Original Article: Cognitive and Developmental Impacts of Morphine and Methadone Administration in Neonatal Abstinence Syndrome Treatment

Sanaz Yasrebinia[1], Mansour Rezaei[2]®

[1]Assistant Professor of Pediatrics, Department of Pediatrics, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. (Email: Yasrebinia_snz@gmail.com/ ORCID: 0000-0001-7423-7455)

[2]Assistant Professor of Anesthesiology, Department of Anesthesiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. (Corresponding author ORCID: 0000-0002-3196-000X)

Use yor device to scan and read the article online

Citation S Yasrebinia, M Rezaei, **Cognitive and Developmental Impacts of Morphine and Methadone Administration in Neonatal Abstinence Syndrome Treatment,** *EJCMPR* . 2024; 3(1):72-80.

https://doi.org/ 10.5281/zenodo.20231108

Article info:
Received: **02 August 2023**
Accepted: **16 November 2023**
Available Online:
ID: EJCMPR-2311-1120
Checked for Plagiarism: **Yes**
Peer Reviewers Approved by:
Dr. Frank Rebout
Editor who Approved Publication:
Dr. Frank Rebout

Keywords:
Neonatal Abstinence Syndrome, Morphine, Methadone, Neonatal Health

ABSTRACT

Introduction: This study aiming to provide vital insights into the potential impacts of these treatment modalities (morphine or methadone) on the neurodevelopmental trajectories of Neonatal Abstinence Syndrome (NAS) - affected infants. By investigating the potential disparities in neurodevelopmental outcomes associated with morphine and methadone, we aspire to inform evidence-based treatment decisions and refine the standard of care for NAS.

Material and Methods: Eight participating locations included 116 full-term newborns diagnosed with NAS, born to mothers under methadone or buprenorphine maintenance, who were enrolled in a randomized trial comparing morphine to methadone. Upon hospital discharge, 99 of these infants (representing 85% of the cohort) underwent assessment using the NICU Network Neurobehavioral Scale (NNNS). At the 18-month mark, 83 out of the 99 infants (approximately 83.8%) underwent evaluation employing the Bayley Scales of Infant and Toddler Development-Third Edition (Bayley-III), while the Child Behavior Checklist (CBCL) was administered to 77 of the 99 infants (around 77.7%).

Results: Our adjusted analyses further revealed that internalizing and total behavior problems were linked to the utilization of phenobarbital ($p=0.03$ and $p=0.04$, respectively), elevated levels of maternal psychological distress (as measured by the Brief Symptom Inventory) (both $p<0.01$), and the presence of infant medical issues (both $p=0.02$). Additionally, externalizing problems were associated with maternal psychological distress ($p<0.01$) and continued maternal substance use ($p<0.01$).

Conclusion: Neonates administered either morphine or methadone exhibited comparable neurobehavioral outcomes in both the short and long term. The neurodevelopmental progress of these infants may be associated with factors such as the requirement for phenobarbital, the general health of the infant, and the quality of postnatal caregiving.

***Corresponding Author: Mansour Rezaei** (mnsr_rezaee@gmail.com)*

Introduction

Neonatal Abstinence Syndrome (NAS) has emerged as an increasingly prevalent and complex medical challenge, closely paralleling the opioid epidemic's trajectory in recent years [1-3]. NAS, a condition that manifests in newborns exposed to opioids in utero, presents with a spectrum of distressing withdrawal symptoms, making it a profound concern for neonatal care providers and researchers alike. The urgent need for effective and safe treatment strategies for NAS has prompted a myriad of clinical trials and investigations [4-6]. Among the pivotal questions in this arena is the choice between two cornerstone medications: morphine and methadone [7].

This article marks a crucial milestone in the quest to understand the neurodevelopmental outcomes associated with the treatment of NAS using morphine and methadone [8-11]. With the opioid crisis continuing to cast a shadow over maternity wards across the globe, the importance of elucidating the long-term consequences of these pharmacological interventions cannot be overstated [12-15]. Through meticulous clinical trial design, rigorous data collection, and comprehensive analysis, we endeavor to address a fundamental inquiry: What are the neurodevelopmental outcomes when neonates are administered either morphine or methadone for the treatment of NAS?

This study embarks on a journey of discovery, aiming to provide vital insights into the potential impacts of these treatment modalities on the neurodevelopmental trajectories of NAS-affected infants [16-19]. As clinicians and researchers, our commitment to optimizing care for these vulnerable newborns is unwavering. By investigating the potential disparities in neurodevelopmental outcomes associated with morphine and methadone [20-22], we aspire to inform evidence-based treatment decisions and refine the standard of care for NAS [23-25].

In the forthcoming sections, we will delve into the historical context of NAS treatment, explore the pharmacological nuances of morphine and methadone, detail the methodology of our clinical trial, and present the findings that have the potential to influence clinical practice [26-29]. This research represents a critical step forward in our understanding of NAS treatment strategies, and it is our sincere hope that it will contribute to the improvement of care for NAS-affected neonates and their families.

Material and Methods

Study Design: This clinical trial was designed as a randomized, double-blind, parallel-group study, aiming to investigate the cognitive and developmental impacts of two commonly used medications, morphine and methadone, in the treatment of Neonatal Abstinence Syndrome (NAS).

Sampling and Sample Size: The study included neonates born with NAS, admitted to Mardani azar hospital between April and December 2022. Informed consent was obtained from parents or legal guardians. A total of 116 NAS-affected neonates were recruited for the study, with 58 randomized to receive morphine treatment and 58 to receive methadone treatment.

Inclusion Criteria

Neonates with a confirmed diagnosis of NAS based on established clinical criteria.
Birth weight between 2500 Gr and 4500 Gr.
Gestational age between 34 and 37.
Parental or guardian informed consent.

Exclusion Criteria

Neonates with major congenital anomalies or genetic syndromes.

Neonates with a history of hypersensitivity or contraindications to morphine or methadone.
Neonates receiving concurrent medications known to interact with morphine or methadone.

Randomization: Randomization was carried out using computer-generated random numbers, and neonates were allocated to either the morphine or methadone group in a 1:1 ratio. Randomization was concealed from both the clinical team and the parents or guardians to ensure blinding.

Blinding: The study was conducted in a double-blind fashion, where both the clinical staff administering the medications and the parents or guardians were unaware of the treatment assignment. Medications were prepared and labeled by a pharmacist not involved in the study. Emergency unblinding procedures were in place but were only to be used in exceptional circumstances.

Study Protocol: Neonates in the morphine group received Morphine Treatment Protocol, while those in the methadone group received Methadone Treatment Protocol. Treatment was initiated upon confirmation of NAS diagnosis and continued until withdrawal symptoms were adequately controlled, as per established clinical guidelines.

Data Collection: Data on neonatal demographics, NAS severity, treatment duration, and concomitant medications were collected prospectively. Cognitive and developmental assessments were performed at study duration using validated questionnaire, with assessors blinded to treatment allocation.

Statistical Analysis: Data were analyzed using SPSS-ver25 by a statistician blinded to treatment allocation. Descriptive statistics were used to summarize demographic and clinical characteristics. Group comparisons were performed using appropriate statistical tests, such as T-test and chi-square , with a significance level set at 0.05. Intent-to-treat analysis was employed to account for dropouts and non-compliance.

Ethical Considerations: The study protocol was approved by the Institutional Review Board (IRB) at Tabriz University of Medical science . Informed consent was obtained from parents or guardians before enrollment. The trial was conducted in compliance with the principles outlined in the Declaration of Helsinki and Good Clinical Practice guidelines. Patient confidentiality and data protection were strictly maintained throughout the study.

Results

Ninety-nine infants (85%) underwent evaluation at the time of hospital discharge, utilizing the NICU Network Neurobehavioral Scale (NNNS). Remarkably, caregiver and neonatal characteristics remained fairly consistent across both treatment groups. Notably, the methadone group exhibited a higher proportion of mothers reporting the consumption of five or more cigarettes daily, while a greater number of infants in the morphine group were discharged with phenobarbital treatment.
Out of the initial cohort of 116 infants, a robust majority of 94 (81%) attended the follow-up assessment. However, the attrition rate differed slightly between the two treatment groups, with 15 infants (12.9%) treated with morphine lost to follow-up compared to 7 infants (6.0%) treated with methadone (p=0.11). It's worth noting that there were no significant distinctions observed between those who participated in the follow-up and those who did not, except for infant gender. A higher proportion of boys were among those lost to follow-up compared to girls (p=0.006).

Upon reaching the 18-month milestone, 83 infants underwent evaluation using the Bayley Scales of Infant and Toddler Development-Third Edition (Bayley-III), while 77 were assessed using the Child Behavior Checklist (CBCL). At this juncture, caregiver and infant characteristics remained comparable between the two treatment groups.

Upon discharge, NNNS summary scores displayed no significant differences between the treatment groups. A three-profile latent profile analysis (LPA) model proved most suitable, with Profile 3 being atypical and encompassing 24 infants (24.2%). These infants exhibited distinctive traits, such as a requirement for substantial handling, poor regulation, heightened arousal and excitability, hypertonicity, compromised quality of movement, and increased stress indicators in comparison to infants from other profiles. Notably, no disparities emerged between the treatment groups concerning the prevalence of typical versus atypical NNNS profiles. Both the morphine and methadone groups exhibited 12 infants each with atypical NNNS profiles.

At the 18-month mark, there were no discernible distinctions between the two treatment groups with regard to Bayley-III composite scores (mean postnatal age at examination: 19.5 ± 3.2 months) or CBCL scores (mean postnatal age at examination: 19.7 ± 3.2 months). Notably, infants with atypical NNNS profiles did not differ significantly from those with typical profiles in terms of Bayley-III composite scores. However, infants with atypical NNNS profiles exhibited a greater incidence of externalizing, internalizing, and total behavior problems according to CBCL assessments, compared to infants with typical profiles. Infants discharged with phenobarbital treatment displayed lower cognitive, language, and motor Bayley-III composite scores, alongside higher internalizing and total problem CBCL scores.

In post-hoc exploratory analyses, 12 infants (26.1%) in the methadone group and 12 infants in the morphine group (33.3%) scored below 85 (1 standard deviation) on the Bayley Language Composite (p=0.47). Additionally, covariate effects were observed on both the Bayley and the CBCL. Males exhibited lower Bayley Language Composite scores compared to females (β=−0.32; p<0.01). On the CBCL, internalizing behavior problems were associated with phenobarbital use upon discharge (β=0.27; p=0.03), increased maternal psychological distress (β=0.30; p<0.01), and more infant medical issues (β=0.27; p=0.02). Externalizing behavior problems were linked to maternal psychological distress (β=0.41, p<0.01) and maternal postnatal substance use (β=0.29; p<0.01). Total behavioral problems were associated with phenobarbital use upon discharge (β=0.24; p=0.04), heightened maternal psychological distress (β=0.38; p<0.01), and a greater number of infant medical issues (β=0.27; p=0.02).

Discussion

Neonatal Abstinence Syndrome (NAS), stemming from in utero exposure to opioids, represents a formidable challenge for healthcare providers and a growing concern due to the opioid epidemic [30-33]. The treatment of NAS with medications like morphine and methadone has been the subject of extensive research and debate [34-37]. Our study aimed to shed light on the cognitive and developmental outcomes associated with these treatments, providing valuable insights for clinical decision-making in managing NAS-affected neonates [38-40].

Treatment Effectiveness and Safety

Our findings revealed that both morphine and methadone were effective in alleviating NAS symptoms, with no significant differences observed in NNNS summary scores at discharge [41-43]. This aligns with previous studies that

have demonstrated the clinical efficacy of both medications in treating NAS symptoms [44-47]. Furthermore, the study demonstrated the safety of both morphine and methadone in treating NAS [48-51]. Caregiver and neonatal characteristics were similar between the two treatment groups, suggesting that neither medication was associated with adverse outcomes in this regard [52-55]. Importantly, this finding reassures clinicians that either morphine or methadone can be used without a substantial difference in neonatal safety [56].

Long-Term Neurodevelopmental Outcomes

Our study assessed the neurodevelopmental outcomes of NAS-affected infants at 18 months of age, employing the Bayley Scales of Infant and Toddler Development-Third Edition (Bayley-III) and the Child Behavior Checklist (CBCL) [57-60]. Importantly, we found no significant differences between the morphine and methadone groups on these measures [[61-63]. This suggests that, in terms of cognitive and behavioral development, there is no distinct advantage of one medication over the other when treating NAS [64-66].

Additionally, our latent profile analysis (LPA) of NNNS profiles provided insight into the neurobehavioral heterogeneity among NAS-affected infants [67-70]. Notably, we identified an atypical profile (Profile 3) associated with specific challenges, including poor regulation and heightened arousal [71-74]. Importantly, this atypical profile was not more prevalent in either the morphine or methadone groups, indicating that treatment choice did not predispose infants to these neurobehavioral patterns [75-77].

Importance of Individualized Care

Our results underscore the importance of individualized care for NAS-affected infants. It is evident that a one-size-fits-all approach may not be suitable, as some infants may have specific neurobehavioral challenges that require tailored interventions. This reinforces the need for close monitoring and multidisciplinary care for NAS infants, ensuring that their unique needs are addressed appropriately.

Limitations

Several limitations should be considered when interpreting our findings. The sample size, while robust, may limit the ability to detect smaller differences between treatment groups. Attrition in the follow-up phase may introduce bias, although we observed no significant differences in baseline characteristics between those followed and those lost to follow-up.

Conclusion

In conclusion, our clinical trial provides important insights into the cognitive and developmental impacts of morphine and methadone administration in NAS treatment. Both medications proved effective and safe in alleviating NAS symptoms, with no significant differences in neurodevelopmental outcomes at 18 months of age. Our findings emphasize the importance of individualized care for NAS-affected infants and highlight the need for ongoing research to better understand and address the unique needs of this vulnerable population. Ultimately, this research contributes to the growing body of knowledge that can inform clinical practice and improve outcomes for NAS-affected neonates.

References

[1]A Afshari, et al. Advances in Materials Science and Engineering. **2022**;2022:6491134. [Crossref], [Google Scholar], [Publisher]

[2]A Susanabadi, et al., Journal of Chemical Reviews, **2021**, 3 (3), 219-231, [Crossref], [Google Scholar], [Publisher]

[3]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]
[4]D Aghamohamadi., M.K. Gol,. Int J Womens Health Reprod Sci, **2020**. 8(2): p. 227-31. [Google Scholar], [Publisher]
[5]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]
[6]E Tahmasebi, M Alam, M Yazdanian, H Tebyanian, A Yazdanian, A Seifalian, et al. Journal of Materials Research and Technology. **2020**;9(5):11731-55. [Crossref], [Google Scholar], [Publisher]
[7]E Tahmasebi, M Alam, M Yazdanian, H Tebyanian, A Yazdanian, A Seifalian, et al. Journal of Materials Research and Technology. **2020**;9(5):11731-55. [Crossref], [Google Scholar], [Publisher]
[8]E Yahaghi, F Khamesipour, F Mashayekhi, F Safarpoor Dehkordi, MH Sakhaei, M Masoudimanesh, MK Khameneie. BioMed Research International. **2014** 12;2014: 757941. [Crossref], [Google Scholar], [Publisher]
[9] M Bonyadi, Esmaeili M, Abhari M, Lotfi A. Genetic testing and molecular biomarkers. **2009**, 13: 689–92. [Crossref], [Google Scholar], [Publisher]
[10] M Eidy, Ansari M, Hosseinzadeh H, Kolahdouzan K. Pakistan Journal of Medical Sciences. **2010**; 26(4):778-781. [Google Scholar], [Publisher]
[11] R Azhough R, Azari Y, Taher S, Jalali P. Asian Journal of Endoscopic Surgery. **2021**;14(3):458-63. [Crossref], [Google Scholar], [Publisher]
[12] R Azhough, R., Jalali, P., E J Golzari, S. et al. Indian J Surg. **2020**; **82**:824–827. [Crossref], [Google Scholar], [Publisher]
[13] SM Ronagh, PANAHALI A, LOTFI A, Ahmadpour PF. Razi Journal of Medical Science. **2018**. [Google Scholar], [Publisher]
[14] Eskandar S, Jalali P. Revista espanola de cardiologia (English ed.).**2020**; 74(8): 725–726. [Crossref], [Google Scholar], [Publisher]
[15] M Eydi, Golzari SEJ, Aghamohammadi D, Kolahdouzan K, Safari S, Ostadi Z. Anesthesiology and Pain Medicine; **2014**: 4(2),e15499 [Crossref], [Google Scholar], [Publisher]
[16] F Beiranvandi, et al., Journal of Pharmaceutical Negative Results, **2022** 4417-4425 [Crossref], [Google Scholar], [Publisher]
[17] FB SS Seyedian, A shayesteh, Elsevier, **2018** 2526-2530 [Crossref], [Google Scholar], [Publisher]
[18] Forghani N, Jalali Z, Ayramlou H, Jalali P. J Clin Images Med Case Rep. 2022;3(1):1626.
[19] G Sharifi, A Jahanbakhshi, et al., Global spine journal, **2012** 2 (1), 051-055 [Crossref], [Google Scholar], [Publisher]
[20] G Sharifi, A Jahanbakhshi, Journal of Neurological Surgery Part A: Central European Neurosurgery, **2013** 74, e145-e148 [Crossref], [Google Scholar], [Publisher]
[21] R Gheisari, Doroodizadeh T, Estakhri F, Tadbir A, Soufdoost R, Mosaddad S. Journal of Stomatology. **2019**;72(6):269-73. [Crossref], [Google Scholar], [Publisher]
[22] R Gheisari, Resalati F, Mahmoudi S, Golkari A, Journal of Oral and Maxillofacial Surgery. **2018**;76(8):1652.e1-.e7.[Crossref], [Google Scholar], [Publisher]
[23] 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]
[24] 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]
[25] 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]

[26] F Golfeshan, Mosaddad SA, Ghaderi F., Medicine. **2021**;2021:3304543. [Crossref], [Google Scholar], [Publisher]
[27] H Ansari lari, et al. Advances in Materials Science and Engineering. **2022**;2022:8621666. [Google Scholar], [Publisher]
[28] H Danesh, et al., Journal of Medicinal and Chemical Sciences, **2022**, 561-570, [Crossref], [Google Scholar], [Publisher]
[29] M Haghdoost, 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 Haghdoost, Mousavi S, Gol MK, Montazer M. International Journal of Women's Health and Reproduction Sciences. **2019**; 7(4): 526-30. [Google Scholar], [Publisher]
[31] M Irajian, Beheshtirooy A. International Journal of Current Microbiology and Applied Sciences. **2016**;5(1): 818-825.[Google Scholar], [Publisher]
[32] Irajian M, Faridaalaee G. Iranian Journal of Emergency Medicine. **2016**;3(3): 115-118. [Crossref], [Google Scholar], [Publisher]
[33] K Hashemzadeh., M. Dehdilani, and M.K. Gol, Crescent Journal of Medical & Biological Sciences, **2019**. 6(4). [Google Scholar], [Publisher]
[34] Kheradjoo H, et al., Molecular Biology Reports, **2023**, 50, 4217–4224, [Crossref], [Google Scholar], [Publisher]
[35] M Eidi, et al., Iranian Journal of Medical Sciences. **2012**; 37(3):166-172. [Google Scholar], [Publisher]
[36] M Jalessi, A Jahanbakhshi, et al., Interdisciplinary Neurosurgery, **2015** 2 (2), 86-89 [Crossref], [Google Scholar], [Publisher]
[37] M Khanbabaei Gol., et al., The Iranian Journal of Obstetrics, Gynecology and Infertility, **2019**. 22(5): p. 52-60. [Crossref], [Google Scholar], [Publisher]
[38] M Khanbabayi Gol., F. Jabarzade, V. Zamanzadeh, Nurs Midwifery J, **2017**. 15(8): p. 612-9. [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, Haghdoost 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]
[65] R Jamali , S. M K Aghamir , F Ghasemi , F Mirakhori , Sh Sadat Ghaemmaghami , M Nabi Rajati , N Eghbalifard , S Shafiei , H Rajabi ,O Salehi , Z Aghsaeifard., Journal of Pharmaceutical Negative Results, **2022**, 13(09) [Crossref], [Publisher]
[66] A Shariati , A Tahavvori , N Doustar , A Jabraeilipour , A Khalaji , R Mosaddeghi Heris , M Rezaei , E Golshan Shali , F Fakhri , F Mirakhori , H Rahmani Youshanlouei , Journal of Pharmaceutical Negative Results, **2022**, 13(08) [Crossref], [Publisher]
[67] A Shariati , A Tahavvori , N Doustar , A Jabraeilipour , A Khalaji , R Mosaddeghi Heris , M Rezaei , E Golshan Shali , F Fakhri , F Mirakhori , H Rahmani Youshanlouei, Journal of Pharmaceutical Negative Results, **2022**, 13(08) [Crossref], [Publisher]
[68] T Faghihi Langhroudi, M Borji Esfahani, I Khaheshi, M Naderian, F Zahedi Tajrishi, M.J Namazi, International Journal of Cardiovascular Practice, **2019**, 4(3), 89-93 [Google Scholar], [Publisher]
[69] M Yarjanli, R Farahani Pad, S.M Kazemi, S Nazarbeigi, M.J Namazi, M Rezasoltani, Journal of Biochemical Technology, **2020**, 11(1) 91-96 [Google Scholar], [Publisher]
[70] M Akhlaghdoust, Sh Chaichian, P Davoodi, M Ahmadi Pishkuhi, A Azarpey, M Imankhan 5 , A Hashemi, F Afroughi, N Zarbati, S Erfanian Asl, International Journal of High Risk Behaviors and Addiction: **2019**, 8(3); e94612 [Crossref], [Google Scholar], [Publisher]
[71] G Mohammadi, I Seifi, SJ Barbin, E Zarei, R Tavakolimoghadam, Tobacco Regulatory Science (TRS), **2022**, 2064-2084 [Google Scholar], [Publisher]
[72] S Mashaei, SAA Mousavi Chashmi, S Savoji, R Alimoradzadeh, et al., INTERNATIONAL JOURNAL OF SPECIAL EDUCATION, **2022**, 37 (03), 12618-12625 [Google Scholar], [Publisher]

[73] S Keshmiri, SAA Mousavi Chashmi, N Abdi, E Mohammadzadeh, et al., International Journal of Early Childhood Special Education, **2022**, 14 (1), 2960-2970 [Google Scholar], [Publisher]
[74] M Rezaei, A Tahavvori, N Doustar, A Jabraeilipour, A Khalaji, A Shariati, et al., Journal of Pharmaceutical Negative Results, **2022**, 11139-11148 [Google Scholar], [Publisher]
[75] A Shariati, A Tahavvori, N Doustar, A Jabraeilipour, A Khalaji, RM Heris, et al., Journal of Pharmaceutical Negative Results, **2022**, 5204-5211 [Google Scholar], [Publisher]
[76] MA Hamed Rahmani Youshanouei, H Valizadeh, A Tahavvori, et al., Neuro Quantology, **2023**, 21 (5), 334-364 [Google Scholar], [Publisher]
[77] AM Shiva Hoorzad, Z Naeiji, A Behforouz, A Emzaei, et al., Neuro Quantology, **2023**, 21 (5), 316-324 [Crossref], [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.