Original Article

OPEN ACCESS

Efficacy of Melatonin in Treatment of Infantile Colic in Infants Presenting to CMH Quetta OPD

Nidda Arshad Waraich[1], Muhammad Omer Tufail[2], Zainab Akmal Abbasi[3], Muhammad Umer Farooq[4]

[1]Postgraduate Resident, Department of Pediatric Medicine, Combined Military Hospital, Quetta
[2]Associate Professor, Department of Pediatric Medicine, Combined Military Hospital, Quetta
[3]Pediatric Medical officer at Pak Medical & Diagnostic Center, Rawalpindi
[4]DADMS / Medical Officer CR Bigd Quetta

Author`s Contribution

[1]Substantial contributions to the conception or design of the work; or the acquisition, [2]Final approval of the version to be published [3,4]Drafting the work or revising it critically for important intellectual content

Funding Source: None
Conflict of Interest: None

Received: May 04, 2025
Revised: May 18, 2025
Accepted: May 21, 2025

Address of Correspondent
Dr Nidda Arshad Waraich
Postgraduate Resident, Dept of Pediatrics, CMH Quetta
niddaarshad22@gmail.com

ABSTRACT

Objective: To determine the efficacy of melatonin in treatment of infantile colic presenting to a tertiary care hospital or CMH Quetta.

Methodology: This prospective single group interventional study was conducted at Pediatrics department of Combined Military Hospital, Quetta, Pakistan from October 2024 to April 2025 after taking parental informed consent and ethical approval from institution. A total of 146 infants with colic were included, selected through non-probability consecutive sampling technique. All the infants were given oral melatonin for five days and one week after completion of therapy infants were assessed for improvement in the colic severity. Efficacy was considered to be established in case of achievement of complete resolution of colic. Analysis of data was performed through SPSS version 22.

Results: In this study, 146 infants were included. Median age was 4.00 (2.00) months. There were 77 (52.70%) male and 69 (47.30%) female infants. Median weight was 9.00 (3.00) kg. A total of 65 (44.50%) infants were receiving breast feeding, 52 (35.60%) infants were receiving formula milk feeding and 29 (19.90%) infants were receiving cow milk. Complete improvement/efficacy was achieved in 80 (54.80%) infants, partial improvement was observed in 43 (29.50%) infants while 23 (15.80%) infants had no improvement.

Conclusion: Melatonin is an effective intervention in the management of infantile colic. It resulted in complete recovery in 54.80% of the infants and partial improvement in 29.50% of the infants with colic.

Keywords: Colic, Efficacy, Infantile, Melatonin.

Cite this article as: Waraich NA, Tufail MO, Abbasi ZA, Farooq MU. Efficacy of Melatonin in Treatment of Infantile Colic in Infants Presenting to CMH Quetta OPD. Ann Pak Inst Med Sci. 2025; 21(3):549-553. doi. 10.48036/apims.v20i3.1519.

Introduction

Infantile colic is one of the commonly encountered problem by the pediatricians globally. [1] In this condition, parents present with distress and apprehension due to the excessive crying of a baby while thinking there may be something wrong.[1,2] However, these episodes of excessive, inconsolable and unexplained crying are usually not due to any organic problem, rather it is due to infantile colic which may affect a large proportion of infants, particularly during the initial months of life. [3] It is such a common condition that according to previous literature, approximately up to 15% of infant population having age between birth and six months are affected by it. [4] Compared to this, a recent epidemiological survey was conducted in Pakistan and it was found that the burden of colic in Pakistani infants was much higher compared to the rest of the world and was reported to reach as high as 40%. [5]

When it comes to the pathophysiology of this common pediatric condition, no clear-cut mechanism of its development has yet been discovered, however, multiple possibilities have been proposed. One of the mechanism, hypothesized to be linked with the development of this condition is the imbalance of the natural gut microbiota and gut immaturity, both of which result in excessive

production of gas and dysmotility of the gut. [6, 7] Another hypothesized possibility is that this condition may occur due to a combination of gastrointestinal, neurodevelopmental and the psychological factors through a complex inter-factorial interaction. [8]

One recently discovered association of infantile colic with the melatonin levels with infants that tend to have colic having much less concentration of serum melatonin as compared to those without colic.[9] Owing to this recently surfaced hypothesis of association of melatonin and colic in infants, an opportunity, in the form of therapeutic use of melatonin, has emerged regarding the management options for treating this condition. However, till date and to the best of the knowledge, clinical trials have not been conducted on national, regional or local level to assess that whether therapeutic melatonin administration is useful in managing infants with colic or not. In fact, even at international level, the availability of clinical research regarding the efficacy of melatonin in treatment of infantile colic is quite scarce, therefore, present study was conducted for determining the efficacy of melatonin in treatment of infantile colic.

Methodology

This prospective single group interventional study was conducted at Pediatrics department of Combined Military Hospital, Quetta, Pakistan from October-2024 to April-2025 after getting approval from institutional ethical committee (Ref No: CMH QTA-IERB 44/2024). Sample size calculation was performed using Raosoft ® sample size calculator. Sample size calculation was performed by using confidence level of 95%, absolute precision of 8% and anticipated efficacy of melatonin in infantile colic of 57.7%. [10] This gave a sample size of 146 which was selected by using non-probability consecutive sampling technique.

Male and female infants who were aged up to six months and presented with infantile colic were included. Infants who were born premature, had ongoing fever at presentation, had history and physical examination suggestive of some organic disease and those with history of perinatal asphyxia or congenital anomalies were excluded from the study. Presence of infantile colic was defined based on Wessel criteria by positive history of crying spells of three hours duration in a day for more than three days in a week for three weeks in association with increased flatulence and sleep disturbance.

Before inclusion of an infant in the study, all the parents were explained regarding the purpose and methodology of the study and informed written consent was taken from the parents. Baseline demographics were age, gender, weight and type of milk being given to infant, which were documented in a patient demographic proforma. After this, oral melatonin was prescribed to all the infants at a dose of 0.25 mg once daily for a period of five days. Parents were given a follow up schedule of visiting in outdoor department at the end of therapy and after one week from the day of completion of therapy. Through subjective assessment, the degree of improvement in colic was assessed and was graded as no, partial or complete. Efficacy was considered to be established in case of achievement of complete resolution of colic at follow up visit scheduled after one week from the day of completion of therapy.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 22. Quantitative variables normality was checked by Shapiro-Wilk test which showed that age and weight were not normally distributed and were thus presented as median interquartile range (IQR). Qualitative variables (gender, type of milk being given to infant, degree of improvement and efficacy) was presented as frequency and percentages. Efficacy was stratified by age, gender and type of milk being given to infants to control effect modifiers and post-stratification comparison was performed by using Chi-square test. A p-value of ≤ 0.05 was considered as statistically significant.

Results

In this study, 146 patients were included. Median age was 4.00 (2.00) months. Among these infants, 68 (46.60%) were aged 0-3 months and 78 (53.40%) were aged 3-6 months. There were 77 (52.70%) male and 69 (47.30%) female infants. Median weight was 9.00 (3.00) kg. A total of 65 (44.50%) infants were receiving breast feeding, 52 (35.60%) infants were receiving formula milk feeding and 29 (19.90%) infants were receiving cow milk. Pre-treatment patients' demographics are given in Table I.

Table I: Pre-treatment patients demographics. (n = 146)

Parameter	Median (IQR); N (%)
Median age	4.00 (2.00) months
0-3 months	68 (46.60%)
4-6 months	78 (53.40%)
Gender	
Male	77 (52.70%)
Female	69 (47.30%)
Median weight	9.00 (3.00) kg
Type of feeding	
Breast Milk	65 (44.50%)
Formula Milk	52 (35.60%)
Cow Milk	29 (19.90%)

Complete improvement/efficacy was achieved in 80 (54.80%) infants, partial improvement was observed in 43 (29.50%) infants while 23 (15.80%) infants had no improvement. Status of improvement of colic after one week of melatonin therapy is given in Table II. Stratification of efficacy by age is given in Table III

Stratification of efficacy by gender is given in Table IV

Table II: Status of improvement of colic after one week of melatonin therapy. (n = 146)

Improvement	N (%)
Complete improvement/Efficacy	80 (54.80%)
Partial improvement	43 (29.50%)
No improvement	23 (15.80%)

Table III: Stratification of efficacy by age. (N = 146)

	0-3 months (n = 68)	4-6 months (n = 78)	p-value
Efficacy	32 (47.06%)	48 (61.54%)	0.080

Table IV: Stratification of efficacy by gender. (N = 146)

	Male (n = 77)	Female (n = 69)	p-value
Efficacy	43 (55.84%)	37 (53.62%)	0.788

and by type of milk being given to infants is given in Table V.

Discussion

Melatonin is a naturally occurring hormone in the human body which is produced by the pineal gland and serves in a multitude of physiological functions and also in therapeutic management of various conditions. [11, 12] Its role in infantile colic has recently surfaced by the work of various researchers. [13, 14] This prompted the conductance of current study to determine the therapeutic role of this hormone in infantile colic management. In present study, average age of the infants who presented with colic was four months with most of the infants with colic aged older than three months. This trend was similar to the one presented in a research by Brown et al. [15] in which they found that the most common time of initial presentation of infants at the healthcare facility with the symptoms consistent with colic was at the four months of age. One possible reason behind this could be the heightened alertness and concern of the parents towards crying of the child at this age compared to the earlier months of life.

Upon analysis of the distribution of the colic across the genders it was observed that 52.7% of the affectees of infantile colic were males while remaining were female. Similar to this, a study was conducted by Helseth et al. [16] in which similar male predominance was observed. Similarly, in another study conducted by Evans et al. [17], this slight male predominance was evident with male infants forming approximately 62% of the colic affected infants. In this study, they found almost similar proportion of male population (52.9%) being affected by this condition. [17] In another study conducted by Suklert et al. [18], contrary finding was observed regarding gender distribution with males only constituting 44% of the infants presenting with symptoms of colic. These differences exhibit that there may not be any direct association of colic with any specific gender. Another interesting finding of current study was that colicky infants were mostly breastfed rather than alternative feeding sources like formula or cow's milk. Contrarily, Hafiz et al.[19] found that among colicky infants, commonest source of feeding formula milk rather than the breast milk. Although there is a correct and widespread perception of breast milk being the best food for the infants [20], previous literature has suggested that the complex molecular networks that are found in the human milk formed between the micro-ribonucleic acid and the microbes has the tendency to increase the chances of developing infantile colic. [21]

Upon analysis of the efficacy of therapeutic melatonin administration in infantile colic, it was observed that more than half of the infants (54.80% to be exact) had complete resolution of their colic while partial resolution was observed in 29.50% of the infants. To compare the results of present study with prior available studies, extensive research was conducted at various platforms like Google Scholar, Medline, Scopus, Researchgate, PubMed and Cochrane library but only one study was found that has been conducted in this regard till date. This available trial was conducted by Shakiba et al. [10] in which this achievement of complete colic resolution was observed in 57.7% of the infants and partial improvement was observed in 31.9% of the patients. This effective control of colic symptoms by melatonin administration has also been considered in a recent literature review conducted by Zwierząt et al. [22] in which they found that this naturally occurring hormone may relax the gut and relieve the colic in infants. Another important and unique finding of present study, which has not been studied

Table-V: Stratification of efficacy by type of milk being given to infants. (n = 146)

	Breast Milk (n = 65)	Formula Milk (n = 52)	Cow Milk (n = 29)	p-value
Efficacy	34 (52.31%)	35 (67.31%)	11 (37.93%)	0.034

previously, was significantly higher efficacy of exogenous melatonin administration in formula fed infants. This may have occurred due to lack of melatonin in formula milk, which occurs naturally in some amount in the breast milk [23], and a sudden spike in its levels due to exogenous administration resulted in rapid and more pronounced clinical improvement.

Based on the results of present study it is evident that therapeutic exogenous melatonin administration is a useful medication with moderate efficacy in managing infantile colic. However, general lack of clinical trials warrants further studies in this regard. Therefore, it is strongly recommended that further studies may be conducted to establish stronger evidence regarding efficacy of melatonin in this condition. There were a few limitations of present study including lack of control arm and lack of comparison with other trials due to non-availability and non-conductance if such trials in the past.

Conclusion

In conclusion, melatonin is an effective intervention in the management of infantile colic. It resulted in complete recovery in 54.80% of the infants and partial improvement in 29.50% of the infants with colic.

References

1. Muller I, Ghio D, Mobey J, Jones H, Hornsey S, Dobson A, etval. Parental perceptions and experiences of infant crying: A systematic review and synthesis of qualitative research. J Adv Nurs. 2023;79(2):403-417. https://doi.org/10.1111/jan.15492
2. Harskamp-Van Ginkel MW, Klazema W, Hoogsteder MHH, Chinapaw MJM, van Houtum L. The need of having a plan in excessive infant crying - A qualitative study of parents' experiences of healthcare support. Acta Paediatr. 2023;112(3):434-441. https://doi.org/10.1111/apa.16618
3. Indrio F, Dargenio VN, Francavilla R, Szajewska H, Vandenplas Y. Infantile colic: a long-term outcomes in childhood: a narrative synthesis of the evidence. Nutrients. 2023;15(3):615. https://doi.org/10.3390/nu15030615.
4. Muhardi L, Aw MM, Hasosah M, Ng RT, Chong SY, Hegar B, et al. A narrative review on the update in the prevalence of infantile colic, regurgitation, and constipation in young children: implications of the ROME IV criteria. Front Pediatr. 2022;9:778747. https://doi.org/10.3389/fped.2021.778747.
5. Jalal MS, Mehdi SZ, Akber JU, Gowa MA, Lifschitz C. Infantile colic: a survey of physicians in Pakistan. Pediatr Gastroenterol Hepatol Nutr. 2024;27(3):186-195. https://doi.org/10.5223/pghn.2024.27.3.186
6. Johnson JM, Adams ED. The gastrointestinal microbiome in infant colic: a scoping review. MCN Am J Matern Child Nurs.2022;47(4):195-206. https://doi.org/10.1097/NMC.0000000000000832.
7. Kozhakhmetov S, Meiirmanova Z, Mukhanbetzhanov N, Jarmukhanov Z, Vinogradova E, Mureyev S, et al. Compositional and functional variability of the gut microbiome in children with infantile colic. Sci Rep. 2023;13(1):9530. https://doi.org/10.1038/s41598-023-36641-z.
8. Ateş Beşirik S, Geçkil E. The effect of therapeutic touch on colic symptoms in infantile colic infants: A randomised controlled study. J Paediatr Child Health. 2024;60(10):569-578. https://doi.org/10.1111/jpc.16646.
9. Ucuncu Egeli T, Tufekci KU, Ural C, Durur DY, Tuzun Erdogan F, Cavdar Z, et al. A new perspective on the pathogenesis of infantile colic: is infantile colic a biorhythm disorder? J Pediatr Gastroenterol Nutr. 2023;77(2):171-177. https://doi.org/10.1097/MPG.0000000000003815.
10. Shakiba M, Momayezolashjar M, Kaboutarkhani MH. Investigating the effect of melatonin on infantile colic: a clinical trial. J Pharm Neg Result. 2022;13(9):9767-9773. https://doi.org/10.47750/pnr.2022.13.S09.1142.
11. Ahmad SB, Ali A, Bilal M, Rashid SM, Wani AB, Bhat RR, et al. Melatonin and health: insights of melatonin action, biological functions, and associated disorders. Cell Mol Neurobiol.2023;43(6):2437-2458. https://doi.org/10.1007/s10571-023-01324-w
12. Vecchierini MF, Kilic-Huck U, Quera-Salva MA; Members of the MEL consensus group of the SFRMS. Melatonin (MEL) and its use in neurological diseases and insomnia: Recommendations of the French Medical and Research Sleep Society (SFRMS). Rev Neurol (Paris). 2021;177(3):245-259. https://doi.org/10.1016/j.neurol.2020.06.009
13. Paditz, E. Melatonin in infants—physiology, pathophysiology and intervention options. Somnologie. 2024;28:103–109. https://doi.org/10.1007/s11818-024-00456-5.
14. Brett BE, Vacaru S, Beijers R, de Weerth C. Infant colic and HPA axis development across childhood. Psychoneuroendocrinology. 2024;164:106965. https://doi.org/10.1016/j.psyneuen.2024.106965
15. Brown JM, Baran JV, Lamos L, Beacker J, Florio J, Oliveros LV, et al. Infant colic symptoms and amino acid formula: insights from a prospective cohort study. Nutrients. 2025;17(8):1302. https://doi.org/10.3390/nu17081302.
16. Helseth S, Misvær N, Småstuen M, Andenæs R, Valla L. Infant colic, young children's temperament and sleep in a population based longitudinal cohort study. BMC Pediatr. 2022;22(1):163. https://doi.org/10.1186/s12887-022-03231-3
17. Evans C, Lorentz WP. Efficacy and Safety of a Colic Relief Remedy in Infantile Colic. Glob Pediatr Health. 2022;9:2333794X221100810. https://doi.org/10.1177/2333794X221100810
18. Suklert K, Phavichitr N. Incidence and associated factors of infantile colic in Thai infants. Pediatr Gastroenterol Hepatol Nutr. 2022;25(3):276-282. https://doi.org/10.5223/pghn.2022.25.3.276

19. Hafiz AM, Ali MA, Hammad A. Frequency of infantile colic in neonates presenting at tertiary care hospital. Professional Med J. 2020; 27(11):2357-2362. https://doi.org/10.29309/TPMJ/2020.27.11.4588.
20. Nuzzi G, Trambusti I, DI Cicco ME, Peroni DG. Breast milk: more than just nutrition! Minerva Pediatr (Torino). 2021;73(2):111-114. https://doi.org/10.23736/S2724-5276.21.06223-X.
21. Chandran D, Warren K, McKeone D, Hicks SD. The Association between Infant Colic and the Multi-Omic Composition of Human Milk. Biomolecules. 2023;13(3):559. https://doi.org/10.3390/biom13030559.
22. Markowska M. Chrononutrition and the role of melatonin in neonates. Pediatr Med Rodz. 2025;21(1):46–50. https://doi.org/10.15557/PiMR.2025.0005.
23. Häusler S, Lanzinger E, Sams E, Fazelnia C, Allmer K, Binder C, et al. Melatonin in human breast milk and its potential role in circadian entrainment: a nod towards chrononutrition? Nutrients. 2024;16(10):1422. https://doi.org/10.3390/nu16101422.