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Research Article

The comparison between different over-the-counter drugs Analgesics used to relive cramps pain associated with menstrual cycle for females in Jordan on kidney function

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Abstract

Primary dysmenorrhea is an abdomen cramps caused pain for females under menstrual cycle. The majority of females in Jordan are consuming paracetamol and different types of NSAIDs to relive the mentioned pain. In this study a different group of females between ages 18–24 years old either not consuming any analgesic or consuming paracetamol, ibuprofen, or diclofenac salts have been asked to test the blood creatinine concentration after 10 days of consumption and after 5 and 10 days of discontinuation. SPSS analysis technique was used to analyse the results. As a results, consuming of paracetamol for 10 days show similar creatinine clearance for females without consuming any type of analgesics. While ibuprofen and diclofenac salts show change in kidney function after the 10 days of consumption. Ibuprofen normal kidney function was for 94.1% of the females where only 0.9% of the females show a sign of acute renal failure. On the other hand, the females using diclofenac salts show a high percentage of 61.2% with a sign of acute renal failure. Most of females show restored renal function after discontinuation of analgesics for 5 or 10 days. In conclusion, the consumption of analgesics between females should be monitored while the using of diclofenac salts should be considered as a prescribed drug due to the major and serious adverse drug reactions caused by the daily consumption.

Keywords

NSAIDs, Paracetamol, menstrual cycle, primary Dysmenorrhea

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) is a class of drug widely and heavily used in the world for the relieving of pain, fever, and inflammation (Moore et al. 2019). Most NSAIDs reversibly inhibit cyclo-oxygenase enzyme (COX) which will cause an inhibition in prostaglandins synthesis (Moore et al. 2019). Prostaglandin has a diverse activity in human body which explain the wide range of adverse effects associated with the consumption of NSAIDs (Moore et al. 2019). These adverse effects such as gastrointestinal bleeding, heart problems, renal failure, and hepatic problem are all associated with high consumption of NSAIDs for long period (Behmanesh et al. 2019). In Jordan, primary dysmenorrhea and heavy menstrual cycle bleeding are very common complaints among

young women (De Sanctis et al. 2015). These changes and symptoms associated with the menstrual cycle have a major contribution on females' quality of life socially and professionally every month (Munro et al. 2012). Primary dysmenorrhea is the abdominal pain associated with the ovulatory menstrual cycle (De Sanctis et al. 2015). This pain is a common in young females and affects more than 50% of them (Ferries-Rowe et al. 2020). On the other hand, heavy menstrual cycle bleeding is a massive and the most common cause of gynaecological referral for females in countries such as the United Kingdom (UK) (Davies and Kadir 2017). NSAIDs and contraceptives are the most common drugs used by females especially females with ages between 18–25 years old (Fisher et al. 2016). A study conducted in Jordan population indicates that 90.1% of the young females are using NSAIDs for primary dysmenorrhea including 42% ibuprofen, 34% paracetamol, 10% diclofenac salts, and less than 5% using prifinium bromide (Fisher et al. 2016). In this research, the authors are comparing between different analgesics used as an over-the-counter drug to relive the pain associated with menstrual cycle. Data were collected from the kidney centres at different private and governmental hospitals for young female patients with daily consumption of the major NSAIDs to reduce the effect of dysmenorrhea. The data were analysed using different statistical analysis techniques through the SPSS program. A final recommendation of the least NSAIDs renal adverse drug reaction was conducted to change Jordanian females' habit of using such drugs.

Materials and methods

Females selection

A 402 Normal Females (no underlaying diseases) with ages between 18–24 years old have been selected for this study. A physical examination and diagnostic testing were performed on the selected females to measure creatinine serum concentration and calculate glomerular filtration rate (GFR). The selected females have taken the drugs listed in Table 1 with the following doses to relive primary dysmenorrhea caused by menstrual cycle for 10 days continuously.

Table 1. Numbers of normal females with each drug and drug dose.

Analgesic type	Number females	Dose (mg)	Frequency/day
No analgesic	101	–	–
Paracetamol	99	1000	3
Ibuprofen	101	400	3
Diclofenac Sodium	101	100	3

Parameters used to monitor kidney function

Creatinine serum concentration

Creatinine serum concentration were measured for females after 10 days of paracetamol and NSAIDs consumption in addition to 5 and 10 days of discontinuation. All samples were collected at Prince Hamza Hospital in Amman, Jordan.

GFR calculation and albumin urea evaluation

All females participated in the study have been given a urine bag to analyse the concentration in albumin on the same time scale mentioned in creatinine section. In addition, GFR has been calculated and females have been categorized accordingly.

Ethical approval

Ethical approval has been taken from Hashemite Kingdom of Jordan ministry of health to use the clinical date from females participated in this study. Ethical approval code: MH-2022-1385.

Statistical analysis

IBM SPSS v25.0 was used for the statistical analysis. The data was presented as frequency and percentage (%). Columns were used for data visualization; each column represents a percentage of the population and not absolute numbers to avoid misrepresentation errors (one group is larger than the other). Differences between groups were analysed using the Chi-Square test of independence and the Z-test for column proportion. A P value of less than 0.05 was considered statistically significant. A Bonferroni correction was applied for all pairwise comparisons using the Z-test.

Results

The effect of using different analgesics for 10 days on kidney function

During menstrual cycle, females without using any kind of analgesics show no change in kidney function as GFR, creatinine serum level, and albuminuria concentration were normal. Thus, females with no use of analgesics have been chosen as a control to be compared with females used NSAIDs and paracetamol. After 10 days of using paracetamol, kidney function was not affected and 100% of females were found to have a normal GFR, creatinine serum level, and albuminuria concentration of ≥ 60 ml/min, < 2 mg/dL, and < 3 mg/mmole respectively. While ibuprofen show some effect on female's kidney function as 5.9% of them show increase in albuminuria level to be between 3–29 mg/mmole, with a lower GFR and a higher creatinine serum level of 15–59 ml/min and 2–4 mg/dL respectively. On the other hand, the majority of females used diclofenac sodium for pain relive show impaired renal function with signs of acute renal failure. Only 11.9% with normal albuminuria level and 9.9% of them with normal serum creatinine level and GFR. All correlation between type of analgesics and their effect on creatinine serum level, GFR, and albuminuria produced a *P*-value of less than 0.05 with confidence interval of 95%. The effect of paracetamol and NSAIDs, continually for 10 days are presented in Figs 1–3.

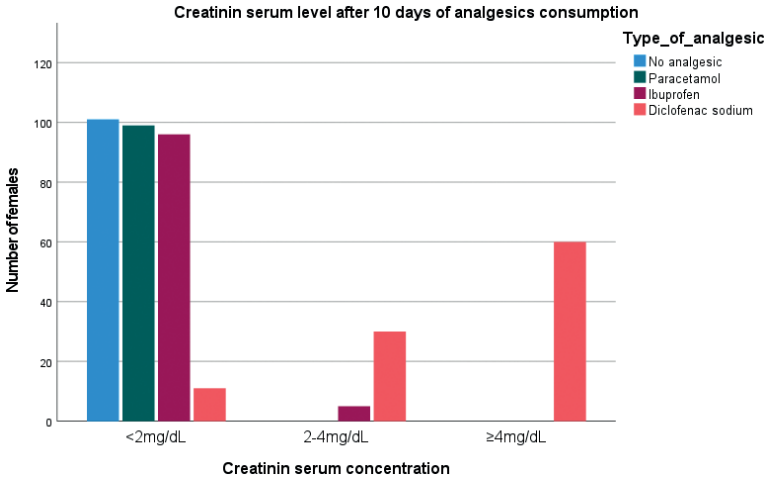

Figure 1. Creatinine serum level after analgesics consumption for 10 days in comparison with no use of analgesics.

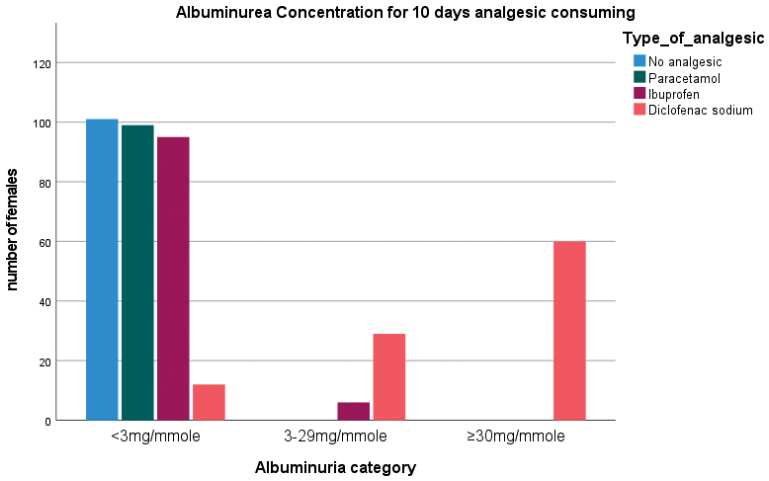

Figure 2. Albumin concentration after analgesics consumption for 10 days in comparison with no use of analgesics.

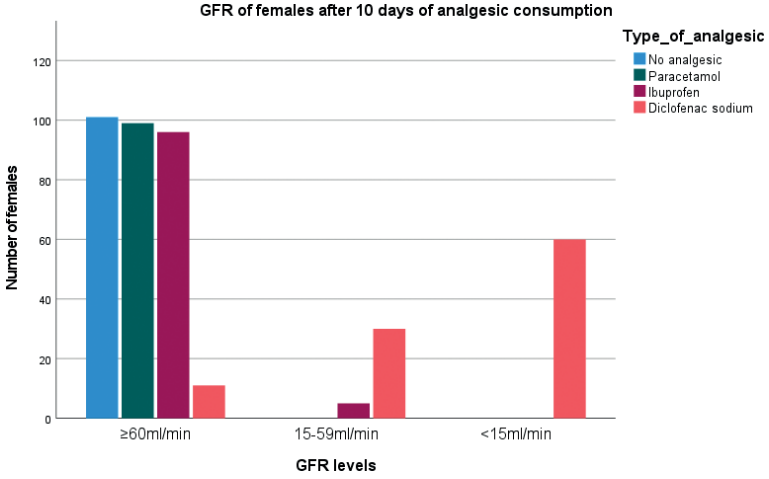

Figure 3. GFR after analgesics consumption for 10 days in comparison with no use of analgesics.

The effect of using different analgesics after 5 days of discontinuation on kidney function

After 5 days of analgesic discontinuation, females using paracetamol show no change and kidney function was normal without any change. On the other hand, both females using ibuprofen and diclofenac sodium were found to returned renal function towards normal as the percentages of females with kidney function has increased to 98 and 21.8% respectively. All correlation between type of analgesics and their effect of creatinine serum level, GFR, and albuminuria produced a *P*-value of less than 0.05 with confidence interval of 95%. Kidney function tests results after 5 days of paracetamol and NSAIDs discontinuation are presented in Figs 4–6.

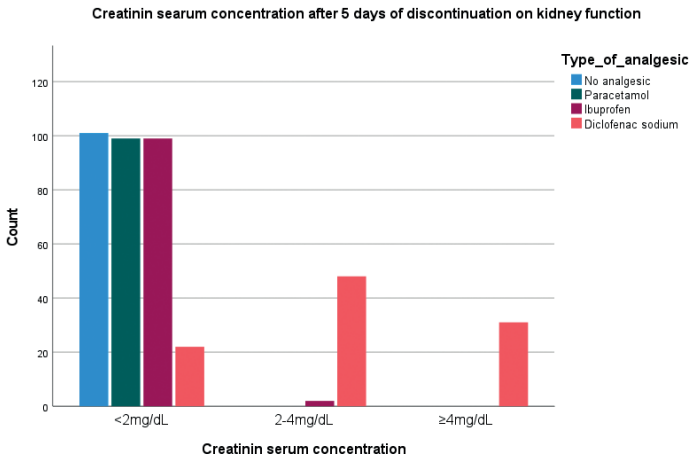

Figure 4. Creatinine serum level after analgesics discontinuation for 5 days.

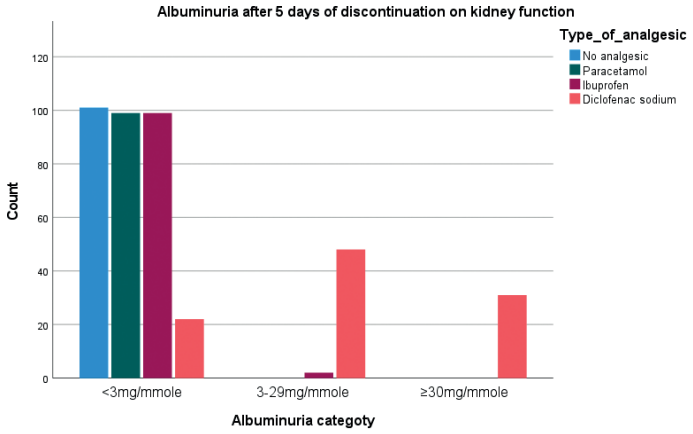

Figure 5. Albumin concentration after analgesics discontinuation for 5 days.

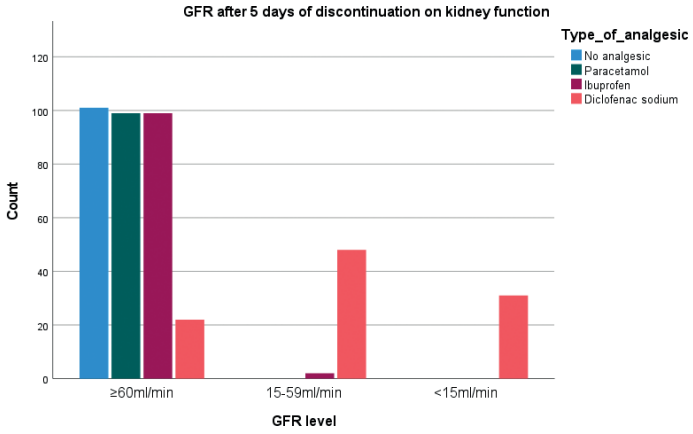

Figure 6. GFR after analgesics discontinuation for 5 days.

The effect of using different analgesics after 10 days of discontinuation on kidney function

Finally, after 10 days of analgesics discontinuation most of all females used paracetamol kidney function still normal and females used ibuprofen have shown a full return to a normal kidney function with a percentage of 100%. In same manner, the percentage females consumed diclofenac sodium returned with normal kidney function have increased to 54.5% with no females with any sign of acute kidney injury. All correlation between type of analgesics and their effect of creatinine serum level, GFR, and albuminuria produced a *P*-value of less than 0.05 with confidence interval of 95%. Kidney function tests results after 5 days of paracetamol and NSAIDs discontinuation are presented in Figs 7–9.

Discussion

Primary dysmenorrhea is a painful abdomen cramps happens with females during menstrual cycle (Dawood 2006).

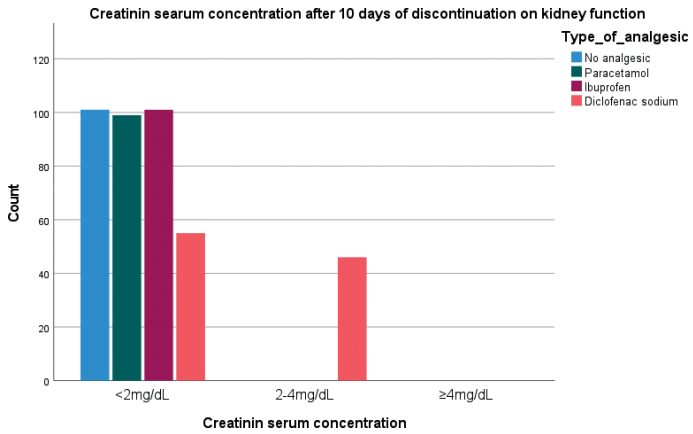

Figure 7. Creatinine serum level after analgesics discontinuation for 10 days.

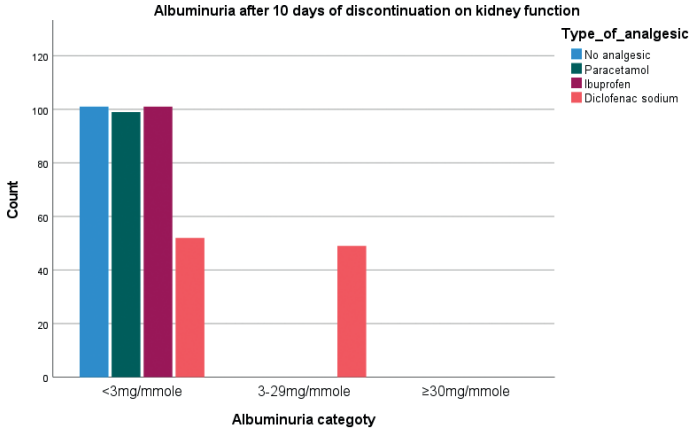

Figure 8. Albumin concentration after analgesics discontinuation for 10 days.

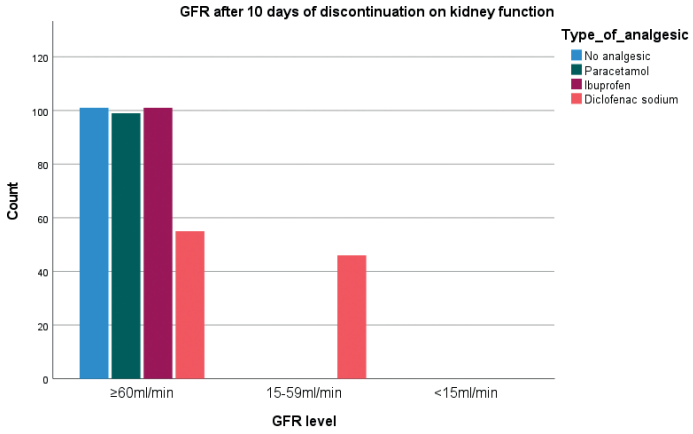

Figure 9. GFR after analgesics discontinuation for 10 days.

In Jordan, females between 18–24 years old are consuming different types of analgesics including paracetamol, ibuprofen, naproxen, and diclofenac salts to relive the mentioned pain. In addition, some females are using herbal remedy from different medicinal plants to reduce the possible adverse drug events caused by the previously mentioned analgesics (Behmanesh et al. 2019). Unfortunately, the using of these herbal remedy was very limited and the majority of females still using either paracetamol or NSAIDs in market (Al Ajeel et al. 2020). The used analgesics especially NSAIDs have been proved to exert a direct adverse drug reaction on cardiac, hepatic, and renal systems at human body (Wong 2019; Schjerning et al. 2020; Ghlichloo and Gerriets 2021). In this research only paracetamol was found to exert similar effect of the control samples of females (without using any drug) and kidney function for 100% of the females were not affected after the consumption 3000 mg of paracetamol for 10 days continuously. This finding was similar to other findings as paracetamol is already the safest drug to be used for patients with liver, cardiac and renal failure as its effect is very low and the therapeutic window is large (Alchin et al. 2022). On the other hand, the using of ibuprofen show aggravated adverse drug reactions for 5–5.9 of females used it after consumption of 1200 mg/daily for 10 days. A similar finding about using Ibuprofen was found that the mentioned drug exert the milder adverse drug reaction between all

NSAIDs as it can be used with patients with impaired renal function with dosing adjustment (Forouzanfar et al. 2019). While the using of 300 mg of diclofenac sodium for 10 days during menstrual cycle have shown a sever adverse drug reaction on renal function. Only 11.9% of the females kept a normal kidney function while the rest had either kidney damage or acute renal failure. In previous study several animal model and case reports have approved that diclofenac salts have a sever and aggressive adverse drug reaction on kidney after continuous consumption for short period of time (Forouzanfar et al. 2019). According to creatinine concentration results in Figs 1, 4, 7, albuminuria concentration results in Figs 2, 5, 8 and calculated GFR results in Figs 3, 6, 9 after discontinuation of ibuprofen and diclofenac sodium for 5 and 10 days the percentage of females with restored renal function have increased. This finding was similar to many findings as most of the patients with acute renal failure and consuming different types of NSAIDs has shown a restore in kidney function after discontinuation (Harężlak et al. 2022)

Conclusion

NSAIDs prescribing for females between ages 18–24 under menstrual cycle should be taken in consideration as its excessively consumed due to primary dysmenorrhea. Paracetamol as an analgesic is the best drug of choice to relive cramps pain for females even with its possible adverse drug reaction on liver. While ibuprofen should be given for severe pain only as many females show aggravated kidney function results. On the other hand, diclofenac salts are recommended to be a prescribed drugs not over the counter drugs as high percentage of young females show acute renal failure signs. Finally, its recommended to enhance the medical awareness about the sever and serious adverse drug reaction of the uncontrolled use of NSAIDs especially between the human population that consume such drugs in a daily basis.

Conflict of interest

This research has no conflict of interest.

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