Article

Evaluation of some prescribed and over-the-counter drugs induced hemato-biochemical changes in mice

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Abstract: The present study was performed in the Department of Physiology and Pharmacology, Faculty of Animal science and Veterinary Medicine, PSTU, Bangladesh. Data were collected using a semi-structured questionnaire from 125 people in Babugonj upazilla, Barishal for using drugs without prescription or at prescription. The experiment was conducted to evaluate the effects of prescribed and over-the-counter drugs on hematological (TEC, Hb and DLC) and biochemical (blood glucose) parameters in mice during the period March to April, 2019. 140 male mice were randomly divided into seven groups (A, B, C, D, E, F and G), each consisting of 20 mice. Group A was kept as control. Paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam were administered orally to mice of group B, C, D, E, F and G, respectively for 28 days. Paracetamol and ranitidine were used by 100% people followed by peantoprazole (80.80%), diclofenac-60%, diazepam-42.40% and clonazepam-24%, respectively without prescription. Paracetamol were used by 100% people followed by peantoprazole (84%), ranitidine-76%, diclofenac-66.40%, clonazepam-53.60% and diazepam 32.80%, respectively at prescription. Paracetamol and diazepam decreased significantly ($p<0.05$) total erythrocyte count (TEC) at 28th day. Paracetamol, diclofenac and diazepam decreased significantly ($p<0.01$ and $p<0.05$) hemoglobin content (Hb) at 28th day. The Differential leukocyte count (DLC) was not significantly changed at 28th day in mice. Paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam increased significantly ($p<0.01$ and $p<0.05$) blood glucose level in mice. It may be concluded that paracetamol is one of the most frequently used and self prescribing drugs in Bangladesh.

Keywords: paracetamol; diclofenac; pantoprazole; ranitidine; diazepam; clonazepam; hemato-biochemical parameter

1. Introduction

Drug is any substance that inhaled, injected, smoked, consumed, absorbed via a patch on the skin, or dissolved under the tongue causes a temporary physiological/psychological change in the body. In pharmacology, drug is a chemical substance when administered to a living organism, produces a biological effect (Adams, 1995). Now-a-days, there is a great problem that so many people use different drugs, either over-the-counter (OTC) drugs or prescription drug, without any concern of physician/doctor or take overdose/subnormal dose of drug

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without following the prescription unconsciously. That causes different side effects, toxicity, hazard and idiosyncrasy on body.

Paracetamol is a widely used analgesic and antipyretic drugs (Anderson *et al.,* 1998; Vane *et al.,* 1998). Diclofenac sodium is a widely circulated drug, used both in humans and animals for the treatment and management of inflammation, fever and pain associated with disease or injury of domestic livestock and humans (Orinya *et al.*, 2016). Pantoprazole are the drug whose main action is pronounced and long-lasting reduction of gastric acid production (Bigoniya *et al.*, 2011). Ranitidine is a medication which established as a potent inhibitor of gastric acid secretion (Pahwa *et al.*, 2016). Diazepam is used for its myorelaxant, anxiolytic, sedative, and anticonvulsant properties (Crestani *et al.*, 2016). Clonazepam acts as sedative, hypnotic, muscle relaxant and anticonvulsants and are especially useful in treating acute anxiety and transient insomnia (Zorzanelli *et al.*, 2019).

To maintain sound health, we should conscious of using drugs. We should follow the prescription and avoiding the overdoses or side effects of drugs. In Bangladesh, there is very few research data of drugs are available. The survey will be build up awareness of people about prescribed and OTC drugs to avoid different side effects, toxicity, hazard and idiosyncrasy on body in Bangladesh. The experiment was conducted to assess the use of different types of prescribed and OTC drugs in Babugonj upazilla of Barishal district at prescription or without prescription. The experiment was also evaluate the effects of prescribed and over-the-counter drugs (paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam) on hematological (TEC, Hb and DLC) and biochemical (blood glucose) parameters in mice.

2. Materials and Methods

The experiment was performed in the laboratory of Department of Physiology and pharmacology, Patuakhali Science and Technology University, Babuganj, Barishal, during a period from 10 March, 2019 to 6 April, 2019. A local level survey of people was conducted in Babugonj upazilla of Barishal district of Bangladesh during January, 2019 to February, 2019. Data (information) were collected by a semi-structured questionnaire from 125 people (Farmer-25, Shopkeeper-25, Rickshaw puller-25, Teacher-25 and Student-25) for using different drugs (paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam) at prescription or without prescription. A total of 140 Swiss Albino male mice were collected from the ICDDR,B, Mohakhali, Dhaka. After procurement, all the mice were kept under close observation in order to acclimatize in the new environmental condition of the experimental Pharmacology Laboratory, Faculty of Animal Science and Veterinary Medicine, Patuakhali Science and Technology University for a period of one week prior to commencement of the experiment. All the mice will be maintained under good housing conditions and provide normal feed. One hundred forty (140) male mice were randomly divided into seven groups (A, B, C, D, E, F and G), each consisting of twenty (20) mice. Group A was kept as control group received only basal feed. Paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam were administered orally to the mice of group B, C, D, E, F and G, respectively with basal feed with standard dose for 28 days. The effects of six patent prescribed and OTC drugs [paracetamol (Tab. Fast® 500, @15 mg/kg b.wt), diclofenac (Tab. Clofenec® 50, @50 mg/kg b.wt), pantoprazole (Tab. Trupan® 20, @15 mg/kg b.wt), ranitidine (Tab. Neotack® 150, @10 mg/kg b.wt), diazepam (Tab. Sedil®, @5 mg/ kg b.wt) and clonazepam (Tab. Epitra® 2, @)2 mg/ kg b.wt] on hemato-biochemical parameters (TEC, Hb, DLC and blood glucose] were evaluated in Swiss Albino male mice. Blood glucose level were recorded on day 0 (pre treatment) and on 7th, 14th, 21st and 28th day of experimental period by the help of Glucometer. Hematological parameters (TEC, Hb and DLC) were determined on the 28th day by the standard method as described by Coffin (1953). Collected data were statistically analyzed by Student's t-test by using the computer statistical package programme of Microsoft Excel.

3. Results and Discussion

3.1. Use of different types of prescribed and OTC drugs in Babugonj upazilla of Barishal district

The use of prescribed and OTC drugs (paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam) in Babugonj upazilla of Barishal district without prescription were shown in the Table 1. Paracetamol and ranitidine were used by 100% people. 80.80% people used peantoprazole (Farmer-72%, Shopkeeper-80%, Rickshaw puller-64%, Teacher-100% and Student-88%) followed by diclofenac-60% (Farmer-52%, Shopkeeper-36%, Rickshaw puller-60%, Teacher-72% and Student-80%), diazepam-42.40% (Farmer-20%, Shopkeeper-36%, Rickshaw puller-16%, Teacher-80% and Student-60%) and clonazepam-24% (Farmer-8%, Shopkeeper-20%, Rickshaw puller-4%, Teacher-56% and Student-32%), respectively. Similar observation has been reported by Chowdhury *et al.* (2012) due to diazepam and clonazepam.

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The use of prescribed and OTC drugs (paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam) in Babugonj upazilla of Barishal district at prescription were shown in the Table 2. Paracetamol were used by 100% people. 84% people used peantoprazole (Farmer-80%, Shopkeeper-88%, Rickshaw puller-72%, Teacher-100% and Student-80%) followed by ranitidine-76% (Farmer-64%, Shopkeeper-88%, Rickshaw puller-80%, Teacher-80% and Student-68%), diclofenac-66.40% (Farmer-68%, Shopkeeper-48%, Rickshaw puller-64%, Teacher-80% and Student-72%), clonazepam-53.60% (Farmer-36%, Shopkeeper-48%, Rickshaw puller-24%, Teacher-88% and Student-72%) and diazepam 32.80% (Farmer-16%, Shopkeeper-24%, Rickshaw puller-12%, Teacher-64% and Student-48%), respectively.

3.2. Effects of prescribed and OTC drugs on hematological parameters in mice
Paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam caused changes on hematological parameters (TEC, Hb and DLC) in mice. The results of the paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam on hematological parameters were shown in the Table 3.

3.2.1. Total erythrocyte count (TEC, million/cu.mm.)
Paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam caused changes on total erythrocyte count (TEC) at 28th day in mice. Paracetamol and diazepam decreased significantly ($p<0.05$) TEC at the mice of group B and F, respectively. On the 28th day TEC was 6.31 ± 0.26, 5.24 ± 0.60, 6.44 ± 0.17, 6.19 ± 0.24, 6.22 ± 0.18, 6.13 ± 0.37 and 6.36 ± 0.32, respectively in groups A, B, C, D, E, F and G. These results are agreeable with the report of Oyedeji *et al.* (2013). He reported that after administrating of paracetamol in albino mice for 42 days significantly decreased total erythrocyte count (TEC). Likewise, Hossain *et al.* (2003) reported that paracetamol significantly decreased TEC. Similar response has been reported by Suresha *et al.* (2012) due to diazepam.

3.2.2. Hemoglobin content (Hb, gm %)
Paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam caused changes on hemoglobin content (Hb) at 28th day in mice. Paracetamol, diclofenac and diazepam decreased significantly ($p<0.01$ and $p<0.05$) Hb at the mice of group B, C and F, respectively. On the 28th day Hb was 10.18 ± 0.22, 9.04 ± 0.40, 11.12 ± 0.28, 10.26 ± 0.23, 10.10 ± 0.40, 9.94 ± 0.45 and 10.16 ± 0.53, respectively in groups A, B, C, D, E, F and G. In confirmatory to the present findings, Ukwueze *et al.* (2014) observed that prolonged use of paracetamol decreased Hb content significantly. This observation is also in agreement with the earlier reports on paracetamol of Oyedeji *et al.* (2013) and Hossain *et al.* (2003). Likewise, Orinya *et al.* (2016) reported that after administrating diclofenac decreased Hb content in wistar rats. Similar results have been observed in dogs following diazepam administration by Suresha *et al.* (2012).

3.2.3. Differential leukocyte count (DLC, %)
Paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam were caused very little changes neutrophil, lymphocyte, eosinophil and monocyte count of differential leukocyte count (DLC) in group B, C, D, E, F and G, respectively at 28th day in mice. On the 28th day neutrophil count was 57.20 ± 1.79, 56.80 ± 1.92, 56.40 ± 1.14, 59.60 ± 2.04, 59.00 ± 1.92, 60.80 ± 0.84 and 60.20 ± 2.77, respectively in groups A, B, C, D, E, F and G. On the 28th day lymphocyte count was 35.20 ± 1.58, 36.20 ± 2.49, 37.80 ± 1.30, 33.20 ± 2.16, 34.60 ± 0.84, 33.40 ± 1.64 and 33.20 ± 1.22, respectively in groups A, B, C, D, E, F and G. On the 28th day eosinophil count was 4.80 ± 0.84, 4.60 ± 1.14, 3.80 ± 0.84, 4.80 ± 0.83, 3.80 ± 0.83, 3.40 ± 0.55 and 4.00 ± 0.70, respectively in groups A, B, C, D, E, F and G. On the 28th day monocyte count was 2.80 ± 0.84, 2.40 ± 0.55, 2.00 ± 0.55, 2.40 ± 0.55, 2.60 ± 0.55, 2.40 ± 0.55 and 2.60 ± 0.55, respectively in groups A, B, C, D, E, F and G.

3.3. Effect of prescribed and OTC drugs on biochemical parameter (blood glucose) in mice
Paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam caused significant changes on blood glucose level in mice. The blood glucose level was increased significantly ($p<0.01$ and $p<0.05$) after Paracetamol, diclofenac, pantoprazole, ranitidine, diazepam and clonazepam treatment in group B, C, E, F and G, respectively. The results of the prescribed and OTC drugs on blood glucose level in mice were shown in the Table 4. Mean blood glucose level of control group on pre-treatment (day 0) was 4.22 ± 0.16. Mean blood glucose level on the 7th, 14th, 21st and 28th day were 4.58 ± 0.30, 4.90 ± 0.26, 5.22 ± 0.34 and 5.39 ± 0.33, respectively in group A. Mean blood glucose level before treatment was 4.35 ± 0.17 and after treatment with paracetamol mean blood glucose level on 7th, 14th, 21st and 28th day were 4.87 ± 0.18, 5.33 ± 0.28, 5.86 ± 0.25 and 6.65 ± 0.40, respectively in group B. Mean blood glucose level before treatment was 4.12 ± 0.13 and after

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treatment with diclofenac mean blood glucose level on 7th, 14th, 21st and 28th day were 4.86±0.22, 5.53±0.36, 6.05±0.48 and 6.71±0.66, respectively in group C. Mean blood glucose level before treatment was 4.51±0.31 and after treatment with pantoprazole mean blood glucose level on 7th, 14th, 21st and 28th day were 4.79±0.34, 5.66±0.53, 5.98±0.48 and 7.87±1.53, respectively in group D. Mean blood glucose level before treatment was 4.33±0.19 and after treatment with ranitidine mean blood glucose level on 7th, 14th, 21st and 28th day were 4.61±0.29, 5.41±0.10, 6.34±0.59 and 7.26±0.94, respectively in group E. Mean blood glucose level before treatment was 4.50±0.37 and after treatment with diazepam mean blood glucose level on 7th, 14th, 21st and 28th day were 4.66±0.38, 5.12±0.59, 5.88±0.43 and 6.59±0.76, respectively in group F. Mean blood glucose level before treatment was 5.41±0.67 and after treatment with clonazepam mean blood glucose level on 7th, 14th, 21st and 28th day were 5.58±0.73, 6.52±0.79, 7.39±0.83 and 7.53±1.10, respectively in group G. In confirmatory to the present findings, Hossain *et al.* (2003) reported that paracetamol significantly increased blood glucose in mice. Similar response has been reported due to paracetamol (Amin *et al.*, 2004), diclofenac (Ahmad *et al.*, 2012), pantoprazole (Agrawal *et al.*, 2018), ranitidine (Gentile *et al.*, 1986), diazepam (Suresha *et al.*, 2012) and clonazepam (Bougherara and Bouaziz, 2014).

Table 1. Use of different types of prescribed and OTC drugs in Babugonj upazilla of Barishal district without prescription (%).

Drug	Farmer	Shopkeeper	Rickshaw puller	Teacher	Student	Total
Paracetamol	100	100	100	100	100	100
Diclofenac	52	36	60	72	80	60
Pantoprazole	72	80	64	100	88	80.80
Ranitidine	100	100	100	100	100	100
Diazepam	20	36	16	80	60	42.40
Clonazepam	8	20	4	56	32	24

Table 2. Use of different types of prescribed and OTC drugs in Babugonj upazilla of Barishal district at prescription (%).

Drug	Farmer	Shopkeeper	Rickshaw puller	Teacher	Student	Total
Paracetamol	100	100	100	100	100	100
Diclofenac	68	48	64	80	72	66.40
Pantoprazole	80	88	72	100	80	84
Ranitidine	64	88	80	80	68	76
Diazepam	16	24	12	64	48	32.80
Clonazepam	36	48	24	88	72	53.60

Table 3. Effects of prescribed and OTC drugs on hematological parameters (TEC, Hb and DLC) in mice.

Group	Treatment	TEC (million /cu.mm.)	Hb content (gm %)	Neutrophil (%)	Lymphocyte (%)	Eosinophil (%)	Monocyte (%)
A	-	6.31 ±0.26	10.18 ±0.22	57.20 ±1.79	35.20 ±1.58	4.80 ±0.84	2.80 ±0.84
B	Paracetamol	5.24 ±0.60*	9.04 ±0.40**	56.80 ±1.92	36.20 ±2.49	4.60 ±1.14	2.40 ±0.55
C	Diclofenac	6.44 ±0.17	11.12 ±0.28**	56.40 ±1.14	37.80 ±1.30	3.80 ±0.84	2.00 ±0.55
D	Pantoprazole	6.19 ±0.24	10.26 ±0.23	59.60 ±2.04	33.20 ±2.16	4.80 ±0.83	2.40 ±0.55
E	Ranitidine	6.22 ±0.18	10.10 ±0.40	59.00 ±1.92	34.60 ±0.84	3.80 ±0.83	2.60 ±0.55
F	Diazepam	6.13 ±0.37*	9.94 ±0.45*	60.80 ±0.84	33.40 ±1.64	3.40 ±0.55	2.40 ±0.55
G	Clonazepam	6.36 ±0.32	10.16 ±0.53	60.20 ±2.77	33.20 ±1.22	4.00 ±0.70	2.60 ±0.55

The above values represent the mean ± standard deviation (SD)
** = Significant at 1 per cent level (p<0.01) * = Significant at 5 per cent level (p<0.05)

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Table 4. Effects of prescribed and OTC drugs on biochemical parameter (blood glucose) in mice.

Group	Treatment	Dose (mg/kg b.wt.)	Pre-treatment '0' day	Post-treatment 7th day	14th day	21st day	28th day
A	-	-	4.22 ±0.16	4.58 ±0.30	4.90 ±0.26	5.22 ±0.34	5.39 ±0.33
B	Paracetamol	15	4.35 ±0.17	4.87 ±0.18*	5.33 ±0.28**	5.86 ±0.25**	6.65 ±0.40**
C	Diclofenac	50	4.12 ±0.13	4.86 ±0.22*	5.53 ±0.36**	6.05 ±0.48**	6.71 ±0.66**
D	Pantoprazole	15	4.51 ±0.31	4.79 ±0.34	5.66 ±0.53**	5.98 ±0.48**	7.87 ±1.53**
E	Ranitidine	10	4.33 ±0.19	4.61 ±0.29*	5.41 ±0.10	6.34 ±0.59	7.26 ±0.94**
F	Diazepam	05	4.50 ±0.37	4.66 ±0.38*	5.12 ±0.59**	5.88 ±0.43**	6.59 ±0.76**
G	Clonazepam	02	5.41 ±0.67	5.58 ±0.73*	6.52 ±0.79**	7.39 ±0.83**	7.53 ±1.10**

The above values represent the mean ± standard deviation (SD)
** = Significant at 1 per cent level ($p < 0.01$) * = Significant at 5 per cent level ($p < 0.05$)

4. Conclusions

Self-medication is one component of self-care, more awareness is needed to foster the level of people's attitudes towards self-medication practices and it is important to consider the manners of drug availability and consumption to decrease unnecessary health risks. The study give some information about the use of some prescribed and OTC drugs.

Conflict of interest

None to declare.

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