

Study Of Off-Label Drug Use In Patients Undergoing Labor In A Regional General Hospital Dr. Loekmono Hadi Kudus

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Abstract. Off label drugs are drugs that are used outside the terms of a product license from an authorized institution of outside product information including dosage, route of administration, indication age and certain population groups. The aims of this study were to find out the pattern of using off-label drugs for childbirth, to find out the accuracy of using off-label drugs for childbirth, and to find out the description of the use off-label drugs for childbirth at dr.Loekmono Hadi Kudus Hospital . Retrospective data collection on medical record data. Samples were taken from patients who had given birth at dr.Loekmono Hadi Kudus Hospital In March 2023. There were 84 samples that met the inclusion criteria using a non experimental quantitative method. Data were analyzed descriptively using DIH 2012 and Medscape 2023 literature and supporting journals related to the use of off-label drugs in patients undergoing labor. The data were analyzed using a frequency test to determine the percentage of delivery patients who received off-label. 84 patients, 68 (82.2%) Gastrul (misoprostrol), while 15 (17.8%) indications of ruptured membranes. There is the use of the drug Gastrul (misoprostrol) which is categorized as appropriate with the categories of off-label indication, off label dose, off label route of administration and off label contraindications as much as 100% while off label drugs are used for delivery in 84 patients (100%), Gastrul (misoprostrol), while 15 (17.8%) indications of ruptured membranes were 15 (17.8%).

Keywords: Off-label , labor

INTRODUCTION

Childbirth is the process of opening and thinning the cervix and the fetus descending into the birth canal, then ending with the expulsion of a full-term or nearly full-term baby or one that can live outside the womb, followed by the expulsion of the placenta and fetal membranes from the mother's body through the birth canal or birth canal, with or without assistance. (Sulfianti *et al*, 2020). Based on *Sampling Registration System* data (SRS) tahun 2018 about 76% of deaths Mother occurs in the phase labor and delivery with proportion of 24% occurs moment pregnant , 36% at the time childbirth and 40% postpartum . Maternal and Infant Mortality , which is more of 62% occurred at home sick . One of the causes is the care that women receive , namely antenatal care or care before giving birth . The efforts made in frame lower number death Mother among them is with increase quality service *antenatal care* (ANC), both For detection and prevention reason death Mother (Achadi, 2019).

According to (Rikomah, 2017), drug *off-label* is drugs used outside provision license product from the authorized institution or outside information product covering dose , route administration , indications , age and group population certain reasons use drug *off-label* is lack of response clinical in treatment previous and contraindications with drug other (Burkle *et al.*, 2014)alternatives . Medicine *off-label* still general used due to the treatment regimen standard No succeed in treat or even No available (Egual, *et al.*, 2016). Drug *off-label* as drug outside the indications listed in the label or outside approval by the agency permission distribution such as the POM Agency and the FDA (*Food and Drug Administration*) used If No There is other alternatives and for interest healing patient . Use medication in patients *obstetrics* and *gynecology* No can carelessly , especially For Mother pregnant. Use medication during pregnancy need attention special , because part big drug can crossing placenta, so that there is possibility drug Can nature teratogenic so that can cause fetal defects (Yulianti *et al.*, 2019)Prescribing medication to pregnant women should be given as a minimum perhaps to avoid the effects possible side effects of the drug. Some studies show 50- 80% of pregnant women take good medication with or without a prescription (Riley, 2005). Provision drug *off-label* is applied at the time childbirth , things the done Because fulfil criteria Medical . Based on a preliminary study at Dr.

Loekmono Hadi Kudus Regional Hospital, doctors often prescribe *off-label medications* to avoid complications. pregnancy such as premature birth, labor, preeclampsia and eclampsia or increased postnatal adaptive capacity may occur for example sepsis or respiratory distress . Then with the description above Researchers are interested in conducting research on the use of *off-label* drugs during labor at Dr. Loekmono Hadi Kudus Regional General Hospital.

METHODS

Writer use type research of a nature quantitative descriptive , because in study This writer want to dig more Far about use drug *off-label* delivery at dr . Loekmono Holy Hadith .

Study This conducted at Dr. Regional Hospital Loekmono Hadi Kudus Loekmono Street Hadi No.19 Kudus Central Java and the research time was conducted in February - March 2023. In the research this, population is all over patients undergoing childbirth at dr. Loekmono Holy Hadith. In this study, the sampling technique used was *Consecutive Sampling* , which is the selection of samples that meet the research criteria (inclusion criteria and exclusion criteria) and are included in the study for a certain period of time, so that the required number of clients is met . study is patients undergoing childbirth at Dr. Loekmono Regional Hospital Holy Spirit

Tools used in study This is sheet data collector and recorder medical patients , as well as literature supporters. Data collection techniques include : Application letter permission research, collecting data, recording and conducting studies literature, Data analysis for use drugs *off label*, as well as Discuss results findings drug *off label*.

Data analysis was conducted using descriptive analysis methods. The collected data was then evaluated to determine the percentage of drugs. Data analysis was performed using SPSS (*Statistical Package for the Social Sciences*). Version 19. Categorized data is displayed as frequency of occurrence. Data analysis using univariate analysis with descriptive frequencies test to determine the percentage of patients childbirth that gets drug *off-label* and analyze variables namely characteristics patient (age, parity, distance pregnancy) and use drug *off-label*.

Results and Discussion

Table 1. Characteristics patient giving birth at dr. Loekmono Hadi Kudus period month July-December 2022 based on age patient .

No	Age	Amount patient	Percentage
1	20-29	49	58.3
2	30-39	25	29.8
3	>40	10	11.9
Total		84	100

Based on percentage data age patient known that aged 20-29 years as many as 49 patients with percentage of 58.3%, while For age 30-39 years as many as 25 patients (29.8%), and at least age on 40 years as many as 10 patients (11.9%). Almost The same with research conducted by Murdiana (2016)the person explaining that part big patient aged 20-30 years as many as 39 (55%) because age the is age safe For giving birth . However , research This different with research by Fadhillah *et al* (2022)the discoverer that patient aged between 26-35 years old as many as 164 (66.1%). This due to a lot of patient data is not complete so that categorized exclusion . Age This Still classified as age No risky in pregnancy .

Table 2. Characteristics patient giving birth at dr. Loekmono Hadi Kudus period month July-December 2022 based on maternity status patient .

No	Delivery status	Amount patient	Percentage
1	Primipara (giving birth to 1 child)	44	52.4
2	Multipara (giving birth) more from 1 time)	40	47.6
Total		84	100

Based on the percentage data of the birth status that has ever occurred experienced by patients at Dr. Hospital Loekmono Holy Hadi is mostly primipara or new give birth to a child as many as 44 (52.4%) respondents while multipara or give birth to twice or more as many as 40 (47.6%) respondents . Distribution frequency the in accordance with findings previously Where part big respondents aged under 30 years old . At the age of the is age productive Where part big women in general give birth to child first and give 3 to 4 years apart in birth next . Almost The same with research conducted by Nyoman *et al* (2017)the discoverer that respondents in the research conducted part big new give birth to child first (primipara) of 26 (33.8%). This explain that Mother Not yet own experience in matter labor so that possibility There is other necessary indications induction . Research This different with study Retnaningsih (2018)which shows that part big respondents Once give birth to previously (multipara) as many as 65 (79.3%).

Table 3. Use drug *off label* on childbirth at RSUD dr Loekmono Hadi Kudus period month July-December 2022

Drug name <i>off label</i>	Indication <i>off label</i>	Indication <i>on label</i>	Amount patient	(%)
Gastrul (Misoprostol)	For induction labor use vaginal /oral	Therapy stomach and small intestine including group NSAID drugs (DIH, 2012)	84	100

Research result This show that gastrul (misoprostol) is drugs used by doctors For childbirth at dr. Loekmono Hadi Kudus as many as 84 (100%) patients . Gastrul (misoprostol) is drug For prevent and reduce symptom ulcer gastric and small intestinal ulcers , especially those triggered by the use of drugs from NSAID class (DIH, 2009) . Drugs types of NSAIDs inhibit production of prostaglandins for reduce pain and inflammation . Prostaglandins are known to is compound natural excretion body For coating channel digestion which also plays a role in the process of inflammation and pain . In the study This gastrula (misoprostol) is categorized as drug major *off-label* Because its use No in accordance indications . The majority use *off-label* Gastrul (misoprostol) at dr. regional hospital Loekmono Holy Spirit as induction childbirth . Research result Wibowo *et al* (2021)who found that use drug *off-label* misoprostol for induction labor as much as 26.92% at Hospital X and as much as 4% at Hospital Y. However , the results different found in research conducted by some of Nyoman *et al* (2017)which big 77 (57%) respondents got drug induction labor oxytocin Because respondents experience first stage indication latent phase . At this time *his* (uterine contractions) take place in a way regular However opening No increase so that need induction oxytocin .

Table 4. Accuracy use gastrul (misoprostol) for patient childbirth at dr. Loekmono Hadi Kudus period month July-December 2022

No	Category	Appropriate		No appropriate		Amount	
		f	%	f	%	f	%
1	<i>Off-label</i> indication	84	100	0	0	84	100
2	<i>Off-label</i> dose	84	100	0	0	84	100
3	<i>Off-label</i> route gift	84	100	0	0	84	100
4	<i>Off label</i> counter indication	84	100	0	0	84	100

Based on results research on the table on known that use drug *off label* gastrul (misoprostol) 100% done appropriate indication , precise dose , right route giving and proper contraindications . *Off label* indications for use gastrul (misoprostol) for patient giving birth at dr. Loekmono Hadi Kudus explained Kimland & Odland (2012)that a drug is categorized as *off-label* if it is used outside the indications listed in the leaflet. The use of gastrula For indication as following :

Table 5. Off label indication use gastrul (misoprostol) for patient childbirth at dr. Loekmono Hadi Kudus period month July-December 2022

No	Drug <i>off label</i>	Indication	Amount patient	(%)
1	Gastrul	Serotinus	69	82.2

(Misoprostol)			
2	amniotic fluid broken early	15	17.8
Total		84	100

Table on explain that the majority induced patients her delivery with drug *off label* gastrula is patient with indication s eroticus that is pregnancy with age pregnancy more from 42 weeks . Patient with Serotinus indications were 68 (82.2%) while indication amniotic fluid broken early as many as 15 (17.8%). Manuaba (2017) define serotonergic pregnancy is pregnancy with age more from 42 weeks complete start from menstruation first . Meanwhile amniotic fluid broken early (KPD) is defined condition the rupture bag amniotic fluid in a way suddenly before the delivery process starts below 37 weeks old . The sac amniotic fluid Alone is part from membrane functioning fetus surround and protect fetus For maintain pregnancy (Metti, 2021).

The medication given with other doses than those listed on the permit distribution or permission sale categorized as drug *off-label* dose . *Off-label* data processing results dosage for use drug gastrula can seen in the table under This :

Table 6. *Off label* dosage for use gastrul (misoprostol) for patient childbirth at dr. Loekmono Hadi Kudus period month July-December 2022

Drug <i>off</i> label	Dose 1 x use	R u t e	Dose usage a day	f	(%)	Dose Medscape literature	
						Very	A day
Gastrul	5 0 µg	Or a l	2 times	23	27, 4	50 µg	100 µg
	25 µg	Intravaginal	1 time	61	72.6	25 µg	50 µg
Total				84	100		

Prescription pattern drug *off label* For help childbirth at dr. Loekmono Hadi Kudus only using 1 type drug that is Gastrul (misoprostol). Based on table on known that use gastrula as *off label* with dose 25 µg with amount 61 (72.6%) patients received the drug once whereas 5 0 µg with many 23 (27.4%) patients were given twice . Gastrul contain material active misoprostol which is prostaglandin analogues . Misoprostol often used in action labor Good For induction labor and For prevention bleeding post labor . Bleeding post labor is cause most in cases death consequence labor (Anggriani *et al.* , 2019)

Drugs are categorized as *off-label* route of administration if they are used outside the procedures regarding the proper way of use. *Off-label* data processing results route provision for use drug gastrula can seen in the table under This :

Table 7. *Off label* route provision for use gastrul (misoprostol) for patient childbirth at dr. Loekmono Hadi Kudus period month July-December 2022

Drug name <i>off</i> label	Route giving	Amount patient	Percentage
Gastrul	Oral	23	27, 4
	Intravaginal	61	72.6
Total		84	100

Based on results study shown in the table on can known that use drug gastrula done with intravaginal method of 61 (72.6%) and orally of 23 (27.4%). Both method giving drug gastrul (misoprostol) already in accordance with indications experienced by the patient that is amniotic fluid broken early and serotonin. Research This supported byDewi & Salmiyati (2016) explain that average time start from use drug misoprostol gastrul until baby born , in use orally obtained time amounting to 7 hours 43 minutes , in total vaginal obtained time as much as 4 hours and 40 minutes . So can concluded that use of misoprostol vaginal more effective and fast compared to orally . There is difference range enough time long between two technique use of misoprostol .

According to Oguz *et al.*, (2012) drug it is said including category *off-label* contraindications If cause contraindications moment given to patient giving birth Because own history health certain like

Once experience miscarriage , position fetus abnormal , and content weak . After giving gastrul (misoprostol), patient experience increased intrauterine tone . In study this , no found contraindications in patients giving birth like placenta previa and bleeding vaginal . According to Wahyuningsih *et al.* (2022) placenta varia is condition Where placenta implanted in an abnormal location in the segment below the uterus so that cover part or all over from the internal uterine ostium (opening) road born). While bleeding vaginal is the exit blood from vagina . Bleeding the can arise from uterus , vaginal walls , or cervix (Juliete, 2021). Use drug gastrula in research This No cause contraindications It means drug *off label* No cause counter indication after given to patient giving birth . In the study this , researcher No find existence counter indications resulting from use drug gastrul (misoprostol).

CONCLUSION

From the results research and discussion can concluded as following :

1. Drug *off label* used For childbirth at dr. Loekmono Holy Hadi is gastrul (misoprostol) in 84 (100%) patients . Gastrul (misoprostol) is used For indication of s erotinus as many as 68 (82.2%) while indication amniotic fluid broken early as many as 15 (17.8%).
2. Accuracy use drug *off label* gastrul (misoprostol) is categorized Already appropriate For childbirth at dr. Loekmono Hadi Kudus with the categories of *off -label* indication, *off -label* dosage, *off -label* route of administration and *off -label* contraindications as much as 100%

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