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Post-marketing surveillance on safety and efficacy of Spasmodart in primary dysmenorrhea: A survey-based study

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Abstract
Dysmenorrhea is one of the most common problems affecting majority of females of reproductive age group. It substantially compromises the overall quality of life of the sufferer almost like a chronic illness. This study was aimed to evaluate the safety and efficacy of Spasmodart Tablet for the complaints of primary dysmenorrhea. A validated survey questionnaire was administered to General Practitioners, Obstetricians, Gynecologists, and General Surgeons. Safety and efficacy data were recorded based on their practice experience. Around 80% of study participants reported no side-effects among patients with Spasmodart and 20% of participants reported mild side-effects of gastric acidity and dizziness (15.1%), acidity, giddiness and nausea (11.3%). More than 60% of participants opined that 1-day dosage was sufficient to get results with Spasmodart in patients with primary dysmenorrhea and more than 30% rated the pain relief score as 8 followed by 7 (15.9%) and 10 (14.3%) (10 being highest/best and 1 being least). Around 85% of study participants responded that their patients felt much better than before with Spasmodart. Around one-fourth of the study participants rated score-8 for the safety of Spasmodart followed by 20.2% participants who rated score-10 score, 18.7% participants rated score-7, 16.3% participants rated score-9. With these results, we conclude that Spasmodart shows promising safety and efficacy in patients presented with primary dysmenorrhea.

Keywords: Dysmenorrhea, primary dysmenorrhea, Spasmodart

1. Introduction
Menstruation is a periodic and cyclical shedding of progestational endometrium which involves many hormonal changes, accompanied by loss of blood. It is a normal physiological process that begins during adolescence and may be associated with various symptoms occurring before or during the menstrual flow [1]. This monthly experience by females adds a powerful tool to the assessment of normal development and the exclusion of pathological conditions among them, and it is one of the determinants of a woman's reproductive health [2].

Disorders in cycles or its irregularities are major gynecological complaints among female adults especially adolescent [3, 4]. This leads to a chief source of anxiety at both individual and family level. Studies have shown that a large proportion of female population of reproductive age suffers from menstruation related health issues [5, 7]. Abnormal menstrual cycle is considered as any deviation from the normal cycle and menstrual disorders prevailing in adolescent girls includes dysmenorrhea, amenorrhea, menorrhagia, hypomenorrhea, polymenorrhea, oligomenorrhea, and premenstrual syndrome.

Dysmenorrhea is one of the most common health problems in young adolescent girls as it affects 50-90% of the general population [8]. Dysmenorrhea refers to a cyclical lower abdominal or pelvic pain which may radiate to the back or to the thighs, occurring during menstruation often accompanied by other biological symptoms including dizziness, fatigue, sweating, backache, headache, nausea, vomiting, and diarrhea. Dysmenorrhea is divided into two types: primary dysmenorrhea and secondary dysmenorrhea. Primary dysmenorrhea is the one, in which there is cramping pain in the lower abdomen at the onset of menstruation in absence of any identifiable pelvic disease. Secondary dysmenorrhea is a menstrual pain associated with underlying pathology and its onset might be years after menarche [9]

The prevalence of dysmenorrhea among young women varies widely from country to country. A recent study on dysmenorrhea showed that there are different prevalence rates among females in different countries and different associated factors with dysmenorrhea or severity of pain [10] Previous studies on university students showed its prevalence to be 34% in Egypt, 64% in Nigeria and Mexico, 84% in Thailand 88% in Turkey, 93% in Taiwan, 74.5% in Malaysia, 70% in Italy, 80% in Australia and 85% among Hispanics. Its lowest prevalence has been so far reported in Japan (16%) [3, 11, 20]. Studies from various parts of India reported the prevalence of dysmenorrhea between 50 to 87.8% [21, 26]. Several studies reported that various physiological, cultural, and psychological factors are involved in dysmenorrhea. Reported risk factors for dysmenorrhea include earlier age at menarche, longer menstrual periods, heavier menstrual flow, family history of dysmenorrhea, and reduced frequency of breakfast meals per week and low body mass index (BMI) [27, 30] Dysmenorrhea is an important public health problem among students and is associated with school absenteeism and poor

quality-of-life. Approximately 10-15% of females experience monthly menstrual pain severe enough to stop normal daily functions at work, home, or school [26, 31, 33].
Due to its importance, different treatments like pharmacological and non-pharmacological treatment approaches such as nonsteroidal anti-inflammatory drugs (NSAIDS), herbal, dietary therapies, yoga, meditation, and acupuncture have been tried to decrease the effects of dysmenorrhea [33]. With this background, the present study was aimed to assess the safety and efficacy of Spasmodart in primary dysmenorrhea.

Materials and Methods

Study design and participants

A questionnaire-based survey was conducted among 252 practicing doctors who were working as General Practitioners, Obstetricians and Gynecologists and General Surgeons across pan India based on the available data in Jagdale Industries Pvt. Ltd. (JIPL) central database. A convenience sampling was adopted to target medical practitioners of the major hospitals from Northern, Southern, Eastern, Western part of India that represent a diversity of geographical area and population size. Hospitals included were public, private and university hospitals. Medical practitioners from each city's major public and private hospitals and health services were invited to participate in the study. All types of primary and secondary care providers were targeted.

Data collection instruments

A validated survey questionnaire was prepared which majorly consisted of three parts. First part was on details regarding purpose of survey and the consent form, second part was on demographic details and third part was on questions on safety and efficacy of Spasmodart. All the eligible doctors who met the Inclusion and exclusion criteria were enrolled into the study. Study questionnaires was distributed to the company Medical Representatives across India to collect the responses from the doctors. Medical Representatives visited the doctor's facility and collected the information from them. All the questionnaires were archived securely and statistically analyzed.

Inclusion and Exclusion Criteria

The inclusion criteria are as follows

- Participants/doctors falling under General Practitioner or Obstetrics and Gynecologist, or General Surgeons
- Willing to provide consent
- Willing to provide information for the survey questions

Exclusion Criteria

The exclusion criteria are as follows

- Participants who are from different specialties
- Not willing to provide consent
- Not willing to provide information for the survey questions

Formulation Details

Table 1: Formulation details of Spasmodart

Brand Name	Spasmodart
Generic Name	Paracetamol, Dicyclomine HCl and Diclofenac Sodium
Composition	Paracetamol IP – 325 mg Dicyclomine HCl – 20 mg Diclofenac Sodium – 50 mg
Product Category	Antispasmodic, Analgesic and Anti-inflammatory
Schedule	Schedule H Drug
Shelf-life	24 months from date of manufacture
Dosage	1 to 3 tablets per day

Statistical Analysis

The analysis of the survey data was processed using Microsoft Excel – Office 365. The data obtained in the form based on the multiple-choice answer was analyzed quantitatively. Findings was presented in the form of percentage of participants reporting each response for particular factor.

Results

Out of 252 study participants, 246 (97.6%) medical practitioners agreed to participate in the survey and to use data for publication. Majority of study participants (71%) responded that in their day-to-day practice, menstrual cramps remains the most common sign and symptom of primary dysmenorrhea, followed by nausea and vomiting, spasmodic pain followed by fever, fatigue, headache and diarrhea (Figure 1).

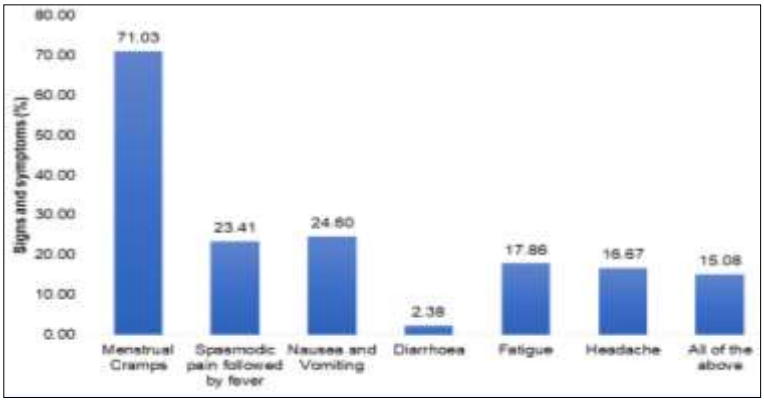

Fig 1: Common signs and symptoms of primary dysmenorrhea

Out of 246 study participants, more than 95% agreed Spasmodart to be commonly prescribed medication for primary dysmenorrhea (Figure 2) and around 67% of study participants responded that Spasmodart was prescribed when patients suffered from primary dysmenorrhea, followed by intestinal colic / renal colic (51.98%), low backache (20.63%) and irritable bowel syndrome (IBS) (7.14%) (Figure 3).

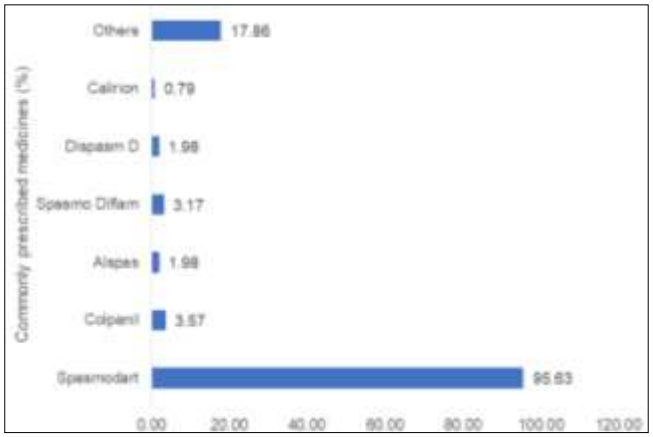

Fig 2: Commonly prescribed medications for primary dysmenorrhea

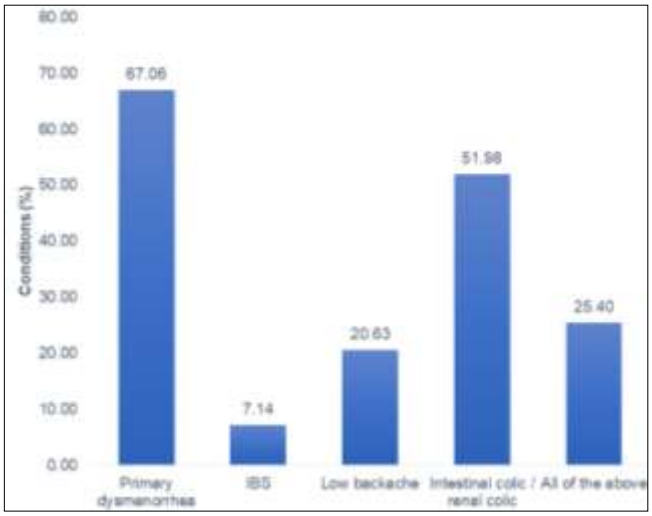

Fig 3: Condition(s) for which Spasmodart is prescribed

More than 40% of study participants replied that they have been prescribing Spasmodart for primary dysmenorrhea during last 1 year to 5 years, followed by 5 years to 10 years (21.0%), less than a year (20.6) and more than 10 years (16.7%) (Table 2).

Table 2: Prescribing duration of Spasmodart in patients with primary dysmenorrhea

Options	No. of participants	Percent
1 year to less than or equal to 5 years	105	41.7
More than 5 years to 10 years	53	21.0
Less than a year	52	20.6
More than 10 years	42	16.7
Total	252	100.0

Out of 246 study participants, more than 60% opined that it takes 1 day to get results with Spasmodart in patients with primary dysmenorrhea. The responses suggest that in some patients it takes 1 to 2 days (33.3%) while in others it takes 2 to 4 days (5.2%) to get desired relief (Table 3). More than 30% study participants rated the pain relief score as 8 in patients with primary dysmenorrhea, followed by 7(15.9%) and 10(14.3%) (Figure 4). Around 85% of study participants believed that their patients felt much better than before with Spasmodart (Table 4).

Table 3: Duration to get results with Spasmodart in patients with primary dysmenorrhea

Options	No. of Participants	Percent
1 day	155	61.5
1 day to less than or equal to 2 days	84	33.3
More than 2 days to 4 days	13	5.2
Total	252	100.0

Table 4: Patient's response to primary dysmenorrhea symptoms with Spasmodart

Options	No. of Participants	Percent
About the same	13	5.2
Much better than before	212	84.1
Much worse than before	2	.8
Somewhat better than previous	24	9.5
Somewhat worse than before	1	.4
Total	252	100.0

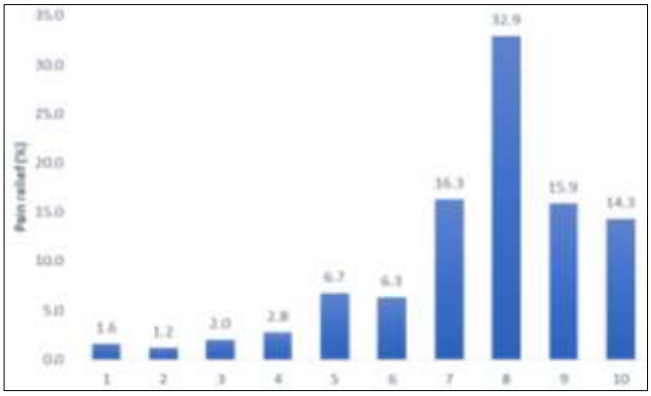

Fig 4: Pain relief rate in patients with primary dysmenorrhea on a scale of 1 to 10

Around 80% study participants reported that they did not notice any side-effects with Spasmodart in their patients (Figure 5).

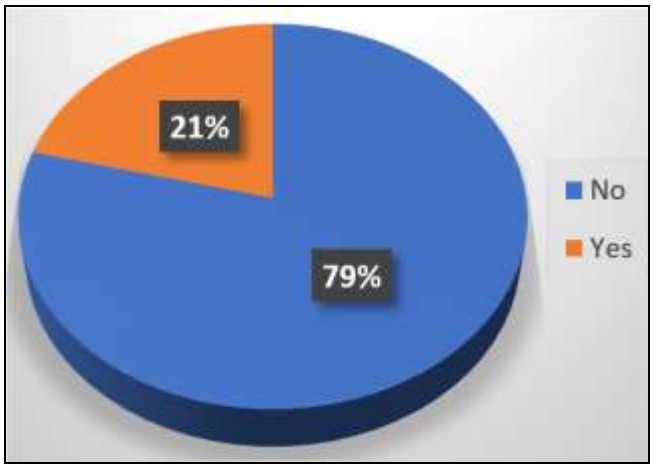

Fig 5: Side-effect(s) with Spasmodart

Of another 20% of study participants, 15.1% study participants reported that patients experienced gastric pain

and dizziness with Spasmodart, followed by 11.3% study participants with acidity, giddiness and nausea (Figure 6). Around one-fourth of the study participants rated score-8 regarding safety of Spasmodart, followed by 20.2% with score-10, 18.7% participants with score-7 and 16.3% participants rated score-9 (Figure 7).

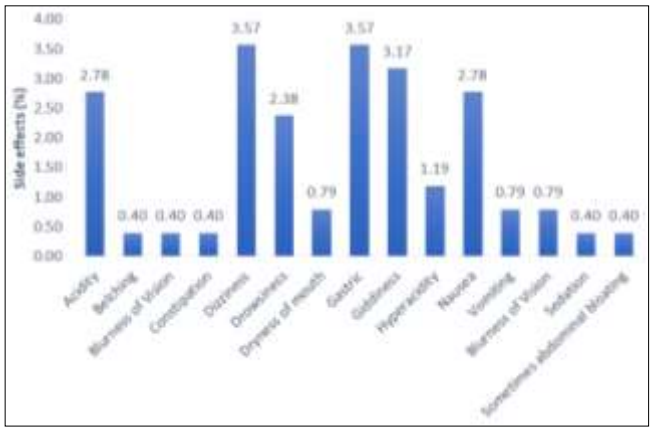

Fig 6: Reported side effects

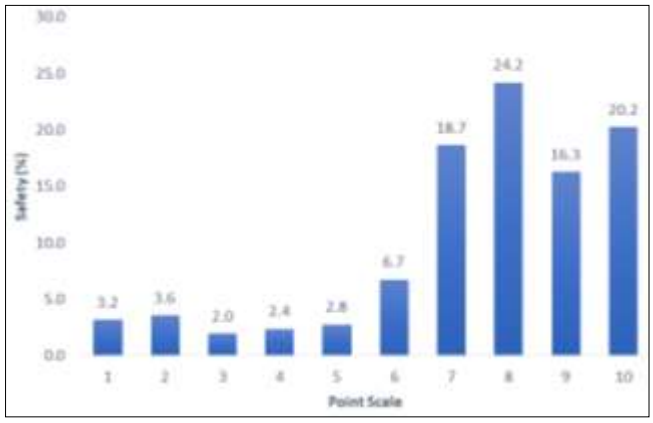

Fig 7: Safety of Spasmodart on a scale of 1 to 10

Discussion

Dysmenorrhea is the most common gynecological disorder among adolescent and young females and is the most common reported complaint during clinical consultations. In the present study, majority of study participants (71%) noticed menstrual cramps to be the most common sign and symptom of primary dysmenorrhea in their practice, followed by nausea and vomiting, spasmodic pain fever, fatigue, headache and diarrhea. The signs and symptoms such as pain or cramping sensations in the lower abdomen accompanied by headaches, dizziness, diarrhea, a bloated feeling, nausea and vomiting, backache, and leg pains have been reported earlier in other studies [34, 35]

Safety and Efficacy

The factors responsible for pain in dysmenorrhea may be multifactorial but the most predominant is excess of Prostaglandin F2α. It has been observed that PgF2α levels are twice higher in dysmenorrhea females than non-dysmenorrhea females during menstruation [36] As prostaglandins are the potent pro-inflammatory agents, the role of NSAIDs and analgesics in combating dysmenorrhea was highlighted in several studies. Various pharmacological agents that were used commonly such as paracetamol, ibuprofen, mefenamic acid, dicyclomine, nimesulide, and diclofenac.

According to the Swanberg and Ulmsten, 23% of patients used analgesics in their study [37] In another study conducted by Hillens reported that most common medication used in primary dysmenorrhea was simple analgesics (53%), followed by NSAIDs [38] According to the Gebeyehu MB, in their study about 36.3% used analgesics, ibuprofen (12.6%), diclofenac (6.9%), and paracetamol (5.4%) were the most frequently used medications [39] In the present study, majority of study participants (95%) reported that they prescribed Spasmodart for primary dysmenorrhea and also for intestinal colic/renal colic (51.98%), low backache (20.63%) and IBS (7.14%) during last 10 years. This response rate clearly shows us the reliability of this Spasmodart amongst the clinicians. Majority of study participants (80%) responded that they have not notice any major side-effects with Spasmodart. Of the remaining 20% study participants, 15.1% reported that patients experienced gastric and dizziness with Spasmodart while the rest 11.3% study participants responded that the patients experienced acidity, giddiness and nausea. These findings clearly show that Spasmodart is associated with very few events of side effects compared to other existing products.

More than 60% of study participants opined that it took 1 day to get results with Spasmodart in patients with primary dysmenorrhea. Some respondents followed by 1 day to 2 day (33.3%) and 2 days to 4 days (5.2%) and more than 30% study participants rated the pain relief score as 8 in patients with primary dysmenorrhea followed by 7 (15.9%) and 10(14.3%). Around 85% study participants responded that their patients felt much better than before with Spasmodart. Around one-fourth of the study participants rated score-8 for the safety of Spasmodart followed by 20.2% participants rated score-10 score, 18.7% participants rated score-7, 16.3% participants rated score-9. This proved the higher efficacy of this product on this indication.

Some of the studies reported the use of NSAIDs alone in the clinical management of both primary and secondary dysmenorrhea. However, the treatment showed less effective when the intake of the drug was delayed until the pain was more severe and also a possibility of side effects especially in women with asthma and allergic disorders and peptic ulcers. Oral contraceptives (OCs) are still used very often as treatment, especially in young women who also require contraception. They reduce uterine contractility, induce endometrial atrophy and reduce endometrial PG concentrations. But, side effects and potential of adverse drug reactions may limit their use in some women. Other treatments such as danazol, GnRH agonists have either too many side effects or ineffective for the treatment of an accompanying disorder, and cannot, therefore, be considered for routine treatment of dysmenorrhea [40]. Instead adopting of these treatment modalities, the fixed dose combination (Paracetamol IP – 325 mg Dicyclomine HCl – 20 mg Diclofenac Sodium – 50 mg) as Spasmodart showed better symptomatic relief in a short duration of time. Spasmodart could thus be considered as a treatment of choice based on our aforementioned observations.

Conclusion

The morbidity of dysmenorrhea has a significant impact on public health as it is the major cause of decrease in the quality of life of those affected. The fixed dose combination of Spasmodart demonstrated greater safety and efficacy in

primary dysmenorrhea condition and we recommend the use of this product under doctor's supervision.

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