoperative outcomes in high-risk surgical patients by reducing postoperative complications, hospital stays, and mortality. In the current study [18], our anesthesiologist had to maintain a sufficient perfusion pressure during rectal surgery to ensure that the heart

and brain received enough blood to meet metabolic needs [19-21]. The anesthesiologist had to rule out any potential negative emergency reactions to the surgery.

During rectal procedures, ephedrine, an indirectly acting beta- and beta-adrenergic agonist, and phenylephrine, a pure beta-adrenergic agonist [22], are frequently administered to treat anesthesia-related hypotension and counteract cardiovascular depression. Vasopressors increase vascular resistance and raise cerebral perfusion pressure, but they can also unintentionally reduce oxygen absorption from the blood by disrupting capillary flow patterns [23-25].

This can happen even if the target cerebral perfusion pressure and the perfusion of other organs (like the heart) are met. G, the kidney) were accomplished [26].

Ephedrine and phenylephrine may affect sublingual microcirculation in elderly patients undergoing laparoscopic surgery for rectal cancer, but this is not well understood. Only a few easily accessible sites can be monitored for microcirculation [27-29]. It is possible to acquire sublingual microcirculation sequences using a portable vital microscope, a sidestream dark field imaging tool. It is a non-invasive method and a useful tool for evaluating microvascular factors like heterogeneity index, percentage of perfused vessels, microvascular flow index, and perfused vessel density. Few studies have examined the behavior of microcirculation in epidural patients and cardiopulmonary bypass surgery; however, in the elderly, microcirculation changes during rectal cancer surgery [30-32].

Microvascular perfusion changes can result in mortality and organ dysfunction in hemorrhagic and septic shocks; associations between microcirculation and macrovascular hemodynamic optimization in the state of a shock have been explored by several research groups [33-35]. The purpose of the current

study was to test the theory that elderly patients undergoing laparoscopic rectal cancer surgery have impaired microvascular perfusion, which recovers following the administration of phenylephrine and ephedrine [36].

Material and Methods

Trial design

This prospective parallel-group, double-blinded, single-center, enrolled, and randomized trial was conducted.

Patients and setting

Those who were scheduled for laparoscopic surgery for rectal cancer between the ages of 65 and 85 and had an American Society of Anesthesiologists grade of I-II underwent screening. The following conditions were excluded: (1) Loose teeth; (2) Hb; (3) Oral bleeding or damage; (4) difficulty opening the mouth; and (5) difficulty performing sublingual microcirculation monitoring.

Study protocol

Patients were divided into one of the two groups using a random number sheet produced by computer software. Anesthetist (MXW) sealed the opaque envelope with the random number sheet before starting the clinical trial. Ephedrine and phenylephrine were infused into the patients in two different groups. Anesthetist (MXW) who was not involved in controlling the patients' hemodynamics prepared the study drug, which was diluted to 50 mL in identical 50-mL infusion syringes under sterile conditions.

Sublingual microcirculation monitoring

We recorded videos of sublingual microcirculation using a sidestream dark field imaging device. This gadget uses a method that was developed from polarized spectral imaging technology. With the aid of these videos, we were able to see the sublingual blood flow within the microvascular networks in real time. Each

erythrocyte was visible in black on a white background because the light being emitted had a wavelength that matched the wavelength of hemoglobin. Internationally accepted standards were followed for the acquisition of images and image analysis. A great deal of care was taken to prevent pressure artifacts based on published recommendations. "Massey et al.". The evaluation was then completed using MicroSee Information Management Software, which had previously described the "microcirculation image quality score," which was used for systematic evaluation of the sequence quality. Poor-quality sequences were removed right there at the bedside. Another round of sequence acquisition was done in order to guarantee the availability of two high quality sequences for each measurement point. Here, a blinded analysis was made possible by hiding the patient's identity as well as the video's identification information and replacing these identifiers with a randomly generated alphanumeric code.

Clinical management

The patients were randomly assigned to receive either an ephedrine (6 mg/mL) or a phenylephrine (0.05 mg/mL) infusion, ensuring a 1:1 distribution. Ephedrine or phenylephrine was given when the MAP dropped below 80% of the baseline value or 65 mmHg for longer than 3 minutes. In this instance, it was given using a target-controlled infusion to keep the perioperative blood pressure stable following a bolus injection. One g/kg/min of phenylephrine and eighty g/kg/min of ephedrine were infused, respectively. Atropine dosages of 0–3–5 mg were used to normalize patients whose heart rates dropped below 50 beats per minute. The end-tidal carbon dioxide was maintained between 36 and 45 mmHg, and the respiratory rate was set so that it was 8 mL/kg-1 of the ideal body weight.

Sample size estimation

Using Power Analysis and Sample Size (PASS version 11.0), sample size was determined using the Cochran-Armitage Test. 7; Kaysville, Utah, USA-based NCSS, LLC). Calculations were made based on early preliminary data that revealed 82 percent of patients had hypotension for more than one minute during the induction of anesthesia. Using a Z-test with continuity correction, we calculated that a sample size of 88 patients (44 patients per group) would have 90% power to identify a linear trend in the proportion of patients with hypotension between groups at a significance level of 0.05. The sample size was raised to 100 patients to account for potential dropouts.

Statistical analysis

Before and after the administration of anesthesia, changes in macrovascular and microvascular parameters were assessed. These variables changed over time, and the changes in macrovascular parameters (HR and MAP) as well as microvascular parameters (microvascular flow index, percentage of perfused vessels, and perfused vessel density) were examined by comparing the values related to the time of ephedrine or phenylephrine administration. In addition, the time points were recorded using the Wilcoxon signed-rank test for microvascular parameters showing non-G.

Results

In this study, 100 patients were included. Five patients received neither phenylephrine nor ephedrine because changes in their MAP following anesthesia induction did not meet the predetermined criteria. Additionally, image analysis was rendered impossible in four patients due to strong signal interference, which resulted in their exclusion. Additionally, each patient gave both oral and written informed consent before taking part in the study. The included patients' average age was 72.2 years old, and their average New York Heart Association score was 1. To determine eligibility, 100 patients in total were examined. 5 patients did not meet the eligibility requirements (5 with a changed surgical approach), and 3 patients chose not to participate, making up the 8 patients who were excluded after screening. Before receiving anesthesia, 1 patient revoked their consent. The study was successfully completed by 91 patients.

91 patients had a low blood pressure episode during the induction of anesthesia. Furthermore, general anesthesia markedly decreased the MAP. Therefore, the prescribed dosages of phenylephrine and ephedrine were administered. Both groups' MAP results clearly indicated changes (Fig 1).

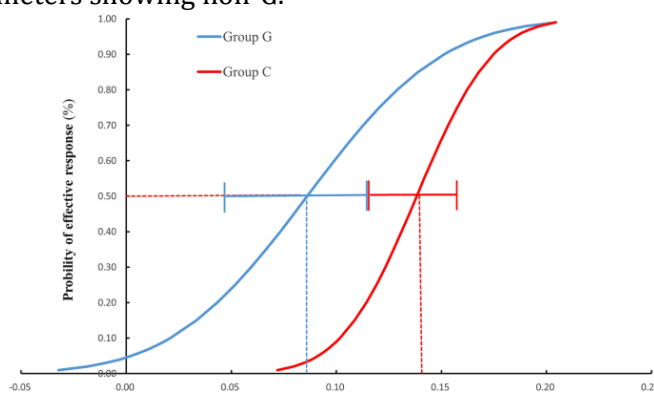


Figure 1. BP response between study groups

10 minutes after drug administration, a reduction in the microvascular flow index was observed from 2.85 ± 0.23 at baseline to 1.86

± 0.39 at the time of ephedrine injection. At the same time, the percentage of perfused vessels decreased from $98.71 \pm 2.19\%$ to 61.37%

17.87 % (and the density of perfused vessels dropped from 15.97 mm/mm². Ten minutes later, 90 point 23 percent of the vessels were

perfused, which was 14 point 17 percent higher(Fig 2).

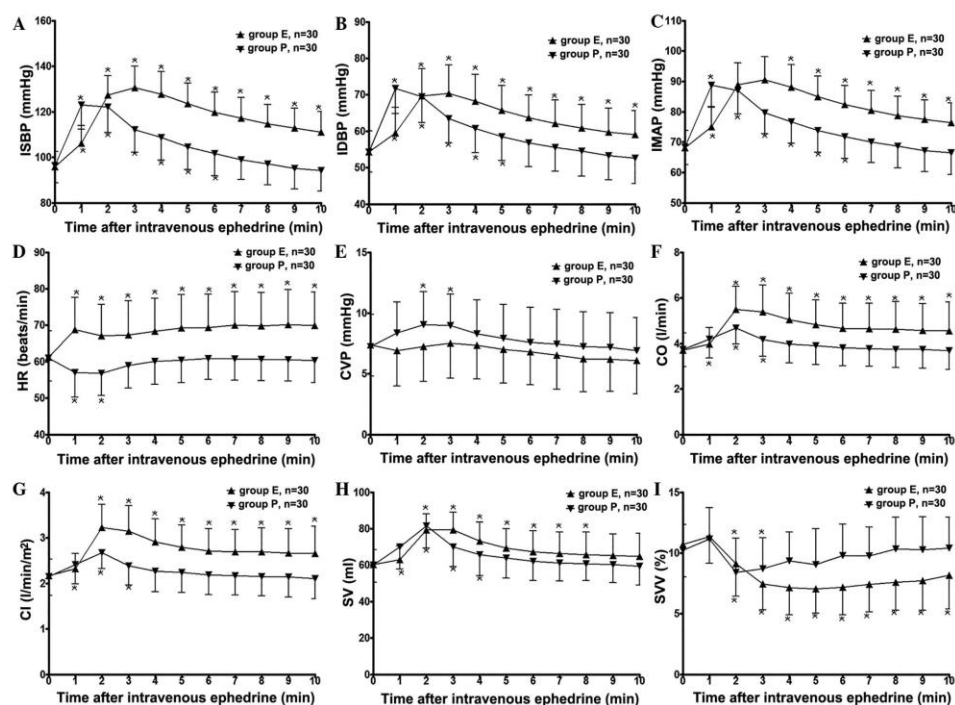


Figure 2. Changes in blood pressure during different times after the intervention

At the time of the phenylephrine injection, the microvascular flow index in the phenylephrine group decreased from 2.89 ± 0.16 at baseline to 1.85 ± 0.36 . At the same time, the number of perfused vessels decreased from 99.16 ± 1.74 percent to 64.02 ± 16.05 percent, and the density of perfused vessels decreased from 16.33 ± 4.24 mm/mm² to 10 point videos of the sublingual

microcirculation's side stream dark field images. Three images of the patients' baseline states, 10 min after anesthesia induction, and 5 min after ephedrine administration have been provided. Images for the phenylephrine group at the same time points have also been provided(Fig 3).

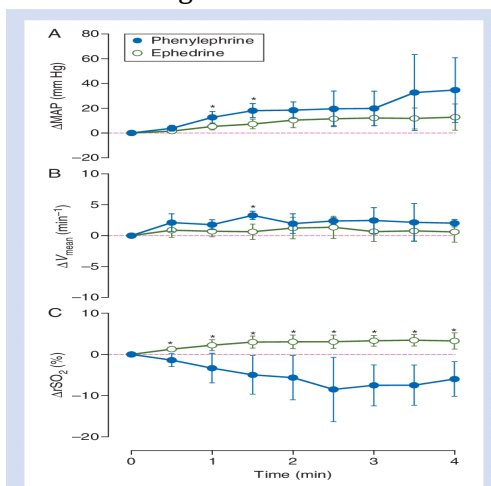


Figure 3. blood pressure changes between different times after the intervention

Discussion

Our study provides a thorough evaluation of sublingual microcirculation in elderly patients undergoing laparoscopic rectal cancer surgery and quantitatively illustrates its heterogeneity, perfusion, and density components [37-39]. Our study's main finding was that elderly patients showed obvious sublingual microcirculatory changes along with lower MAP and HR [40].

The disorder manifested as decreases in the proportion of perfused vessels, vascular density, and the presence of capillaries with hyperdynamic flow. In order to treat hypertension, we used ephedrine and phenylephrine [41-43]. We discovered that phenylephrine significantly reduced HR. Comparing the two groups, the ephedrine group displayed a higher percentage of perfused vessels for sublingual microcirculation [44]. The latter was more effective than the former in lowering the parameters of the heterogeneity index [45].

This study demonstrates a link between anesthesia-induced hypertension and sublingual microcirculation disorder in patients undergoing laparoscopic rectal cancer surgery. However, our results show that sublingual microcirculation parameters were not positively correlated with MAP and HR, and interestingly, MAP was negatively correlated with PVD. According to our research, these patients' declining blood pressure was associated with reduced sublingual microcirculation [46-48]. We did observe impaired microvascular perfusion during anesthesia, though, after MAP declined.

In order to raise MAP, adrenergic agonists like ephedrine or phenylephrine were used, and it was discovered that both treatments resulted in a recovery of microvascular perfusion [49-51]. In fact, some sublingual microcirculatory parameters, including the proportion of perfused vessels, the density of perfused vessels,

and the microvascular flow index, significantly dropped along with the decline in MAP. Ephedrine and phenylephrine both restored the MAP and microvascular variables, though [52]. Nevertheless, it is noteworthy how differently they impacted the HR and the intensity of sublingual microvascular variables. The microvascular flow index, MAP, the percentage of perfused vessels, and the perfused vessel density all showed clear increases after receiving ephedrine and phenylephrine, whereas the HR clearly decreased in the phenylephrine group [53].

Hypotension was defined as a MAP of in a previous study involving 255 patients. The decrease in sympathetic activity brought on by propofol and sufentanil in elderly patients is what leads to their hypotension [54-56]. The combined effects of myocardial contractility depression, venous and impaired baroreflex, and mechanism arterial vasodilation result in a decrease in cardiac output as well as a rise in systemic vascular resistance [57].

The MAP increased after phenylephrine and ephedrine treatments, and the PPV and microvascular flow index also increased at the same time [58-60]. Unknown at this time is the true mechanism. Although only sublingual microcirculation was found in the current study, many studies have shown a correlation between sublingual microcirculatory changes and changes in the gut and renal microcirculatory systems. In this investigation, we evaluated the sublingual microcirculation characteristics in patients undergoing laparoscopic rectal cancer surgery [61].

In order to maintain or restore oxygen delivery to the tissues, ephedrine and phenylephrine are frequently used [62-64]. It is difficult to predict microcirculation patterns solely from changes in macrocirculatory variables. In fact, the physiologic microvascular response appears primarily focused on maintaining tissue

perfusion in light of the decreased cardiac output, which was followed by decreases in the MAP. It should be noted, however, that altered microcirculation during shock is still possible despite the improvement of macrocirculation. This finding is due to the fact that microcirculation is altered in particular ways when in shock and exhibits changes in viscosity and endothelial dysfunction. There could be variations in the severity of microcirculatory alterations; it may change over time as well as with the difference in the intensities of in shock dot [64]. This is significant because persistent hypotension can inadvertently harm vital organs.

Improvements in microcirculation were seen in early hypotension after ephedrine and phenylephrine treatments. In the current study, patients with prior microvascular impairment and hemodynamic instability had their sublingual microcirculatory variables assessed. In patients undergoing colorectal cancer surgery, our study suggests that anesthesia induction with sufentanil and propofol affects sublingual microcirculation (and possibly microcirculation in other sites as well). It should be noted that it can be difficult to predict changes in microcirculatory patterns solely based on changes in macrocirculatory variables. The microcirculation characteristics of the microvascular flow index must recover to baseline levels for the MAP to reach them. The HR level was clearly different between the phenylephrine and ephedrine groups, which was an intriguing finding of our study according to our clinical observations. A phenylephrine injection may reduce heart rate. Bradycardia in the elderly can be brought on by heart block, myocardial ischemia, and abnormal sinus node function. As a result, any negative effects in elderly patients receiving phenylephrine should be closely monitored.

In elderly patients undergoing laparoscopic surgery for rectal cancer, we noticed changes in

sublingual microcirculation. This finding may be related to three factors: (1) elderly patients' decreased vascular compliance; (2) anesthetic drugs like propofol and sufentanil that cause vasoplegia; (3) changes in arterial tone brought on by fasting and enema that cause the loss of body fluids and electrolytes. This observational study has a number of drawbacks. The video was acquired by a non-blinded investigator, even though a blinded researcher performed the retrospective microvascular analysis. The study's restriction to the use of ephedrine and phenylephrine also limits the applicability of our findings because other vasopressors and fluid therapy may have different effects on cerebral blood flow and sublingual microcirculation.

Conclusion

MAP decline and sublingual microcirculation changes were observed in elderly patients undergoing laparoscopic surgery for rectal cancer. With the help of phenylephrine and ephedrine, sublingual microcirculation was successfully recovered. Therefore, in order to increase MAP and prevent decreased microcirculation, it is advised to administer ephedrine or phenylephrine right away based on our findings. Sublingual microvascular parameters may be used as additional microcirculation indicators in the future.

References

- [1]Jiang, S., et al., Journal of Drug Delivery Science and Technology, **2022**: p. 103792. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [2]A Afshari, et al. Advances in Materials Science and Engineering. **2022**;2022:6491134. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [3]A Susanabadi, et al., Journal of Chemical Reviews, **2021**, 3 (3), 219-231, [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [4]AR Baghestani, P Shahmirzalou, S Sayad, ME Akbari, F Zayeri, Asian Pacific journal of cancer

- prevention: APJCP, **2018** 19 (6), 1601 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [5] R Azhough R, Azari Y, Taher S, Jalali P. Asian Journal of Endoscopic Surgery. **2021**;14(3):458-63. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [6] R Azhough, R., Jalali, P., E J Golzari, S. et al. Indian J Surg. **2020**; **82**:824–827. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [7] D Aghamohamadi, M.K. Gol, Int J Womens Health Reprod Sci, **2020**. 8(2): p. 227-31. [[Google Scholar](#)], [[Publisher](#)]
- [8] D Alvandfar, M. Alizadeh, M. Khanbabayi Gol, The Iranian Journal of Obstetrics, Gynecology and Infertility, **2019**. 22(9): p. 1-7. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [9] E Tahmasebi, M Alam, M Yazdani, H Tebyanian, A Yazdani, A Seifalian, et al. Journal of Materials Research and Technology. **2020**;9(5):11731-55. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [10] E Tahmasebi, M Alam, M Yazdani, H Tebyanian, A Yazdani, A Seifalian, et al. Journal of Materials Research and Technology. **2020**;9(5):11731-55. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [11] E Yahaghi, F Khamesipour, F Mashayekhi, F Safarpour Dehkordi, MH Sakhaei, M Masoudimanesh, MK Khameneie. BioMed Research International. **2014** 12;2014: 757941. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [12] M Eidy, Ansari M, Hosseinzadeh H, Kolahdouzan K. Pakistan Journal of Medical Sciences. **2010**; 26(4):778-781. [[Google Scholar](#)], [[Publisher](#)]
- [13] Eskandar S, Jalali P. Revista espanola de cardiologia (English ed.). **2020**; 74(8): 725–726. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [14] M Eydi, Golzari SEJ, Aghamohammadi D, Kolahdouzan K, Safari S, Ostadi Z. Anesthesiology and Pain Medicine; **2014**: 4(2), e15499 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [15] F Beiranvandi, et al., Journal of Pharmaceutical Negative Results, **2022** 4417-4425 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [16] FB SS Seyedian, A shayesteh, Elsevier, **2018** 2526-2530 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [17] Forghani N, Jalali Z, Ayramlou H, Jalali P. J Clin Images Med Case Rep. **2022**;3(1):1626.
- [18] G Sharifi, A Jahanbakhshi, et al., Global spine journal, **2012** 2 (1), 051-055 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [19] G Sharifi, A Jahanbakhshi, Journal of Neurological Surgery Part A: Central European Neurosurgery, **2013** 74, e145-e148 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [20] R Gheisari, Doroodizadeh T, Estakhri F, Tadbir A, Soufdoost R, Mosaddad S. Journal of Stomatology. **2019**;72(6):269-73. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [21] R Gheisari, Resalati F, Mahmoudi S, Golkari A, Journal of Oral and Maxillofacial Surgery. **2018**;76(8):1652.e1-e7. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [22] R Gheisari, Resalati F, Mahmoudi S, Golkari A, Mosaddad SA. Journal of Oral and Maxillofacial Surgery. **2018**;76(8):1652.e1-e7. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [23] Golfeshan F, Ajami S, Khalvandi Y, Mosaddad SA, Nematollahi H. Journal of Biological Research - Bollettino della Società Italiana di Biologia Sperimentale. **2020**;93(1). [[Google Scholar](#)], [[Publisher](#)]
- [24] F Golfeshan, Mosaddad SA, Babavalian H, Tebyanian H, Mehrjuyan E, Shakeri F. India Section B: Biological Sciences. **2022**;92(1):5-10. [[Google Scholar](#)], [[Publisher](#)]
- [25] F Golfeshan, Mosaddad SA, Ghaderi F., Medicine. **2021**;2021:3304543. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [26] H Ansari lari, et al. Advances in Materials Science and Engineering. **2022**;2022:8621666. [[Google Scholar](#)], [[Publisher](#)]

- [27] H Danesh, et al., Journal of Medicinal and Chemical Sciences, **2022**, 561-570, [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [28] M Haghdooost, Mousavi S, Gol MK, Montazer M. International Journal of Women's Health and Reproduction Sciences. **2019**; 7(4): 526-30. [[Google Scholar](#)], [[Publisher](#)]
- [29] M Haghdooost, Mousavi S, Gol MK, Montazer M. International Journal of Women's Health and Reproduction Sciences. **2019**; 7(4): 526-30. [[Google Scholar](#)], [[Publisher](#)]
- [30] M Irajian, Beheshtirooy A. International Journal of Current Microbiology and Applied Sciences. **2016**;5(1): 818-825.[[Google Scholar](#)], [[Publisher](#)]
- [31] Irajian M, Faridaalae G. Iranian Journal of Emergency Medicine. **2016**;3(3): 115-118. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [32] K Hashemzadeh., M. Dehdilani, and M.K. Gol, Crescent Journal of Medical & Biological Sciences, **2019**. 6(4). [[Google Scholar](#)], [[Publisher](#)]
- [33] Kheradjoo H, et al., Molecular Biology Reports, **2023**, 50, 4217–4224, [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [34] M Eidi, et al., Iranian Journal of Medical Sciences. **2012**; 37(3):166-172. [[Google Scholar](#)], [[Publisher](#)]
- [35] M Jalessi, A Jahanbakhshi, et al., Interdisciplinary Neurosurgery, **2015** 2 (2), 86-89 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [36] M Khanbabaei Gol, et al., The Iranian Journal of Obstetrics, Gynecology and Infertility, **2019**. 22(5): p. 52-60. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [37] M Khanbabayi Gol, F. Jabarzade, V. Zamanzadeh, Nurs Midwifery J, **2017**. 15(8): p. 612-9. [[Google Scholar](#)], [[Publisher](#)]
- [38] M Milanifard, Weakness and Irritability, GMJ Medicine, **2021** 5 (1), 391-395 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [39] M Montazer., et al., Gynecology and Infertility, **2019**. 22(8): p. 10-18. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [40] M Najafi, A Jahanbakhshi, et al., Current Oncology, **2022** 29 (5), 2995-3012 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [41] M Yazdanian, A Rahmani, E Tahmasebi, H Tebyanian, A Yazdanian, SA Mosaddad. in Medicinal Chemistry. **2021**;21(7):899-918. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [42] M.K Gol., A. Dorosti, and M. Montazer, Journal of education and health promotion, **2019**. 8. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [43] Mahdavi F, Osquee HO.2020; 23(3): 34-39. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [44] Mahmoudi H, et al., Nanomedicine Research Journal, **2022**, 7(3), 288-293, [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [45] MH Abdollahi, et al. Nigerian medical journal: journal of the Nigeria Medical Association. **2014**; 55(5): 379. [[Google Scholar](#)], [[Publisher](#)]
- [46] MN Darestani, et al., Photobiomodulation, Photomedicine, and Laser Surgery. **2023**. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [47] Mobaraki-Asl N, Ghavami Z, Gol MK. Journal of education and health promotion. **2019**;8:179.
- [48] Moharrami M, Nazari B, Anvari HM. Trauma Monthly. **2021**; 26(4):228-234. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [49] Mokhtari Ardekani AB, et al., BioMed Research International, **2022**, Article ID 5744008, [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [50] Namanloo RA, Ommani M, Abbasi K, Alam M, Badkoobeh A, Rahbar M, et al. Advances in Materials Science and Engineering. **2022** :2489399. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [51] Nazari B, Amani L, Ghaderi L, Gol MK. Trauma Monthly.**2020**; 25(6): 262-268. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [52] Owaysee HO, Pourjafar H, Taghizadeh S, Haghdooost M, Ansari F. Journal of Infection. **2017**; 74(4): 418-420. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]

- [53] R Dargahi, et al., International Journal of Women's Health and Reproduction Sciences. **2021**; 9(4):268-273. [[Google Scholar](#)], [[Publisher](#)]
- [54] Rostami F, Osquee HO, Mahdavi F, Dousti S. International Journal of Women's Health and Reproduction Sciences. **2020**; 8(3): 297-302. [[Google Scholar](#)], [[Publisher](#)]
- [55] S Cozzi, M Najafi, et al., Current Oncology, **2022** 29 (2), 881-891 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [56] S Torkan, MH Shahreza. VacA, CagA, IceA and Oip. Tropical Journal of Pharmaceutical Research. **2016** 4;15(2):377-84. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [57] SAY Ahmadi, S Sayad, et al., Current Pharmacogenomics and Personalized Medicine, **2020** 17(3) 197-205 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [58] SE Ahmadi, et al., Romanian Journal of Military Medicine, **2022**,356-365, [[Google Scholar](#)], [[Publisher](#)]
- [59] Shahidi N, Mahdavi F, Gol MK. Journal of Education and Health Promotion. **2020**;9: 153. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [60] Shahsavarinia K, Gharekhani A, Mousavi Z, Aminzadeh S, Jalali P. J Clin Images Med Case Rep. **2022**;3(2):1634. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [61] Shirvani M, et al., BioMed Research International, **2022**, Article ID 5744008, [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [62] SS Aghili, et al., Open Access Maced J Med Sci. **2022** Nov 04; 10(F):763-772. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [63] SS Beladi Mousavi, et al., Jundishapur Scientific Medical Journal (JSMJ), **2014** 13 (1), 11-20 [[Google Scholar](#)], [[Publisher](#)]
- [64] Susanabadi A, et al., Annals of the Romanian Society for Cell Biology, **2021**, 25 (6), 2703-2716, [[Google Scholar](#)], [[Publisher](#)]

This journal is a double-blind peer-reviewed journal covering all areas in Chemistry, Medicinal and Petroleum. EJCMPR is published quarterly (6 issues per year) online and in print. Copyright © 2022 by ASC ([Amir Samimi Company](#)) which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.