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OVERVIEW OF MISOPROSTOL STUDIES IN POSTPARTUM HEMORRHAGE

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INTRODUCTION

These tables of peer-reviewed misoprostol studies were compiled to provide the reader with comprehensive references to the use of misoprostol in practice since 1997, for both prevention and treatment of postpartum hemorrhage. The tables include both randomized and non-randomized trials, and they represent a diversity of situations. Table 1 provides an overview of 32 studies in the prevention of postpartum hemorrhage (including dosage and route of administration). Table 2 gives an overview of seven studies in the treatment of postpartum hemorrhage (including dosage and route of administration).

Table 1 Misoprostol for prevention

Authors	*Institutions*	*Study title*	*Journal*	*n*	*Participants in misoprostol group*	*Dosage of misoprostol*	*Route of administration*	*Participants in control group(s)*	*Control agent(s)*
Prata N, Hamza S, Gypson R, *et al.*	Bixby Program in Population, Family Planning and Maternal Health, School of Public Health, University of California, Berkeley, USA	Misoprostol and active management of the third stage of labor	*Int J Gynaecol Obstet* 2006 Jul 6 [epub ahead of print]	2532	1189	600 µg	oral	1343	current AMTSL practices
Nellore V, Mittal S, Dadhwal V	Dept. of Obstetrics and Gynecology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India	Rectal misoprostol vs. 15-methyl prostaglandin $F_{2\alpha}$ for the prevention of PPH	*Int J Gynaecol Obstet* 2006; 94:45–6	120	60	400 µg	rectal	60	125 µg 15-methyl prostaglandin $F_{2\alpha}$ i.m.
Chandhiok N, Dhillon BS, Datey S, *et al.*	Division of Reproductive Health and Nutrition, Indian Council of Medical Research, New Delhi, India	Oral misoprostol for prevention of PPH by paramedical workers in India	*Int J Gynaecol Obstet* 2006; 92:170–5	1200	600	600 µg	oral	600	current government guidelines for PPH prevention
Zachariah ES, Naidu M, Seshadri L	Dept. of Obstetrics and Gynecology, Christian Medical College Hospital Vellore, India	Oral misoprostol in the third stage of labor	*Int J Gynaecol Obstet* 2006; 92:23–6	2023	730	400 µg	oral	[1] 617 [2] 676	[1] 10 IU oxytocin i.m. [2] 2 mg ergometrine i.v.
Garg P, Batra S, Gandhi G	Maulana Azad Medical College and Lok Nayak Hospital, Delhi, India	Oral misoprostol vs. injectable methylergometrine in management of the third stage of labor	*Int J Gynaecol Obstet* 2005; 91:160–1	200	100	600 µg	oral	100	0.2 mg methylergometrine i.v.
Ozkaya O, Sezik M, Kaya H, *et al.*	Dept. of Obstetrics and Gynecology, School of Medicine, Suleyman Demirel University, Turkey	Placebo-controlled randomized comparison of vaginal with rectal misoprostol in the prevention of PPH	*J Obstet Gynaecol Res* 2005;31: 389–93	150	[1] 50 [2] 50	400 µg	[1] rectal [2] oral	50	placebo
Hoj L, Cardoso P, Nielsen BB, *et al.*	Dept. of Obstetrics and Gynecology, Aarhus University Hospital, Denmark	Effect of sublingual misoprostol on severe PPH in a primary health center in Guinea-Bissau: randomized double-blind clinical trial	*BMJ* 2005; 331:723	661	330	600 µg	sublingual	331	placebo

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Table 1 *Continued*

Authors	*Institutions*	*Study title*	*Journal*	*n*	*Participants in misoprostol group*	*Dosage of misoprostol*	*Route of administration*	*Participants in control group(s)*	*Control agent(s)*
Walraven G, Blum J, Dampha Y, *et al.*	Farafenni Field Station, Medical Research Council Laboratories, Farafenni, Gambia	Misoprostol in the management of the third stage of labor in the home delivery setting in rural Gambia: a randomized controlled trial	*BJOG* 2005; 112:1277–83	1229	630	600 µg	oral	599	2 mg ergometrine oral
Vimala N, Mittal S, Kumar S, *et al.*	Dept. of Obstetrics and Gynecology, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India	Sublingual misoprostol versus methylergometrine for active management of the third stage of labor	*Int J Gynaecol Obstet* 2004; 87:1–5	120	60	400 µg	sublingual	60	0.2 mg methylergometrine i.v.
Lam H, Tang OS, Lee CP, *et al.*	Dept. of Obstetrics and Gynecology, Queen Mary Hospital, Hong Kong SAR, China	A pilot-randomized comparison of sublingual misoprostol with syntometrine on the blood loss in third stage of labor	*Acta Obstet Gynecol Scand* 2004;83: 647–50	60	30	600 µg	sublingual	30	1 ml syntometrine i.v. (5 IU syntocinone and 0.5 mg ergometrine maleate)
Caliskan E, Dilbaz B, Meydanli MM, *et al.*	SSK Maternity and Women's Health Teaching Hospital, Ankara, Turkey	Oral misoprostol for the third stage of labor: a randomized controlled trial	*Obstet Gynecol* 2003;101: 921–8	1574	388	600 µg	oral	[1] 404 [2] 384 [3] 398	[1] 600 µg misoprostol plus 10 IU oxytocin i.v. [2] 10 IU oxytocin i.v. [3] 10 IU oxytocin i.v. plus 0.2 mg methylergonovine maleate
Oboro VO, Tabowei TO	Maternity Unit, Zonal General Hospital, Kwale, Delta State, Nigeria	A randomized controlled trial of misoprostol vs. oxytocin in the active management of the third stage of labor	*Obstet Gynecol* 2003;23: 13–16	496	247	600 µg	oral	249	10 IU oxytocin i.m.
Lumbiganon P, Villar J, Piaggio G, *et al.*	Dept. of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Thailand	Side-effects of oral misoprostol during the first 24 h after administration in the third stage of labor	*BJOG* 2002;109: 1222–6	1686	843	600 µg	oral	843	10 IU oxytocin i.m. or i.v.

Quiroga Diaz R, Esparaza Arechiga M, Batiza Resendiz V, *et al.*	Hospital de Ginecologia y Obstetricia de Monterrey, N. L. Mexico	Vaginal misoprostol in the prevention of PPH	*Ginecol Obstet Mex* 2002;70: 572–5	400	208	800 µg	vaginal	192	current AMTSL practices
Caliskan E, Meydanli MM, Dilbaz B, *et al.*	Social Security Council: Maternity and Women's Health Teaching Hospital, Kucukesat, Ankara, Turkey	Is rectal misoprostol really effective in the treatment of third stage of labor? A randomized controlled trial	*Am J Obstet Gynecol* 2002; 187:1038–45	1606	396	600 µg	rectal	[1] 401 [2] 407 [3] 402	[1] 10 IU oxytocin i.v. plus 600 µg misoprostol rectal [2] 10 IU oxytocin i.v. [3] 10 IU oxytocin i.v. plus 1 ml methylergometrine i.m.
Karkanis SG, Caloia D, Salenieks ME, *et al.*	University of Toronto, Toronto, Canada	Randomized controlled trial of rectal misoprostol vs. oxytocin in third stage management	*J Obstet Gynaecol Can* 2002;24: 149–54	214	110	400 µg	rectal	113	5 IU oxytocin i.v. or 10 IU oxytocin i.m.
Kundodyiwa TW, Majoko F, Rusakaniko S	Dept. of Obstetrics and Gynecology, University of Zimbabwe, Harare, Zimbabwe	Misoprostol vs. oxytocin in the third stage of labor	*Int J Gynaecol Obstet* 2001; 75:235–41	499	243	400 µg	oral	256	10 IU oxytocin i.m.
Benchimol M, Gondry J, Mention JE, *et al.*	Centre de Gynecologie Obstetrique, Amiens, France	Role of misoprostol in the delivery outcome	*J Gynecol Obstet Biol Reprod (Paris)* 2001;30: 576–83	600	200	600 µg	oral	[1] 200 [2] 200	[1] 2.5 IU oxytocin i.v. [2] placebo
Gerstenfeld TS, Wing DA	Women's and Children's Hospital, Dept. of Obstetrics and Gynecology, University of Southern California Keck School of Medicine, Los Angeles, USA	Rectal misoprostol vs. intravenous oxytocin for the prevention of PPH after vaginal delivery	*Am J Obstet Gynecol* 2001; 185:878–82	325	159	400 µg	rectal	166	20 IU oxytocin i.v.
Gulmezoglu AM, Villar J, Ngoc NT, *et al.*	WHO Collaborative Group to Evaluate Misoprostol in the Management of the Third Stage of Labour	WHO multicenter randomized trial of misoprostol in the management of the third stage of labor	*Lancet* 2001; 358:689–95	18 530	9264	600 µg	oral	9266	10 IU oxytocin i.m. or i.v.

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Table 1 *Continued*

Authors	*Institutions*	*Study title*	*Journal*	*n*	*Participants in misoprostol group*	*Dosage of misoprostol*	*Route of administration*	*Participants in control group(s)*	*Control agent(s)*
Hofmeyr GJ, Nikodem VC, de Jager M, *et al.*	Dept. of Obstetrics and Gynecology, Coronation Hospital and Effective Care Research Unit, University of the Witwatersrand, Johannesburg, South Africa	Side-effects of oral misoprostol in the third stage of labor – a randomized placebo-controlled trial	*S Afr Med J* 2001;91: 432–5	600	300	600 µg	oral	300	placebo
Bugalho A, Daniel A, Faundes A, *et al.*	Maternity of the Hospital Central de Maputo, Maputo, Mozambique	Misoprostol for prevention of PPH	*Int J Gynaecol Obstet* 2001; 73:1–6	663	324	400 µg	rectal	339	10 IU oxytocin i.m.
Ng PS, Chan AS, Sin WK, *et al.*	Dept. of Obstetrics and Gynecology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories	A multicenter randomized controlled trial of oral misoprostol and i.m syntometrine in the management of the third stage of labor	*Hum Reprod* 2001;16: 31–5	2058	1026	600 µg	oral	1032	1 ml syntometrine i.v. (5 IU syntocinone and 0.5 mg ergometrine maleate 0.5 mg)
Walley RL, Wilson JB, Crane JM, *et al.*	Dept. of Obstetrics and Gynaecology, St John's, Memorial University of Newfoundland, Canada	A double-blind placebo controlled randomized trial of misoprostol and oxytocin in the management of the third stage of labor	*BJOG* 2000; 107:1111–15	401	203	400 µg	oral	198	10 IU oxytocin i.m.
El-Refaey H, Nooh R, O'Brien P, *et al.*	Dept. of Obstetrics and Gynaecology, University College Hospital, London, UK	The misoprostol third stage of labor study: a randomized controlled comparison between orally administered misoprostol and standard management	*BJOG* 2000; 107:1104–10	1000	501	500 µg	oral	499	standard oxytocic regimens (10 IU oxytocin or 0.5 mg ergometrine or 1 ml syntometrine)
Cook CM, Spurrett B, Murray H	Dept. of Obstetrics and Gynaecology, University of Sydney at Nepean Hospital Penrith, New South Wales, Australia	A randomized clinical trial comparing oral misoprostol with synthetic oxytocin or syntometrine in the third stage of labor	*Aust N Z J Obstet Gynaecol* 1999;39: 414–19	863	424	400 µg	oral	439	standard oxytocic regimens (10 IU oxytocin i.m. or 1 ml syntometrine i.m.)

Amant F, Spitz B, Timmerman D, *et al.*	Dept. of Obstetrics and Gynaecology, University Hospitals Leuven, Belgium	Misoprostol compared with methylergometrine for the prevention of PPH: a double-blind randomized trial	*Br J Obstet Gynaecol* 1999;106: 1066–70	200	100	600 µg	oral	100	0.2 mg methylergometrine i.v.
Surbek DV, Fehr PM, Hosli I, *et al.*	Dept. of Obstetrics and Gynecology, University of Basel, Switzerland	Oral misoprostol for the third stage of labor: a randomized placebo-controlled trial	*Obstet Gynecol* 1999;94: 255–8	65	31	600 µg	oral	34	placebo
Bamigboye AA, Hofmeyr GJ, Merrell DA	Dept. of Obstetrics and Gynecology, Coronation Hospital, and University of the Witwatersrand, Johannesburg, South Africa	Rectal misoprostol in the prevention of PPH: a placebo-controlled trial	*Am J Obstet Gynecol* 1998; 179:1043–6	546	271	400 µg	rectal	275	placebo
Hofmeyr GJ, Nikodem VC, de Jager M, *et al.*	Dept. of Obstetrics and Gynaecology, Coronation Hospital and University of the Witwatersrand, Johannesburg, South Africa	A randomized placebo controlled trial of oral misoprostol in the third stage of labor	*Br J Obstet Gynaecol* 1998;105: 971–5	500	250	400 µg	oral	250	placebo
Bamigboye AA, Merrell DA, Hofmeyr GJ, *et al.*	Dept. of Obstetrics and Gynecology, Natalspruit Hospital and the University of the Witwatersrand, Johannesburg, South Africa	Randomized comparison of rectal misoprostol with syntometrine for management of third stage of labor	*Acta Obstet Gynecol Scand* 1998;77: 178–81	491	241	400 µg	rectal	250	1 ml syntometrine i.m. (5 IU syntocinone and 0.5 mg ergometrine maleate 0.5 mg)
El-Refaey H, O'Brien P, Morafa W, *et al.*	Dept. of Obstetrics and Gynaecology, University College Hospital, London, UK	Use of oral misoprostol in the prevention of PPH	*BJOG* 1997; 104:336–9	237	237	600 µg	oral	0	–

PPH, postpartum hemorrhage

Table 2 Misoprostol for treatment

Authors	*Institutions*	*Study title*	*Journal*	*n*	*Participants in misoprostol group*	*Dosage of misoprostol*	*Route of administration*	*Participants in control group(s)*	*Control agent(s)*
Prata N, Mbaruku G, Campbell M, *et al.*	Bixby Population Program, School of Public Health, University of California, Berkeley, USA	Controlling PPH after home births in Tanzania	*Int J Gynaecol Obstet* 2005; 90:51–5	849	454	1000 µg	rectal	395	current practices
Walraven G, Dampha Y, Bittave B, *et al.*	Reproductive Health Programme, Medical Research Council Laboratories, Farafenni, The Gambia, South Africa	Misoprostol in the treatment of PPH in addition to routine management: a placebo randomized controlled trial	*BJOG* 2004; 111:1014–17	160	79	600 µg	200 µg oral and 400 µg sublingual	81	placebo
Hofmeyr GJ, Ferreira S, Nikodem VC, *et al.*	Effective Care Research Unit, University of Witwatersrand and Fort Hare, and East London Hospital Complex, East London, South Africa	Misoprostol for treating PPH: a randomized controlled trial [ISRCTN72263357]	*BMC Pregnancy Childbirth* 2004;4:16	238	117	1000 µg	200 µg oral and 400 µg sublingual and 400 µg rectal	121	placebo
Shojai R, Desbriere R, Dhifallah S, *et al.*	Service de gynecologie-obstetrique, CHU Nord, Marseille, France	[Rectal misoprostol for PPH]	*Gynecol Obstet Fertil* 2004; 32:703–7	41	41	1000 µg	rectal	0	–
Lokugamage AU, Sullivan KR, Niculescu I, *et al.*	Dept. of Obstetrics & Gynaecology, Royal Free and University College London School, London, UK	A randomized study comparing rectally administered misoprostol versus Syntometrine combined with an oxytocin infusion for the cessation of primary PPH	*Acta Obstet Gynecol Scand* 2001;80: 835–9	64	32	800 µg	rectal	32	1 ml syntometrine i.m. (5 IU syntocinone and 0.5 mg ergometrine maleate) plus 10 IU oxytocin i.v.
Abdel-Aleem H, El-Nashar I, Abdel-Aleem A	Dept. of Obstetrics & Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt	Management of severe PPH with misoprostol	*Int J Gynaecol Obstet* 2001; 72:75–6	18	18	600 µg or 1000 µg	rectal	0	–
O'Brien P, El-Refaey H, Gordon A, *et al.*	Dept. of Obstetrics and Gynaecology, University College Hospital, London, UK	Rectally administered misoprostol for the treatment of PPH unresponsive to oxytocin and ergometrine: a descriptive study	*Obstet Gynecol* 1998;92: 212–14	14	14	1000 µg	rectal	0	–

PPH, postpartum hemorrhage